SIAF

Swiss Institute of Allergy and Asthma Research

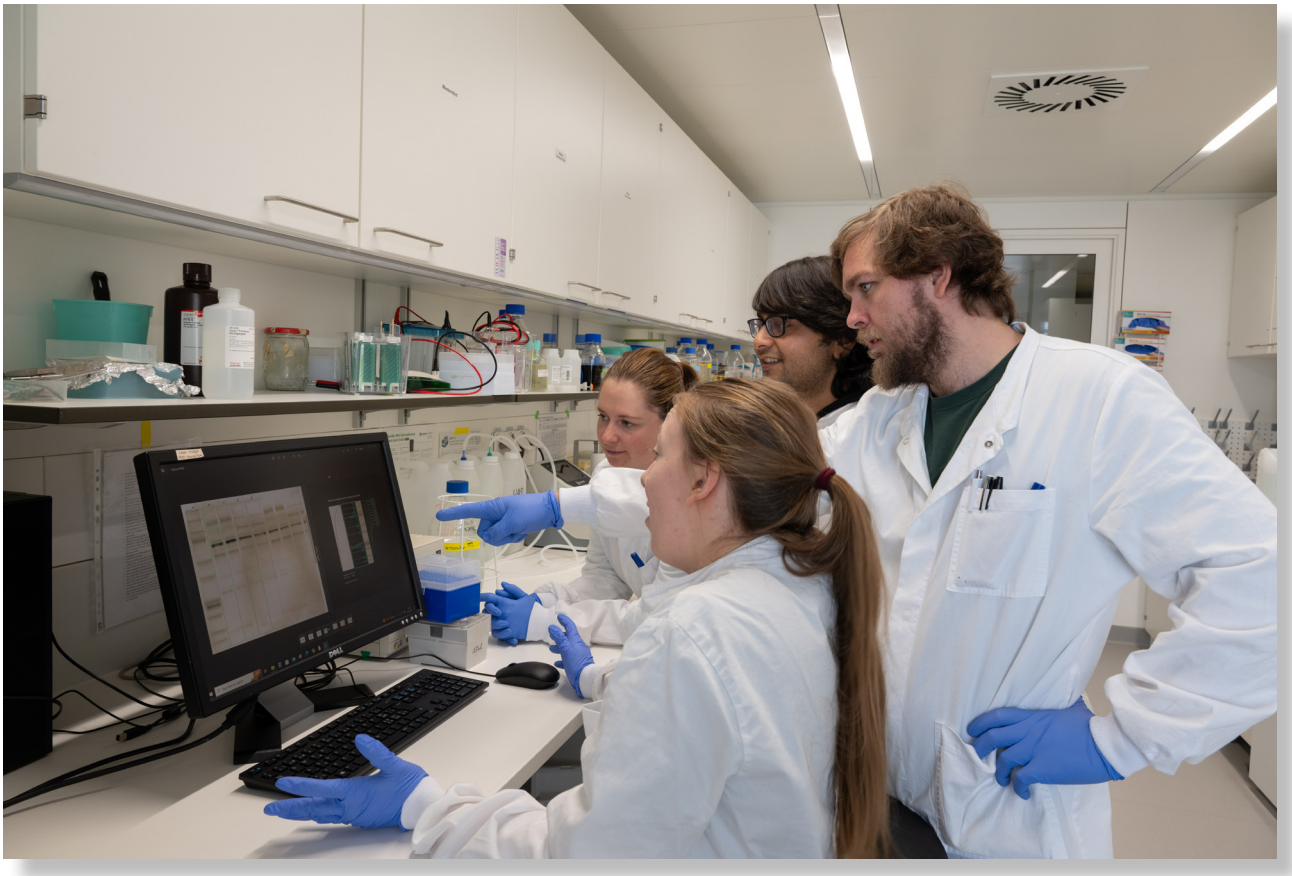
ANNUAL REPORT 2023

Universität Zürich[UZH]

Index

The Swiss Institute of Allergy and Asthma Research (SIAF) is a department of the foundation Swiss Research Institutes for High Altitude Climate and Medicine Davos (SFI) and an affiliated institute of the University of Zurich and member of the Life Science Zurich Graduate School. The institute in its current form arised from the medical department of SFI in 1988. Since this time the research activities at SIAF are focused on basic research in the field of allergies and asthma.

1905	Tuberculosis Research Institute Davos
	Medical Society Davos, Community of Davos, K. Turban
1907	Physical-Meteorological Observatory Davos, C. Dorno
1922	Swiss Research Institute for High Altitude Climate and Tuberculosis
1922-1933	A. Loewy, High Altitude Physiology
1934-1937	F. Roulet, Chemistry of Mycobacterium Tuberculosis
1938-1954	W. Berblinger, Pathology of Tuberculosis
1954-1960	W. A. Vischer, Resistance to Mycobacterium Tuberculosis
1961	Swiss Research Institute for High Altitude Climate and Medicine
1961-1985	E. Sorkin, Neuroendocrine-Immune Interactions
1985-1987	H. Basedowsky, Neuroendocrine-Immune Interactions
1988	Swiss Insitute of Allergy and Asthma Research (SIAF)
1988-2006	K. Blaser, Mechanisms of Allergy and Asthma
2006-present	C. A. Akdis, Mechanisms and Novel Methods for the Diagnosis and Treatment of Allergy and Asthma



Bericht des Direktors

Prof. Dr. Cezmi A. Akdis

Das Schweizerische Institut für Allergie- und Asthmaforschung (SIAF), gegründet 1988 von der Medizinischen Abteilung des Schweizerischen Forschungsinstituts für Hochgebirgsklima und Medizin Davos (SFI), hat das Ziel durch seine Forschung das Verständnis von Allergien und Asthma zu verbessern. Das Ziel ist es, Behandlungen zu entwickeln, die die Zukunft der Betroffenen verbessern. Seit 1996 ist das SIAF der Universität Zürich angeschlossen und seit 2008 Mitglied der Life Science Zurich Graduate School, einem gemeinsamen Bildungsprojekt der Universität Zürich und der ETH Zürich. Diese Zugehörigkeit ermöglicht es dem SIAF umfassende PhD-Ausbildungen anzubieten. Darüber hinaus ist das SIAF ein aktives Mitglied der Academia Raetica und der Graduate School des Kantons Graubünden.

Die Forschung am SIAF ist auf die direkte Zusammenarbeit mit Kliniken in Davos, der Universität Zürich und anderen spezialisierten Instituten ausgelegt. Das Institut konzentriert sich auf patientenrelevante, translationale Forschung und die Untersuchung der immunologischen Grundlagen von allergischen und asthmatischen Erkrankungen, was Einblicke in neue präventive und kurative Behandlungen bietet, die den Betroffenen zugutekommen. Darüber hinaus ist das SIAF in die Europäische Akademie für Allergie und klinische Immunologie (EAACI), die Amerikanische Akademie für Allergie, Asthma und Immunologie (AAAAI) und die Weltallergieorganisation (WAO) eingebunden. Es besteht auch eine intensive Zusammenarbeit mit der Stanford University (Sean Parker Asthma and Allergy Center) und der Harvard University (T.H. Chan School of Public Health). Eine grosse Anzahl von Bioinformatikern arbeitet derzeit im Institut. Projekte zur Künstlichen Intelligenz/Maschinellem Lernen werden kontinuierlich weiterentwickelt.

Im Jahr 2023 wurden 76 wissenschaftliche, durch Gutachter geprüfte Arbeiten in internationalen Zeitschriften mit einem Impact-Factor veröffentlicht. Das SIAF erreichte im Jahr 2023 einen Gesamt-Impact-Faktor-Wert von 1046.4 und einen Durchschnitt von 13.79 Punkten pro Veröffentlichung. Die neuesten Erkenntnisse wurden zudem in 59 Abstracts auf verschiedenen Fachkonferenzen präsentiert. Unsere Mitarbeiter wurden eingeladen, an 111 verschiedenen Seminaren und Präsentationen auf nationalen und internationalen Kongressen teilzunehmen. Solche Einladungen sind wichtig für die Verbreitung der erzielten Ergebnisse und für die internationale Akzeptanz der Forschungsarbeit des Instituts. SIAF-Mitarbeiter leiteten 46 verschiedene Sitzungen. Darüber hinaus bekleiden SIAF-Mitarbeiter 79 wissenschaftliche Positionen in internationalen Gesellschaften und 35 Positionen in internationalen Zeitschriften. Seit 2018 ist Prof. C.A. Akdis Chefredakteur der Zeitschrift Allergy. Unter seiner Leitung stieg der Impact-Faktor des Fachjournals von 6.02 auf 14.71, womit sie zur führenden Zeitschrift im Bereich der Allergie- und Klinischen Immunologie wurde. Aufgrund der international hoch angesehenen wissenschaftlichen Publikationen wurde Prof. Dr. C.A. Akdis 2023 zum achten Mal von Thomson Reuters Clarivate in die Liste der meistzitierten Forscher aus allen wissenschaftlichen Disziplinen weltweit aufgenommen. Das SIAF hat rund 1.705 wissenschaftliche Beiträge veröffentlicht und gehört zu den meistzitierten Instituten weltweit. Die vom SIAF veröffentlichten Artikel wurden 96‘000-mal zitiert.

Die Epithelial-Barrier-Theorie: Ein umfassendes Verständnis der pandemieartigen Entwicklung und Ursachen von allergischen und anderen chronischen nicht übertragbaren Krankheiten. Die Epithelial-Barrier-Theorie, postuliert von C.A. Akdis, liefert eine umfassende Erklärung für den weltweiten Anstieg chronischer Krankheiten in den letzten 65 Jahren. Sie besagt, dass die Exposition gegenüber toxischen Substanzen, die durch die Industrialisierung und Veränderungen des modernen Lebensstils eingeführt wurden, die epitheliale Barriere der Haut, der oberen und unteren Atemwege und der Darmschleimhaut stört, was eine entzündliche Immunreaktion auslösen kann, die viele chronische Entzündungskrankheiten initiiert oder verschlimmert. Die Oberflächen unserer Haut, Atemwege und Innereien sind mit schützenden Zellschichten, den epithelialen Barrieren, ausgekleidet. Intakte epitheliale Barrieren sind entscheidend für die Homöostase, da sie das Wirtsgewebe vor Infektionen, Umweltgiften, Schadstoffen und Allergenen schützen. Es ist bekannt, dass viele chemische Substanzen, die in gängigen Konsumgütern enthalten sind (wie Luftschadstoffe, Mikro- und Nanoplastik, Detergenzien, Zahnpasta, Shampoos, Reinigungsmittel und verarbeitete Lebensmittel), diese kritischen Barrieren schädigen und die Durchlässigkeit für Bakterien, Toxine, Schadstoffe und Allergene erhöhen. Wenn die epithelialen Barrieren beeinträchtigt oder "undicht" sind können toxische Substanzen, Mikroben und Allergene in tiefere Gewebe eindringen, wo sie nicht hingehören und so eine Immun-/Entzündungsreaktion auslösen, die chronische Entzündungskrankheiten initiieren oder verschlimmern kann.

Störende Effekte von Lebensmittelemulgatoren und Detergenzien auf intestinale Epithelzellen: Untersuchung der Effekte von gängigen Lebensmittelemulgatoren und Detergenzien auf Zytotoxizität, Barrierefunktion, Transkriptom und Proteinexpression in gastrointestinalen Epithelzellen. Die Beeinträchtigung der Integrität der epithelialen Barriere im Gastrointestinaltrakt ist wichtig für die Pathogenese vieler entzündlicher Erkrankungen. Dementsprechend haben wir das Potenzial von Biomarkern für die Disfunktion der epithelialen Barriere zur Vorhersage von Krankheiten wie COVID-19 und Asthma bewertet. Um die Effekte von Störsubstanzen und Rettungsagenten auf intestinale Epithelzellen zu untersuchen, haben wir humane intestinale Organoide entwickelt, die aus induzierten pluripotenten Stammzellen stammen, sowie Organ-on-a-Chip-Modelle.

Waschmittel und Funktion der epithelialen Barriere: Mit Waschmitteln und dem Hauptaktivbestandteil Natriumlaurylsulfat behandelte ex vivo Hautproben von Menschen zeigten eine signifikante Reduktion der Hautbarriere im Vergleich zu unbehandelter Haut. Eine Reduktion der Expression mehrerer Gene, die für die Integrität der Hautbarriere essenziell sind, wie Tight Junctions und Adhärenzkontaktproteine, wurde beobachtet. Im Gegensatz dazu wurden als Teil des Heilungsprozesses die Verhornung, lipidmetabolische Prozesse und die Differenzierung epidermaler Zellen hochreguliert. Zusammenfassend lässt sich sagen, dass Waschmittel und ihr Hauptbestandteil SDS die epidermale Barriere in vivo und ex vivo menschlicher Haut beeinträchtigen. Tägliche Waschmittelexposition kann zu Hautbarriere-störungen führen und zur Entwicklung atopischer Krankheiten beitragen.

Precision Proteomics Center: Eines der Schlüsselprojekte des Instituts ist die Einrichtung des Precision Proteomics Center am SIAF in Zusammenarbeit mit dem Kanton Graubünden und der Universität Zürich. Das Zentrum wurde erfolgreich eingerichtet und befindet sich nun unter der Leitung von Prof. Christoph Messner in der Phase der Personal- und Infrastrukturerweiterung. Das Zentrum entwickelt und wendet modernste massenspektrometrie-basierte Technologien für die Proteomanalyse klinischer Proben an. Ziel des Zentrums ist es, neue Biomarker und Krankheitsmechanismen zu identifizieren, die zur Entwicklung der nächsten Generation personalisierter Behandlungen beitragen werden.

· Etablierung von Hochdurchsatz-Proteomik-Technologien für Anwendungen in der Biomarker-Entdeckung bei Allergien, Hautkrankheiten und Onkologie.

· Neue Technik 'OxoScan-MS' für grossangelegte Plasma-Glycoproteomik: Wir haben eine Methode entwickelt, die eine quantitative Kartierung von Glykopeptiden in großen Kohorten ermöglicht und eine differenzielle Glycosylierung bei COVID-19-Patienten aufzeigt.

· Integration von Lymphom-Proteomen in eine biomedizinische Informatikplattform: Wir erstellen den grössten Proteomik-Datensatz für Lymphome mit dem Ziel, Diagnose und Behandlung zu verbessern.

· Studie an PDAC-Patienten, die eine Immuntherapie und Chemotherapie erhalten: Wir haben Patientengruppen mit prognostischen Markern für Überlebensraten identifiziert.

· Systematische Gen-Knockout-Studie in Hefe zur Untersuchung von Protein-Funktionen: Wir haben funktionelle Genomik mit Proteomik kombiniert, um Prinzipien der Protein-Funktion aufzuklären.

Molekulare Allergologie: Im Rahmen des DAViS-Zentrums wurde das GeneSelectR R-Paket erstellt und auf CRAN verfügbar gemacht. Es ermöglicht die Analyse komplexer RNA-Sequenzierungsdatensätze mit verschiedenen maschinellen Lernmethoden und die Bewertung der Klassifikationsleistung und biologischen Relevanz der Ergebnisse. Es ist Teil unserer fortlaufenden Bemühungen, molekulare und klinische Datensätze im ML-SOS-ALL-Projekt zu integrieren. Durch die Bestimmung der relativen Häufigkeit verschiedener SARS-CoV-2-Varianten im Abwasser haben wir gezeigt, dass sich eine neue Variante bei internationalen Sportveranstaltungen im Dezember 2021 und beim WEF im Januar 2023 verbreitete. Wir haben gezielte Proteomik in ex vivo differenzierten Th1-Zellen eingesetzt, um Peptide zu erkennen, die zuvor durch nicht-kodierende RNAs übersetzt wurden. In einem anderen Projekt haben wir nach Allergenproteinen in Lebensmitteln gesucht, indem wir gezielte Proteomik verwendeten.

Wir haben die Proteinisoprenylierung in aktivierten Th1-Zellen weiter untersucht und die aktuelle Ansicht zu den Zielen und Orten der Proteinisoprenylierung herausgefordert. Zusätzlich zur Installation der IT-Infrastruktur gab es weitere Projekte in Zusammenarbeit zwischen dem DAViS-Zentrum und dem Zentrum für Präzisionsproteomik. Dazu gehörten ein Projekt zur verbesserten statistischen Analyse von Massenspektrometrie-Daten angereicherter Proteine sowie ein Projekt mit dem Schweizerischen Institut für Sportmedizin (SRISM) zur statistischen Analyse nicht massenspektrometriebasierter Proteomik-Daten. Eine Veröffentlichung erfolgte in Zusammenarbeit mit der Fachhochschule Graubünden (FHGR), dem SIAF und der Medizinischen Universität Lodz in Polen, im Rahmen der gemeinsamen COVID-19-Studie. Die Studie identifizierte diagnostische Laborparameter und Prädiktoren für einen schweren Verlauf von COVID-19. Im ML-SOS-ALL-Projekt wurden Daten südafrikanischer Kinder mit und ohne atopischer Dermatitis analysiert, um relevante Transkriptlisten zu erstellen. Die Analyse von Abwasserproben und die Sequenzierung von SARS-CoV-2-RNA-Fragmenten wurden fortgesetzt und wird bis WEF23 abgeschlossen.

Immunmetabolismus: Die Forschung zum Immunmetabolismus am Institut konzentrierte sich auf folgende Hauptbereiche:

· Immunologie viraler Infektionen und deren langfristige Konsequenzen: Infektionen mit Rhinoviren, respiratorischen Synzytialviren und Coronaviren verändern die angeborenen und adaptiven Immunantworten bei Patienten mit chronischen Atemwegs- und Allergieerkrankungen. Wir haben abnormale Mechanismen gegenüber Viren in den Atemwegen sowie kurz- und langfristige immunologische Konsequenzen von Infektionen bei Patienten mit Asthma und Allergien charakterisiert.

· Immunmetabolismus bei viralen Infektionen, Immuntoleranz, Allergien und Asthma: Mit Einzelzell- und Bulk-Sequenzierung, räumlicher Transkriptomik, Proteomik und Metabolomik, gekoppelt mit Gen-Editing, Durchflusszytometrie, konfokaler Mikroskopie, Einzelzell-Metabolismus-Assays und umfassenden bioinformatischen Ansätzen haben wir 1) abnormalen mitochondrialen Metabolismus des Bronchialepithels, der für beeinträchtigte antivirale Antworten bei Asthma verantwortlich ist, 2) metabolische Kontrollpunkte für die Entwicklung menschlicher pathogener Th2-Zellen, 3) immunmetabolische Reprogrammierung von allergen-spezifischen CD4+T-Zellen während der Allergen-Immuntherapie und 4) Auswirkungen von Typ-2-Entzündungen auf den Keratinozyten-Metabolismus bei atopischer Dermatitis charakterisiert.

· Neue Wege für Biomarker, Prävention und Behandlung von Asthma und Allergien: Trainierte Immunität und Toleranz stellen ein neues Konzept der unspezifischen immunologischen Erinnerung über epigenetische und metabolische Modifikationen dar. Wir haben diese Mechanismen in verschiedenen Zellen und ihre Biomarker im Serum von Patienten mit Allergien und unter Allergen-Immuntherapie untersucht.

B-Zell-Immunologie: Wie aus den unten aufgeführten Projekten ersichtlich ist, ist die B-Zell-Immunologie-Gruppe hervorragend mit modernsten Techniken ausgestattet, um menschliche B-Zellen in Gesundheit und Krankheit zu untersuchen. 25 Jahre in vivo-Verfolgung von allergenspezifischen Gedächtnis-B-Zellen beim Menschen: Die Immunantwort auf Giftallergen bei Imkern stellt eines der besten Modelle dar, um die Toleranz gegenüber hohen Allergenmengen zu untersuchen. Imker und AIT-Reaktionen bei bienengiftallergischen Individuen werden im Vergleich untersucht. Charakterisierung von Gedächtnis-B-Zellen, die spezifisch für Milchallergene sind: Unsere vorläufigen Daten zeigten eine differenzielle Expression von 30 Genen, die mit der Toleranz gegenüber Lebensmittelantigenen in Zusammenhang stehen. Wir werden diese Gene mit gezielter Proteomik und B-Zell-Knock-in- und Knock-out-Experimenten eingehend analysieren. Histamin reguliert Immunantworten durch differenzielle Expression von H1- und H2-Rezeptoren: Histamin und der Histaminrezeptor (HR) 2 fördern die Entwicklung

der peripheren Toleranz während der SIT und der Exposition gegenüber hohen Dosen von Gift bei Imkern. Mit diesem umfassenden Hintergrund schlagen wir vor, unsere vorläufigen Daten zur differenziellen Expression von HR1 und HR2 auf B-Zell-Untergruppen weiter zu verfolgen. Umfassende Untersuchung von Immunzellen aus asthma-diskordanten eineiigen Zwillingen: Wir untersuchen zirkulierende T- und B-Zell-Untergruppen durch umfassende Einzelzellsequenzierung kombiniert mit Einzelzell-Proteomik, um die Mechanismen der Immuntoleranz während der erdnussspezifischen OIT umfassend zu charakterisieren. Umfassende Methoden zur Untersuchung von antigenspezifischen B-Zellen werden auf Erdnussallergene und die Untersuchung von allergenspezifischen B-Zellen angewendet. Zirkulierende Lebensmittelallergen-spezifische Antikörper bei Patienten mit eosinophiler Ösophagitis: Diese Studie untersucht die zugrunde liegenden Mechanismen der eosinophilen Ösophagitis (EoE) mit Fokus auf antigenspezifische Reaktionen. Unsere Ergebnisse zeigen erhöhte Spiegel von IgG, IgG4, IgA1 und IgA2 gegen verschiedene Lebensmittelantigene bei EoE-Patienten mit signifikanten Unterschieden zwischen aktiver und inaktiver EoE. Typ 2-polarisierte Gedächtnis-B-Zellen (MBC2s): Diese Studie zeigt, dass die Dupilumab-Behandlung bei pädiatrischen Patienten mit atopischer Dermatitis (AD) die Typ 2-polarisierten Gedächtnis-B-Zellen (MBC2) und die Gesamtheit der IgE-Spiegel signifikant reduziert. Die Ergebnisse deuten darauf hin, dass MBC2- und Gesamt-IgE-Spiegel von der IL-4-Signalgebung abhängig sind und dass die Hemmung der IL-4- und IL-13-Wege durch Dupilumab AD durch die Verringerung dieser Marker effektiv behandelt. Durchflusszytometrische Analysen der Immunglobulin-Schwerketten-Isoformen des B-Zell-Rezeptors: Die genaue Erkennung der B-Zell-Rezeptor (BCR)-Schwerketten-Isoformen ist entscheidend für das Studium der B-Zell-Immunologie. In dieser Studie haben wir den Einfluss verschiedener Fc-Rezeptor (FcR)-Blockierungsreagenzien auf die Detektionsgenauigkeit der BCR-Schwerketten-Isoformen mithilfe der Durchflusszytometrie bewertet und eine optimierte Färbemethode für BCR-Isoformen entwickelt. Menschliche Askaris-Infektion und IL-10-produzierende B-Zellen: Unsere Studie ergab, dass eine Infektion mit Ascaris lumbricoides mit höheren Frequenzen von IL-10-produzierenden regulatorischen B-Zellen verbunden ist, was auf eine immunsuppressive Reaktion bei infizierten Personen hinweist. Darüber hinaus korreliert die Infektion mit reduzierten Spiegeln zirkulierender ABA-1-spezifischer IgG1- und IgE-Antikörper, was auf eine Modulation der Antikörperantworten hinweist.

Alpine Medical Campus: Das SIAF führt in enger Zusammenarbeit mit seinen unabhängigen Partnern CK-CARE, HGK, Cardio-CARE und der gestifteten Professur MC Brüggen auf dem Alpine Medical Campus medizinische Forschung auf höchstem Niveau durch. Diagnostik, Forschung und Therapie ergänzen sich ideal auf dem medizinischen Campus. Diese Synergien kommen den Patienten direkt zugute: Forschungsergebnisse werden in Therapieoptionen und Behandlungen umgesetzt, wodurch ein umfassendes diagnostisches und therapeutisches Konzept entsteht. Darüber hinaus sind Ausbildung, Fort- und Weiterbildung von Akademikern (MSc, PhD und Postdocs) und medizinischem Fachpersonal zentrale Bestandteile des Dienstleistungsportfolios. Das strategische Ziel des medizinischen Campus ist es, ein international anerkanntes Exzellenzzentrum im Bereich der personalisierten Prävention und Behandlung von allergischen und kardiovaskulären Erkrankungen zu schaffen. Wir freuen uns sehr auf eine umfangreiche Zusammenarbeit im Rahmen des neu entstehenden Alpine Innovationszentrums.

Schweizerisches Forschungsinstitut für Sportmedizin: Nach der Gründung des Schweizerischen Forschungsinstituts für Sportmedizin (SRISM) hat sich unsere Forschungszusammenarbeit effizient weiterentwickelt und konzentriert sich auf Eishockeyspieler, Langläufer, nicht-professionelle Athleten und nicht sportliche Kontrollen. Wir untersuchten die Mechanismen häufiger Atemwegsinfektionen und Infektionskrankheiten bei Athleten sowie die immunologischen Mechanismen des Trainings. Wir erreichten die Veröffentlichung des 5. gemeinsamen Artikels und mehrere Schlüsselstudien sind im Gange, die sich auf die Auswirkungen des Trainings, des Immunstoffwechsels, des Geschlechts, der Auswirkungen der Umweltbelastung, der körperlichen Leistungsfähigkeit und Leistung konzentrieren.

Auszeichnungen: Milena Sokolowska erhielt den European Academy of Allergy and Clinical Immunology (EAACI)-Phadia Research (PhARF) Award. Mubeccel Akdis erhielt den Women in Science Award der Asia Pacific Society of Allergy and Clinical Immunology, den EAACI Fellow Award, den FEBS National Lecture Award und den Dr. Nejat Eczacıbaşı Medicine Awards; Medical Science award. Cezmi Akdis erhielt den APAACI award: Asia Pacific Society of Allergy Asthma Immunology, life time achievement award und den Award für Jack Peppy's honorary Lecture: British Society of Allergy Clinical Immunology. Mubeccel und Cezmi Akdis erhielten die Ehrenprofessur der Harvard University, Abteilung für Umwelt und Gesundheit Harvard T.H. Chan School of Public Health, Harvard University.

Klinischer Dienst: Seit 2019 ist das SIAF Dienstleister der OLINK-Technologie und bietet seinen akademischen und industriellen Kunden spezielle Messungen zur Bestimmung von Biomarkern an, die als Parameter zur Beurteilung der Krankheitsentwicklung und -überwachung dienen. Diese Messungen helfen auch, verschiedene Manifestationen und Verläufe von Krankheiten besser zu verstehen. Derzeit ist das SIAF das einzige Labor in der Schweiz, das diese speziellen Messungen sowohl für nationale als auch für internationale Zwecke anbietet. Das SIAF stellt der Davoser Klinik und allen anderen interessierten Kliniken und praktizierenden Ärzten spezielle zelluläre immunologische Untersuchungen zur Verfügung. Mithilfe der Durchflusszytometrie (FACS-Analyse) von Blut, bronchoalveolärer Lavage (BAL) sowie anderen Gewebeflüssigkeiten werden die verschiedenen Immunzellen und Unterpopulationen in Bezug auf ihre Entwicklung, Anteile und Aktivierungszustand gemessen.

Ausbildung, Lehre, Kongresse: Das SIAF spielt eine wichtige Rolle in der Ausbildung von Studenten und Postgraduierten. Gleichzeitig erfüllt das SIAF Lehrverpflichtungen an der Universität Zürich. Diese Verpflichtungen umfassen verschiedene Vorlesungsstunden im Rahmen der Biochemie am Biochemischen Institut. Prof. C. A. Akdis ist Mitglied der Medizinischen Fakultät der Universität Zürich mit dem Recht zur Promotion in der Fakultät für Mathematik und

Naturwissenschaften. Prof. C. A. Akdis und Prof. M. Akdis halten ausserdem Ehrenprofessuren am Tongren Hospital der Peking University, der Universität Bursa-Uludag und der Wuhan University. Kürzlich erhielten C. Akdis und M. Akdis Ehrenprofessuren der Harvard University, Harvard T.H. Chan School of Public Health, Department of Environmental Medicine. PD Dr. K. Bärenfaller und PD Dr. M. Sokolowska sind Mitglieder des Lehrkörpers der UZH.

Biomedical Data Mining Block Course: Vom 5. bis 23. Juni 2023 fand der vierte Biomedical Data Mining Blockkurs statt. Wie im Jahr 2022 wurde er eine Woche lang vor Ort am SIAF und anschliessend zwei Wochen online abgehalten. Die verantwortlichen Dozenten waren PD Dr. K. Bärenfaller und PD Dr. M. Sokolowska. Die Studierenden bekamen Daten aus verschiedenen RNA-Sequenzierungs- oder Proteomikprojekten und sollten diese Listen in verschiedenen Aufgaben mit R analysieren und die Ergebnisse dann kontextualisieren. Um die Studierenden mit den nötigen Fähigkeiten und Hintergründen auszustatten, wurde der praktische Teil durch Vorlesungen zu Proteomik, Transkriptomik, Metabolomik, Immunoassays, Durchflusszytometrie, experimentellem Design und statistischen Methoden, funktioneller Kategorisierung, maschinellen Lern- und KI-Tools sowie durch Einführungen in verschiedene Tools wie STRING, Cytoscape und Genevestigator ergänzt. Am Ende des Kurses mussten die Studierenden eine mündliche Präsentation halten und einen schriftlichen Bericht über ihre Datenanalyseaufgabe einreichen.

Weltkonferenz zur Immunregulation: Nach den Jahren der Pandemie konnte die 17. Ausgabe der Weltkonferenz zur Immunregulation (WIRM) zum zweiten Mal in Folge wieder als Präsenzveranstaltung im Kongresszentrum Davos stattfinden. Rund 500 Wissenschaftler aus über 37 Ländern der Welt versammelten sich vom 6. bis 9. Juli 2023 zu dem viertägigen Kongress, um die neuesten Erkenntnisse in der Immunologie auszutauschen. Talentierte junge Forscher trafen auf erfahrene Experten, als Wissenschaftler 119 Vorträge hielten und 167 Abstracts präsentierten, in denen sie ihre neuesten Erkenntnisse in der Immunologie teilten. Dieser globale Austausch aktueller Erkenntnisse hilft, neue Therapieansätze und innovative Behandlungsmethoden für Patienten zu entwickeln.

Finanzielle Basis: Die Ausgaben und Einnahmen des SIAF haben sich im Vergleich zu den Vorjahren nur geringfügig verändert. Die Grundfinanzierung des Instituts wird derzeit durch die Hauptsponsoren sichergestellt. Sie besteht hauptsächlich aus einem Beitrag des Bundes (Forschungsgesetz Art. 15), Beiträgen des Kantons Graubünden und der Gemeinde Davos, Beiträgen der Universität Zürich, Beiträgen des Schweizerischen Nationalfonds, EU-Konsortialzuschüssen CURE und Syn-Air-G sowie Beiträgen von Stiftungen wie der PROMEDICA Stiftung und der Stiftung vormals Bündner Heilstätte Arosa, die Doktorandenprogramme unterstützen. Die zusätzlichen Ausgaben wurden durch Einnahmen aus zusätzlich wettbewerblich erworbenen Drittmitteln und dem WIRM-Kongress gedeckt.

Danksagungen:
Ich möchte allen Mitarbeitern herzlich für ihre grossartige Arbeit und das gute Arbeitsklima am SIAF danken. Gleichzeitig danke ich den Davoser Kliniken, ihren Chefärzten und ihrem Personal sowie der Universität Zürich für ihre konstante und effektive Unterstützung unseres Instituts.

Besonders hervorheben möchte ich unsere fruchtbare Zusammenarbeit mit CK-CARE, die es uns ermöglicht, patientenorientierte Forschung bei atopischer Dermatitis durchzuführen. Ich danke insbesondere Frau und Herrn Kühne für ihre Unterstützung, die unsere Forschung befähigt, nachhaltige Lösungen für bessere Diagnosen und Behandlungen von Patienten mit atopischer Dermatitis zu finden. Dank dieser Unterstützung wurden im Institut viele Master- und Doktorgrade erworben und eine grosse Anzahl internationaler Stipendien vergeben, ein sehr erfolgreiches Projekt, das seit der Gründung von CK-CARE über 60 kurzfristige internationale Stipendien unterstützt hat.

Mein ausserordentlicher Dank gilt auch der Stiftung Schweizerisches Forschungsinstitut für Hochgebirgsklima und Medizin (SFI), ihrem Stiftungsrat und ihrem Ausschuss für die stets gewährte Unterstützung. Ebenso bin ich und das gesamte SIAF Dr. Walter Ammann, der Ende 2022 von seiner Position als SFI-Präsident zurückgetreten ist, für seine ständigen und unermüdlichen Support sehr dankbar. Herzlichen Dank an Philipp Wilhelm, dem Stadtpräsidenten von Davos, der im letzten Jahr Präsident unserer Stiftung war, für seine unermüdliche Hilfe und Unterstützung der Davoser Forschungsinstitute. Mein Dank und meine besten Wünsche für viel Erfolg gehen an Brigitta Gadient, die neue Präsidentin unserer Stiftung. Last but not least, mein besonderer Dank geht an den Kanton Graubünden, das Staatssekretariat für Bildung, Forschung und Innovation und alle Behörden, die ein entschlossenes Interesse an der Forschung des SIAF gezeigt haben und das Institut in jeder Hinsicht unterstützen.

Davos, Mai 2024

Report of the director

Prof. Dr. Cezmi A. Akdis

The Swiss Institute of Allergy and Asthma Research (SIAF), founded in 1988 by the Medical Department of the Swiss Research Institute for High Altitude Climate and Medicine Davos (SFI), aims to improve understanding of allergies and asthma through its research. The goal is to develop treatments that will improve the future of those affected. Since 1996, SIAF has been affiliated with the University of Zurich and has been a member of the Life Science Zurich Graduate School since 2008, which is a joint education project of the University of Zurich and ETH Zurich. This affiliation allows SIAF to offer comprehensive PhD training. Additionally, SIAF is an active member of Academia Raetica and the Graduate School of the Canton of Graubünden.

Research at SIAF is designed for direct collaboration with clinics in Davos, the University of Zurich, and other specialized institutes. The institute focuses on patient-relevant translational research and the investigation of the immunological basis of allergic and asthmatic diseases, which provides insights for new preventive and curative treatments benefiting those affected. Furthermore, SIAF is involved in the European Academy of Allergy and Clinical Immunology (EAACI), the American Academy of Allergy, Asthma, and Immunology (AAAAI), and the World Allergy Organization (WAO). There is also an intensive collaboration with Stanford University (Sean Parker Asthma and Allergy Center) and Harvard University (T.H. Chan School of Public Health). A high number of bioinformaticians are currently working in the institute. Artificial Intelligence/ Machine learning projects are continuously developing.

In 2023, 76 scientific papers were published or are still in press in peer-reviewed international journals with an "Impact Factor." The SIAF achieved a total "Impact Factor" value of 1046.4 and an average of 13.79 points per publication in 2023. The latest findings were also presented in 59 abstracts at various professional conferences. Our employees were invited to participate in 111 different seminars and presentations at national and international congresses. Such invitations are important for disseminating the achieved results and for the international acceptance of the institute's research. SIAF employees chaired 46 different sessions. Additionally, SIAF employees hold 79 scientific positions in international societies and 35 positions in international journals. Furthermore, since 2018, Prof. CA. Akdis has held the position of Editor-in-Chief of the journal Allergy. With his leadership the impact factor of Allergy increased from 6.02 to 14.71 which became the number one journal of the specialty of Allergy and Clinical Immunology, As a result of the internationally highly esteemed scientific publications, Prof. Dr. CA. Akdis was included in Thomson Reuters Clarivate's list of most cited researchers from all scientific disciplines worldwide for the eighth time in 2023. The SIAF has published around 1,705 scientific contributions and is among the most cited institutes worldwide. The articles published by the SIAF have been cited 96'000 times.

The Epithelial Barrier Theory: A comprehensive understanding of the pandemic size develeopment and causes of allergic and other chronic non-communicable diseases. The epithelial barrier theory provides a comprehensive explanation for the worldwide epidemic rise of chronic diseases in the last 65 years. Postulated by C.A. Akdis, it states that exposure to toxic substances introduced by industrialization and changes in modern lifestyle disrupts the epithelial barrier of the skin, upper and lower respiratory tract, and intestinal mucosa, triggering an inflammatory immune response that can initiate or exacerbate many chronic inflammatory diseases. The surfaces of our skin, respiratory tract, and intestines are lined with protective cell layers called epithelial barriers. Intact epithelial barriers are essential for homeostasis as they protect the host tissue from infections, environmental toxins, pollutants, and allergens. It is known that many chemical substances found in common consumer products (such as air pollutants, micro and nanoplastic, detergents, toothpaste, shampoos, cleaning agents, and processed foods) damage these critical barriers and increase permeability to bacteria, toxins, pollutants, and allergens. When the epithelial barriers are compromised (or "leaky"), toxic substances, microbes and allergens can penetrate towards deeper tissues, where they do not belong, triggering an immune/inflammatory reaction that can initiate or exacerbate many chronic inflammatory diseases.

Disturbing effects of food emulsifiers and detergents on intestinal epithelial cells: Investigation of the effects of commonly used food emulsifiers and detergents on cytotoxicity, barrier function, transcriptome, and protein expression in gastrointestinal epithelial cells. Impaired integrity of the epithelial barrier in the gastrointestinal tract is important for the pathogenesis of many inflammatory diseases. Accordingly, we evaluated the potential of biomarkers for epithelial barrier dysfunction in predicting diseases such as COVID-19 and asthma. To investigate the effects of disruptors and rescue agents on intestinal epithelial cells, we have developed human intestinal organoids derived from induced pluripotent stem cells and organoid organ-on-a-chip models.

Laundry detergents and epithelial barrier function: Laundry detergent- and main active surfactant sodium lauryl sufate-treated human ex vivo skins showed a significant reduction in skin barrier compared to untreated skin. A reduction of the expression of several genes essential for skin barrier integrity, such as tight junctions and adherens junction proteins was observed. In contrast, as a part of the healing process, keratinization, lipid metabolic processes, and epidermal cell differentiation were upregulated. In conclusion, laundry detergents and its main component, SDS impaired the epidermal barrier in vivo and ex vivo human skin. Daily detergent exposure may cause skin barrier disruption and may contribute to the development of atopic diseases.

Precision Proteomics Center: One of the key projects of the Institute is the establishment of the Precision Proteomics Center at SIAF in collaboration with the Canton of Grisons and the University of Zurich. The center was successfully established and is now in the process of staffing and infrastructure expansion under the direction of Prof. Christoph Messner. The center develops and applies state-of-the-art mass spectrometry-based technologies for proteome analysis of clinical samples. The goal of the center is to identify novel biomarkers and disease mechanisms that will contribute to the development of the next generation of personalized treatments.
· Established high-throughput proteomics technologies for applications in biomarker discovery studies for allergies, skin diseases, and oncology.

· New technique 'OxoScan-MS' for large-scale plasma glycoproteomics: We developed a method that enables quantitative mapping of glycopeptides in large cohorts, revealing differential glycosylation in COVID-19 patients.
· Integrating lymphoma proteomes into a biomedical informatics platform: We are generating the largest proteomics dataset for lymphoma, aiming to improve diagnosis and treatment.
· Study on PDAC patients receiving immunotherapy and chemotherapy: We identified patient subgroups with prognostic markers for survival outcomes.
· Systematic gene knockout in yeast to study protein functions: We combined functional genomics with proteomics to reveal principles of protein.

Molecuar Allergology: In the context of the DAViS Center, the GeneSelectR R package was created and made available on CRAN. It allows the analysis of complex RNA sequencing datasets using different machine learning methods and assessing the classification performance and biological relevance of the results. It is part of our continuing efforts to integrate molecular and clinical datasets in the ML-SOS-ALL project. By determining the relative prevalence of different SARS-CoV-2 variants in wastewater, we showed that a new variant spread at international sports events in December 2021 and at the WEF in January 2023. We used targeted proteomics in ex vivo differentiated Th1 cells to detect peptides with previous evidence of translation from non-coding RNAs. In another project, we searched for allergen proteins contaminating food using targeted proteomics.
We continued investigating protein prenylation in activated Th1 cells, challenging the current view on the targets and sites of protein prenylation.In addition to the IT infrastructure installation, there were further projects in collaboration between the DAViS Center and the Center for Precision Proteomics. These included a project for improved statistical analysis of mass spectrometry data of enriched proteins, as well as a project with the Swiss Institute for Sports Medicine (SRISM) for the statistical analysis of non-mass spectrometry-based proteomics data. A publication was made in collaboration with the University of Applied Sciences Graubünden (FHGR), SIAF, and the Medical University of Lodz, Poland, as part of the collaborative COVID-19 study. The study identified diagnostic laboratory parameters and predictors for a severe course of COVID-19. In the ML-SOS-ALL project, data on South African children with and without atopic dermatitis were analyzed to create relevant transcript lists. The analysis of wastewater samples and sequencing of SARS-CoV-2 RNA fragments were continued and will be completed by WEF23.

Immunometabolism: Immune metabolism research in the institute has been focused on the following major areas:
· Immunology of viral infections and their long-term consequences: Infections with rhinoviruses, respiratory syncytial viruses and coronaviruses alter innate and adaptive immune responses in patients with chronic respiratory and allergic diseases. We have characterised abnormal mechanisms to viruses in the airways and short- and long immune consequences of infections in patients with asthma and allergies.
· Immunometabolism in viral infections, immune tolerance, allergy and asthma: Using single-cell and bulk sequencing, spatial transcriptomics, proteomics, and metabolomics, coupled with gene editing, flow cytometry, confocal microscopy, single-cell metabolic assays, and comprehensive bioinformatic approaches, we have characterised 1) abnormal mitochondrial metabolism of bronchial epithelium responsible for impaired antiviral responses in asthma, 2) metabolic checkpoints for development of human pathogenic Th2 cells, 3) immunometabolic reprogramming of allergen-specific CD4+T cells during allergen immunotherapy, and 4) effects of type 2 inflammation on keratinocyte metabolism in atopic dermatitis.
· Novel avenues for biomarkers, prevention and treatment in asthma and allergy: Trained immunity and tolerance constitute a novel concept of unspecific immunological memory via epigenetic and metabolic modifications. We have been investigating these mechanisms in various cells and their biomarkers in serum of patients with allergies and undergoing allergen immunotherapy.

B cell Immunology: As can be seen from the below projects, the B cell immunology group has been extremely well equiped with front techniqes to invstigate human B cells in health and diseases. 25 years in vivo follow up of allergen-specific memory B cells in humans: Immune response to venom allergen in beekeepers represents one of the best models to investigate high dose allergen tolerance. Bee keepers and AIT response in bee venom allergic individuals will be investigated in comparison. Characterization of memory B cells specific for milk allergens: Our preliminary data demonstrated differential expression of 30 food antigen tolerance-related genes. We will perform in-depth analysis of these genes with targeted proteomics and B cell knock-in and knockout experiments. Histamine regulates immune responses by differential expression of H1 and H2 receptors: Histamine and Histamine receptor (HR) 2 promotes the development of peripheral tolerance during SIT and high dose venom exposure in beekeepers. With this extensive background, we propose to pursue our preliminary data on the differential expression of HR1 and HR2 on B cell subsets.
In depth investigation of immune cells from asthma-discordant monozygotic twins: We are investigating circulating T and B cell subsets by extensive single cell sequencing combined with single cell proteomics.To comprehensively characterize the mechanisms of immune tolerance during the peanut-specific OIT. Extensive methodology to investigate antigen-specific B cells is goingto be applied to peanut allergens and the investigation of allergen-specific B cells. Circulating food allergen-specific antibodies in eosinophilic esophagitis patients: This study investigates the underlying mechanisms of eosinophilic esophagitis (EoE), focusing on antigen-specific responses. Our findings indicate elevated levels of IgG, IgG4, IgA1, and IgA2 against various food antigens in EoE patients, with notable differences between active and inactive EoE.
Type 2 polarized memory B cells (MBC2s): This study demonstrates that dupilumab treatment in pediatric atopic dermatitis (AD) patients significantly reduces Type 2–polarized memory B cells (MBC2) and total IgE levels. The findings suggest that MBC2 and total IgE levels are dependent on IL-4 signaling, with dupilumab's inhibition of IL-4 and IL-13 pathways effectively managing AD by decreasing these markers. Flow Cytometric Analyses of B-Cell Receptor Immunoglobulin Heavy Chain Isotypes: Accurate detection of B-cell receptor (BCR) heavy chain isotypes is critical for studying B-cell

immunology. In this study, we evaluated the impact of various Fc receptor (FcR) blocking reagents on the detection accuracy of BCR heavy chain isotypes using flow cytometry and developed an optimized staining method for BCR isotypes. Human Ascaris infection and IL-10 producing B cells: Our study found that Ascaris lumbricoides infection is associated with higher frequencies of IL-10 producing regulatory B cells, suggesting an immunosuppressive response in infected individuals. Additionally, the infection correlates with reduced levels of circulating ABA-1-specific IgG1 and IgE, indicating a modulation of antibody responses.

Alpine Medical Campus: The SIAF, in close collaboration with its independent partners CK-CARE, HGK, Cardio-CARE and the and the endowed professorship MC Brüggen on the Alpine Medical Campus, conducts cutting-edge medical research. Diagnostics, research, and therapy complement each other ideally on the medical campus. These synergies directly benefit the patients: research findings are translated into therapy options and treatments, allowing for a comprehensive diagnostic and therapeutic concept. Furthermore, education, training, and continuing education of academics (MSc, PhD, and postdocs) and medical professionals are central components of the service portfolio. The strategic goal of the medical campus is to create an internationally recognized center of excellence in the field of personalized prevention and treatment of allergic and cardiovascular diseases. We very much look forward to extensive collaboration in the fremework of the newly developing Alpine Innnovation Center.

Swiss Research Institute for Sports Medicine: After the establishment of Swiss Research Institute for Sports Medicine (SRISM) our research collaboration has been efficiently growing focusing on ice hockey players, cross-country players, non professional athletes and nonsportive controls investigated the mechanisms of common respiratory infections infectious diseases in athlethes and immune mechanisms of training. We achieved the publication of the 5th paper together and several key studies are going on focused on effects of training, immune metabolism, gender, effects of environmental exposure, physical capacity and permance.

Education, teaching, congresses

SIAF plays an important role in the education of students and postgraduate studies. At the same time, SIAF fulfills teaching obligations at the University of Zurich. These obligations include various lecture hours within the framework of biochemistry at the Biochemical Institute. Prof. C. A. Akdis is a faculty member of the Medical Faculty of the University of Zurich with the right to confer doctorates in the Faculty of Mathematics and Natural Sciences and an honorary professor at Bezmialem University Istanbul. Prof. C. A. Akdis and Prof. M. Akdis also hold honorary professorships at Tungren Hospital of Peking University, University of Bursa-Uludag, and Wuhan University. PD Dr. K. Bärenfaller and PD Dr. M. Sokolowska are members of the teaching staff at UZH.

Recent important awards: Milena Sokolowska received the European Academy of Allergy and Clinical Immunology (EAACI)-Phadia Research (PhARF) Award. Mubeccel Akdis received Asia Pacific Society of Allergy and Clinical Immunology Women in Science Award, the EAACI Fellow Award, the FEBS National Lecture Award and the Dr Nejat Eczacıbaşı Medical Science award.
Cezmi Akdis received the APAACI award: Asia Pacific Society of Allergy Asthma Immunology, life time achievement award and the award for Jack Peppy's honourary lecture: British Society of Allergy and Clinical Immunology.
Mübeccel and Cezmi Akdis Received Adjunct Professorship From Harvard University, Department of Environmental Health, Harvard T.H. Chan School of Public Health, Harvard University.

Clinical service: Since 2019, SIAF has been a service provider of OLINK technology, offering its academic and industrial customers special measurements to determine biomarkers that serve as parameters for assessing disease development and monitoring. These measurements also help in better understanding various manifestations and progressions of diseases. Currently, SIAF is the only laboratory in Switzerland offering these specialized measurements for both domestic and international purposes. The SIAF offers special cellular immunological investigations to the Davos clinic and all other interested clinics and practicing physicians. Using flow cytometric analysis (FACS analysis) of blood, bronchoalveolar lavage (BAL), as well as other tissue fluids, the different immune cells and subpopulations are measured in terms of their development, proportions, and activation state.

Biomedical Data Mining Block Course: From June 5 to 23, 2023, the fourth edition of the Biomedical Data Mining block course took place. As in 2022, it was held on-site at SIAF for one week, followed by two weeks online. The responsible lecturers were PD Dr. K. Bärenfaller and PD Dr. M. Sokolowska. Applying the didactic project method, the students were given data from different RNA sequencing or proteomics projects, and and were asked to analyze these lists using R in various tasks and then contextualize the results. To equip the students with the necessary skills and background, the hands-on part was supplemented with lectures on proteomics, transcriptomics, metabolomics, immunoassays, flow cytometry, experimental design and statistical methods, functional categorization, machine learning and AI tools, and with introductions to various tools including STRING, Cytoscape, abd Genevestigator. At the end of the course, the students had to give an oral presentation and to submit a written report on their data mining task.

17th World Immune Regulation Meeting: After years of the pandemic, the 17th edition of the World Immune Regulation Meetings (WIRM) could finally be held for the second time in a row as a face-to-face meeting at the Davos Congress Centre. Around 500 scientists from over 37 countries around the world gathered from July 6-9, 2023, for the four-day congress to exchange the latest findings in immunology. Talented young researchers met experienced experts, as scientists delivered 119 presentations and presented 167 abstracts, sharing their latest insights in immunology. This global exchange of current knowledge helps develop new treatment therapies and innovative approaches for patients.

Financial basis: SIAF's expenses and financial income have changed only insignificantly compared to previous years. Basic funding of the Institute is currently ensured by the main sponsors. It consists mainly of a contribution from the federal government (Research Promotion Act Art. 15), contributions from the Canton of Graubünden and the municipality of Davos, contributions from the University of Zurich, contributions from the Swiss National Science Foundation, EU Consortium Grants CURE and Syn-Air-G and contributions from foundations, such as the PROMEDICA Foundation and the Foundation formerly Bündner Heilstätte Arosa, which support doctoral programs. The additional expenses were covered by income from additional competitively acquired third-party funds and the WIRM congress.

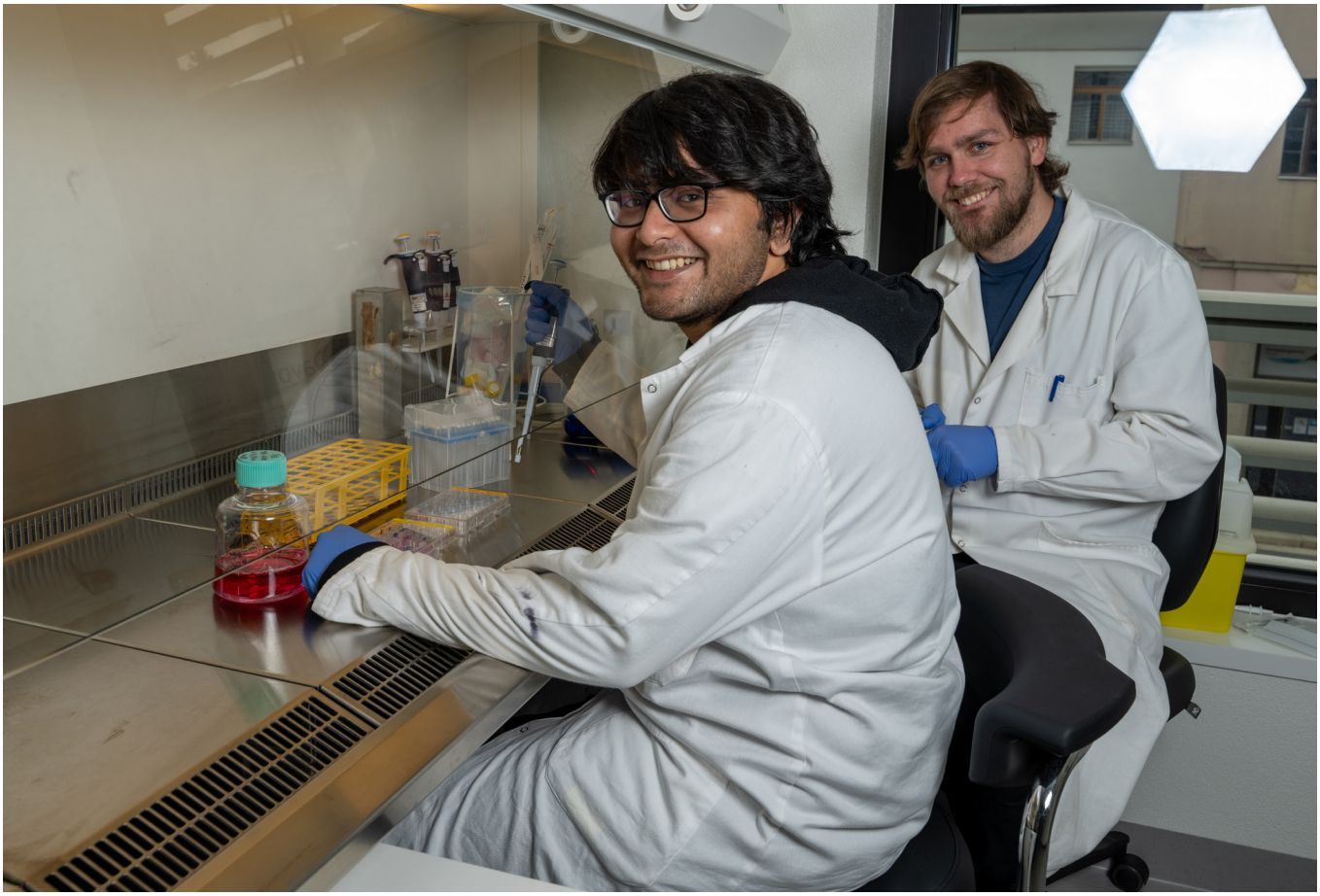
Acknowledgements: I would like to sincerely thank all employees for their great work and the good working atmosphere at SIAF. At the same time, I would like to thank the Davos clinics, their chief physicians and their staff, as well as the University of Zurich for their constant and effective support of our institute.

In particular, I would like to emphasize our fruitful collaboration with CK-CARE, which enables us to conduct patient-oriented research in atopic dermatitis. I especially thank Mrs. and Mr. Kühne for their support, which enables our research to find sustainable solutions for better diagnoses and treatments of atopic dermatitis patients.

Thanks to this support, many Master's degrees and PhD degrees have been obtained in the Institute and a huge number of international fellowships have been given, a very successful project that supported more than 60 short term international fellowships since the establishment of CK-CARE.

Above all, my thanks also go to the Swiss Research Institute for High Altitude Climate and Medicine (SFI) Foundation, its Board of Trustees and Executive Board for the support they have always provided. Likewise, I and the entire SIAF are very grateful to Dr. Walter Ammann, who stepped down from his position as SFI President at the end of 2022, for his constant and tireless support. Thank you very much to Philipp Wilhelm, the city mayor of Davos, and who was the president of our foundation during the last year for his tireless helps and support to the research institutes of Davos. My thanks and best wishes for success go to Brigitta Gadient, the new president of our foundation. Last but not least, my special thanks go to the Canton of Graubünden, the State Secretariat for Education, Research and Innovation, and all the authorities who have taken a determined interest in SIAF's research and who support the Institute in every way.

Davos, May 2024



Director

Akdis Cezmi A.	Prof., MD ***

Group Leaders

Akdis Cezmi A.	Prof., MD, Head Immunology ***
Akdis Mübeccel	Prof, MD, PhD, Head Immune Regulation *
Bärenfaller Katja	PD, PhD, Head Molecular Allergology *
Messner Christoph	Prof., PhD, Head Precision Proteomics Center ***
Rhyner Claudio	PhD, Head Vaccine Development *
Sokolowska Milena	PD, MD, PhD, Head Immune Metabolism *
van de Veen Willem	PhD, Head B Cell Immunology *

SIAF Administration

Schultz Anja, Congress Organisation/Administration */***
Zumkehr-Bert Daniela, Head of Administration/HR/Finances *

House Keeping

Stojadinovic Nenad, House keeping *
Dos Santos Fernanda, House cleaning *

Financial Administration

Wälti H., lic. oec. HSG, Wälti Treuhand AG, Bad Ragaz

Scientific Advisory Board

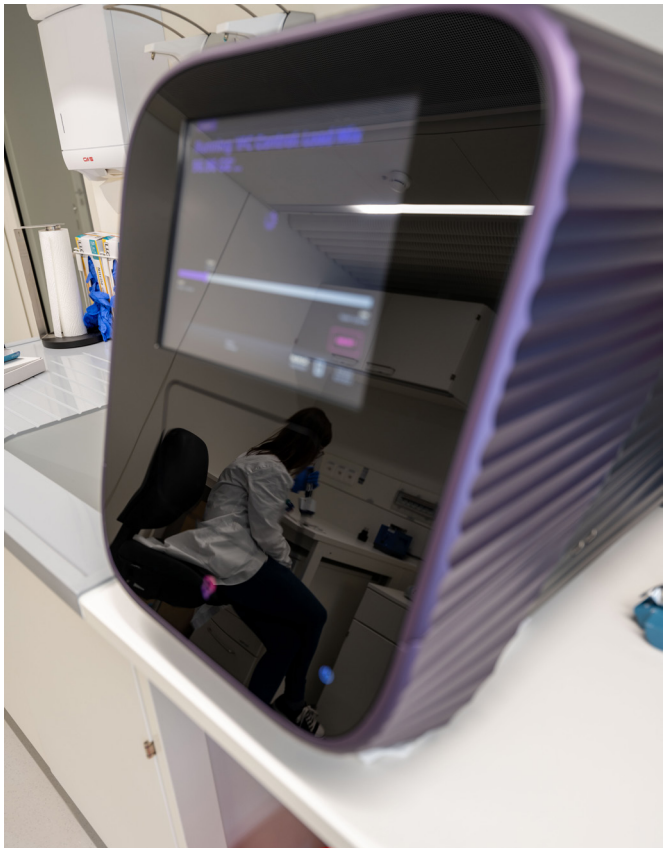
Alini M., Prof., AO Research Institute Davos
P. Wilhelm, Landammann, SFI Davos, Davos
Ferreira F., Prof. Dr., University of Salzburg
Kündig T., Prof. Dr., University Hospital Zurich (Chair SAB)
Schwarze J., Prof., University of Edinburgh
Wenger R.H., Prof. Dr., University Zurich, SFI Davos

SFI Board of Trustees

P. Wilhelm, Landammann, Davos (Präsident a.i.)
C. Appenzeller, Prof. Dr. sc. nat. ETH, Direktor, Bundesamt für Meteorologie und Klimatologie, MeteoSchweiz, Zürich
R. H. Wenger, Prof. Dr. phil. nat., Physiologisches Institut, Universität Zürich, Delegierter der Universitätsleitung der Universität Zürich, Zürich
C. A. Akdis, Prof. Dr. med., Direktor SIAF, Davos (mit beratender Stimme)
L. Harra, Prof. Dr. C. phys., Direktorin PMOD/WRC, Davos (mit beratender Stimme)
H. Wälti, lic. oec. HSG, Quästor, Bad Ragaz (mit beratender Stimme)

SFI Foundation Council

B. Allgöwer, Dr. sc. techn. ETH, Präsidentin Academia Raetica, Davos
Chr. Buol, Dr. med., Delegierter Ärzteverein Davos, Davos
H. J. Christoffel, Rechtsanwalt, Delegierter Davos Destinations-Organisation DDO, Davos
M. Dörig, Dr. iur., Rechtsanwalt, Forch
Th. Fehr, Prof. Dr. med., Chefarzt und Departementsleiter Innere Medizin, Kantonsspital Graubünden, Chur
G. Menz, PD Dr. med., a. Chefarzt und ärztlicher Direktor, HGK, Davos
B. Ottmer, dipl. Umwelt-Natw. ETH, Delegierte der Naturforschenden Gesellschaft Davos, Davos
J. Pfister, Dr., Generalsekretär SCNAT, Delegierter SCNAT, Bern
J. Ring, Prof. Dr. Dr., Direktor Klinik am Biederstein, München
J. Vontobel, Dr. med., Ärztlicher Direktor und Chefarzt Kardiologie, HGK, Davos



Scientific Staff

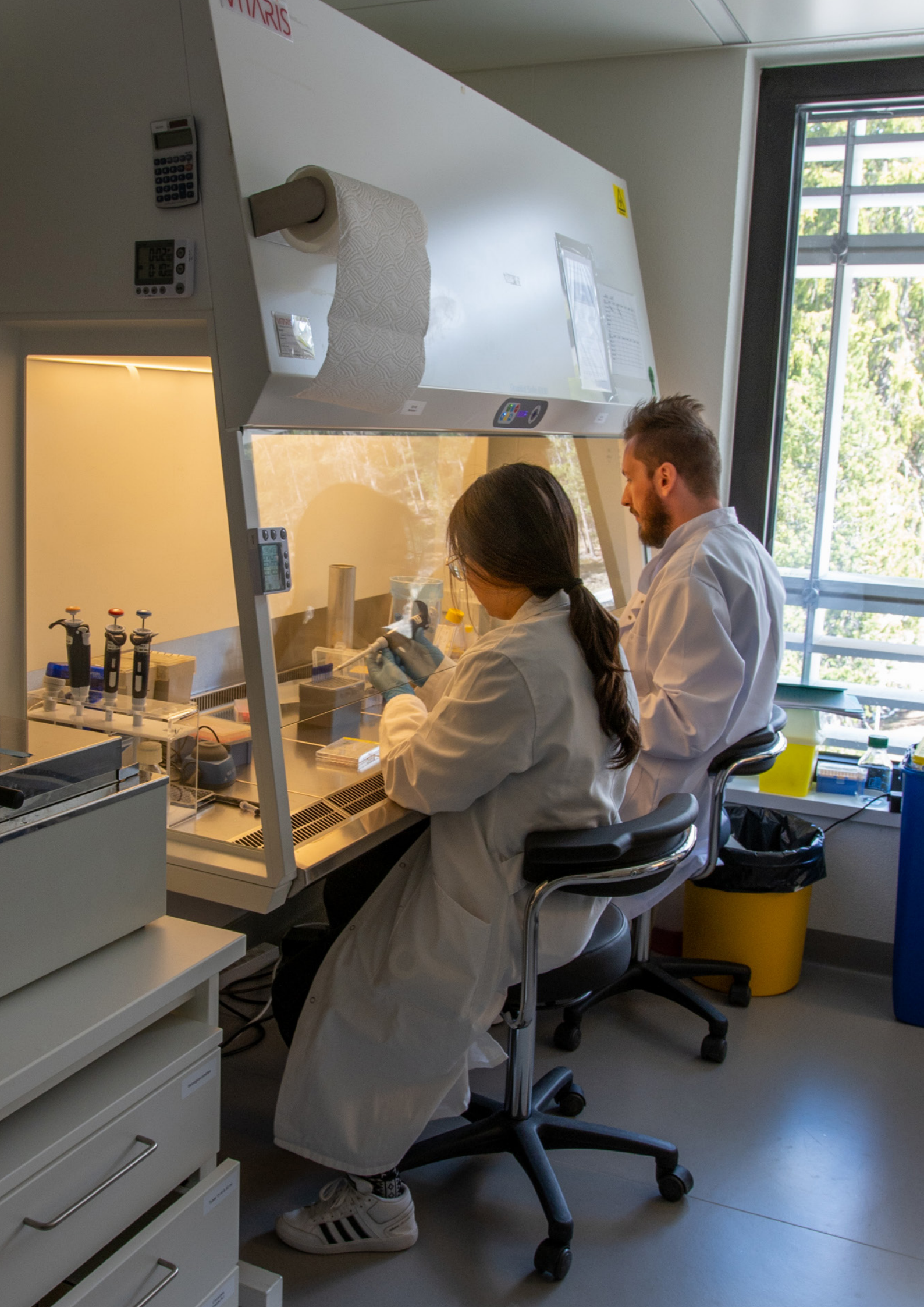
Ardicli Özge	Acad. guest, *** (ab 04/23)
Ardicli Sena	Acad. guest, *** (ab 04/23)
Babayev Huseyn	Acad. guest, MSc *** (ab 03/23)
Bu Xiangting	Acad. guest, MSc *** (bis 11/23)
Barletta Elena	PhD student ***
Bel imam Manal	PhD student ***
Beha Carina	Technician *
Bürgi Laura	Technician *
Duphey Seyram	Acad. guest, (bis 07/23)
Chatterjee Lopamudra	PhD student***
D'Avino Paolo	PhD student ***
Du Hang	PhD student ***
Fieten Karin	Post-doc, PhD ***
Garcia Sanchez Maria	Acad. guest, ***
Gessner Philipp	PhD student ***
Heider Anja	Technician *
Jardón Parages Inés	PhD student ***
Kianfar Roya	Acad. guest, MSc ***
Kim Juno	Acad. guest, MSc *** (ab 05/23)
Koch Jana	PhD student *** (bis 10/23)
Kulkarni Abhijeet	PhD student **
Li Manru	PhD student ***
Lopez Crespo Juan	PhD student**
Maurer Debbie	PhD student *** (bis 07/23)
Meinema Jenne	Acad. guest (ab 11/23)
Öztürk Mustafa	Acad. guest (ab 02-11/23)
Pat Yağız	Post-doc, MD ***
Ram Isika	Acad. guest (bis 01/23)
Radzikowska Urszula	Post-doc, PhD **
Ruggia Alessandra	Acad. guest, MSc, (ab 09/23)
Rückert Beate	Head Technician * (bis 10/23)
Satitsuksanoa Pattraporn	Post-doc, PhD ** (bis 04/23)
Schneider Stephan	PhD student **
Shi Lili	Acad. guest, MD *** (ab 06/23)
Skolnick Stephen	Acad. guest, ***
Sun Na	Acad. guest,, MD *** (bis 07/23)
Sun Xindong	PhD student***
Starrenburg Margot	Acad. guest (03-07/23)
Stocker Nino	Technician *
Wawrocki Sebastian	Post-doc, PhD ***
Westermann Patrick	Technician ***
Xiong Peng	Acad. guest (ab 06/23)
Yang Minling	PhD student ***
Yazici Duygu	Post-doc, PhD ***
Zhao Bingjie	PhD student *** (ab12/23)
Zhakparov Damir	PhD student ***
Zhu Xueyi	Acad. guest, MSc ***

Allergy Office

Alberch Gracia Laura	Managing Editor Allergy ****
Globinska Anna	Graphics Editor Allergy ****
Ögülür Rüya	Online Media Editor Allergy ****

Salary paid by

* SIAF
** Swiss National Science Foundation
*** Other
**** EAACI



Prof. Dr. Cezmi A. Akdis, MD

The epithelial barrier theory: History and Molecular Mechanisms

What is epithelial barrier theory

Exposure to harmful substances, which have become more prevalent in our daily lives due to industrialization and modernization, can disrupt the protective barriers in the skin, respiratory system, and gastrointestinal tract. This disruption can lead to imbalances in the microbial community and cause inflammation. Examples of substances that can damage these barriers include surfactants and enzymes found in cleaning products, as well as chlorine in swimming pools, microplastics, and air pollutants like ozone, particulate matter, and diesel exhaust. Our understanding of epithelial barriers stepwise developed in the last 26 years came to the proposal of an extended “epithelial barrier theory”.

The history of our discoveries on epithelial barrier theory

Our initial research into the epithelial barrier hypothesis began in 1998 when we delved into intensive skin research. During this time, we successfully created the first artificial 3D human skins and published a groundbreaking paper in the Journal of Clinical Investigation in 2000, shedding light on the nature of eczema. Eczema manifests when the skin's T cells are triggered by allergens, substances, and microbial products, migrating to the epidermis where they engage with and eliminate keratinocytes. This discovery led us to formulate the epithelial barrier theory in skin health, which we later expanded to encompass the respiratory system, sinuses, and gut.

In 2006, we authored an editorial elucidating that the epithelial barrier functions not only as a physical defense mechanism, creating a 'keep away' effect, but also plays a crucial role in immune regulation with a 'wash away' effect. When internal inflammation reaches a certain threshold, the barrier opens to expel cells outward.

By 2008, our research highlighted the immune system's role in modulating the epithelial barrier, revealing how cytokines and soluble molecules from the immune system can either open or close these barriers. This period also saw advancements in our comprehension of skin and mucosal tight junctions. Simultaneously, a pivotal discovery regarding filaggrin mutations in the stratum corneum underscored the clinical significance of maintaining epithelial barrier integrity. While tight junctions in the skin are situated beneath the stratum corneum in the stratum granulosum, they hold even greater importance in the gut, lungs, and sinuses, where they serve as the primary line of defense due to the absence of a protective stratum corneum.

In around 2013, as we delved into understanding the role of the immune response and inflammation in regulating epithelial barriers, our focus turned to investigating the impact of various environmental factors. These included air pollution, particulate matter, microplastics, detergents, household cleaners, and food emulsifiers. What surprised us were the effects we observed on skin, particularly in the context of these factors opening tight junctions and triggering the release of inflammatory factors. For instance, surfactants like sodium lauryl sulfate, commonly found in soaps and detergents, were found to alter surface tension and compromise the integrity of the epithelial barrier.

Our initial research, which centered on skin, led us to further exploration using human organoids on a chip, and now we are conducting studies with human native skin explants, employing robust skin cultures. Through this research, we have come to realize that since the 1960s, humans have been inadvertently exposed to various environmental substances. Sodium lauryl sulfate's (SLS or SDS: sodium dodecyl sulfate) introduction into household detergents and cleaners marked the beginning of this exposure, followed by the addition of enzymes like amylase, lipase, and protease to detergents. This trend continued with exposure to air pollution, food emulsifiers, and additives that compromise epithelial barriers.

The breakdown of epithelial barriers, whether short-term or long-term, depending on the dosage of the substances, disrupts the balance of beneficial bacteria in the microbiome, leading to microbial dysbiosis. Failure of skin, gut, or respiratory tissues to heal properly creates opportunities for pathogenic microorganisms to colonize. In skin conditions like eczema, the colonization of Staphylococcus aureus triggers epithelial cells and an immune response. This cascade of events results in keratinocytes signaling immune cells to the skin's surface, where high levels of cytokines are produced. Consequently, chronic changes in epithelial cells weaken the barrier, exacerbating conditions such as colitis, diabetes, obesity, asthma, rhinosinusitis, and atopic dermatitis in patients.

Development of Human Research Models

Human research was not sufficient and currently not possible because of known toxicity; animal research must be replaced to analyze the dose and molecular toxicity mechanisms of these substances. In vivo-like human models are needed to be developed. Accordingly, our epithelial group developed human in vivo-like experimental models by combining induced pluripotent stem cell (iPSC)-derived intestine organoids and organ-on-a-chips to demonstrate the activation and regulation of epithelial cells in response to environmental toxic substances. We demonstrated the molecular mechanisms of action of these substances on intestinal epithelial cells through transcriptomics, proteomics, and deletion studies using CRISPR/Cas9 and siRNA technologies. In this way, we are now able to guide strategies to reduce related diseases, control substance doses, develop less-toxic products, and explore new therapeutic approaches. More information can be found in ***www.epithelialbariertheory.com.***

Molecular Mechanisms of Epithelial Barrier Theory

Disturbed epithelial barriers: The presence of epithelial barrier disruptions in these conditions indicates that the primary defense mechanism of our body against harmful pathogens is not functioning properly. Evidence of epithelial barrier damage in most cases is typically observed through direct biopsies of affected tissues, with three main reasons identified for this disruption: I. Genetic defects and mutations in barrier proteins: Mutations in proteins like filaggrin, as well as polymorphisms in genes related to tight junctions (TJ) such as claudin and occludin, can impact the integrity of the epithelial barrier. For example, in the skin, the stratum corneum forms a robust barrier with filaggrin repeats and other molecules like loricrin, involucrin, and hornerin. II. Exposure to toxic substances in the environment (exposome): Direct exposure to elements in the exposome can disrupt epithelial barriers, affecting the microbiome and immune system. III. Inflammation in affected epithelial barriers: Conditions like asthma, atopic dermatitis, rhinitis, sinusitis, and colitis can activate epithelial cells, leading to the opening of their barriers.

Microbial dysbiosis: A healthy microbiota on the mucosal barrier's surface plays a crucial role in regulating various aspects of barrier homeostasis. However, reduced biodiversity and changes in the gut and skin microbiota composition are associated with inflammatory conditions like asthma, allergic diseases, inflammatory bowel disease, type 1 diabetes, and obesity. Dysbiosis, an imbalance in tissue microorganisms, and bacterial translocation are linked to the development and worsening of allergic and autoimmune diseases.

Immune response to commensal bacteria and opportunistic pathogens: In areas with compromised epithelial barriers, the immune system struggles to differentiate between harmful and harmless microorganisms, leading to chronic inflammation triggered by harmless microorganisms. This can reduce biodiversity and contribute to allergic and autoimmune disease development. For instance, the immune response to opportunistic pathogen S. aureus is prevalent in conditions like atopic dermatitis, chronic rhinosinusitis, and asthma, with a high correlation between disease severity and IgE antibodies.

Peri-epithelial inflammation, epithelitis, and expulsion response: Individuals with leaky epithelial barriers may experience local inflammation in their epithelial cells, known as "epithelitis," which attracts proinflammatory cells to the damaged area. This prompts the immune system to expel tissue-invading commensals and opportunistic pathogens through an “expulsion response”, similar to a defense mechanism against helminth parasites in the gastrointestinal system or scabies in the skin.

Migration of inflammatory cells to distant organs: Immune cells activated at sites with compromised barriers can migrate to distant organs, causing inflammation. Additionally, increased inflammatory mediators in the circulation, referred to as "circulating microinflammation," can be detected. Inflammatory cell migration from leaky barrier areas to diseased tissues is evident, such as Cutaneous lymphocyte antigen-expressing T cells getting activated in the gut after exposure to food allergens and then migrating to the skin to exacerbate atopic dermatitis. This mechanism may contribute to the progression of allergic diseases like atopic dermatitis, food allergy, asthma, and allergic rhinitis during childhood, known as the atopic march.

Epigenetic regulation and chronicity: An impaired ability to restore the epithelial barrier function due to inflammation and epigenetic changes instigates a vicious cycle of leaky barriers, microbial dysbiosis and chronic inflammation.

Diseases of the Epithelial Barrier Theory: Diseases linked to “Epithelial Barrier Theory” exhibit common characteristics such as an increasing prevalence since the 1960s or 2000s, independent of changes in diagnostic methods, and involve molecular mechanisms like epithelial barrier dysfunction, epithelitis, microbial imbalance with a decrease in beneficial microbes and an increase in harmful pathogens, as well as systemic microinflammation. Furthermore, there has been an observed emergence of various seemingly unrelated diseases, namely comorbidities/multimorbidities that meet these criteria in the recent years. More than 100 diseases have been identified exploring their epidemiological patterns and providing insight into the evidence supporting epithelial barrier disruption, microbial imbalance, and circulating microinflammation.

A series of conditions like atopic dermatitis, psoriasis, asthma, allergic rhinitis, eosinophilic esophagitis, food allergy, irritable bowel syndrome, ocular allergy, and dry eye are activated by disruptions in the protective tissue barriers in the affected organs, ongoing inflammation, and imbalances in the body's microbial community. These issues typically affect specific organs or tissues such as the skin, respiratory system, digestive system, and eyes.

On the other hand, a different set of diseases, predominantly autoimmune, autoinflammatory, metabolic, in nature, are linked to problems in the intestinal barrier and microbial imbalances. These conditions are often triggered through connections like the gut-thyroid axis, gut-joint axis, gut-liver axis, or gut-brain axis. Examples of such diseases include Hashimoto’s thyroiditis, Graves’ disease, osteoarthritis, obesity, diabetes, rheumatoid arthritis, fatty liver, multiple sclerosis, chronic hepatitis and cirrhosis. In addition, neuropsychiatric diseases, such as autism, Parkinson’s disease, Alzheimer’s disease, chronic depression are compelling to be listed here as they show microbial dysbiosis and gut barrier defects in biopsies and increased prevalence in the last decades.

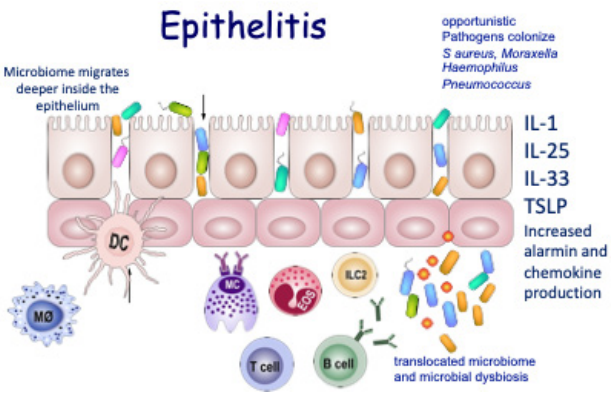


Figure 1. What is Epithelitis? *Epithelitis is a term used to describe inflammation that specifically affects epithelial cells. When these epithelial cells become inflamed, it can indicate an immune response to tissue damage, infection, or other underlying conditions. Upon exposure to environmental toxic substances, allergens and translocated bacteria, epithelial cells release alarmins, such as IL-1, IL-25, IL-33 and TSLP and various chemokines that activate and invite/attract the immune system cells to the affected tissue. In the context of medical conditions involving epithelial barriers, such as the skin, gut, or respiratory tract, epithelitis may be a key feature of the immune response to disruptions in the epithelial barrier. Following disruption of epithelial barriers, microbiome migrates deeper in the tissues and opportunistic pathogens start to colonize. This inflammation can attract immune cells to the damaged area and trigger a cascade of immune responses to help repair the barrier and fight off potential threats by the translocated microbiome and toxic substances.*

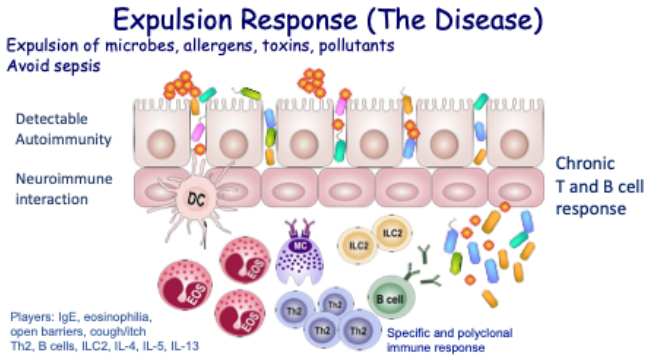


Figure 2. Characteristics of the Expulsion Response. *An immune response develops towards, allergens, autoantigens, commensal bacteria and opportunistic pathogens in the affected organ, such as the skin or the lining of the gut or respiratory tract and systemic inflammation takes place. The term "expulsion response" typically refers to a mechanism by which the body reacts to protect itself against potential threats or harmful substances by expelling them from the epithelial barriers. For example, in the gastrointestinal tract, the expulsion response may involve mechanisms like vomiting or diarrhea to quickly remove harmful pathogens or toxins that have been ingested. In the respiratory tract, expulsion responses like coughing or sneezing help to expel irritant toxic substances or pathogens from the airways. These expulsion responses are important for maintaining the integrity of the epithelial barriers and protecting the body from infections and other threats. They are part of the body's innate defence mechanisms and play a crucial role in maintaining homeostasis and overall healing. In allergic diseases, the type 2 immune response with the involvement of Th2 cells, type 2 innate lymphoid cells, M2 macrophages, eosinophils, IL-4, IL-5, IL-13 and IgE response.*

Studies on Electric Impedance Spectroscopy & Epithelial Barrier Theory

Household laundry detergents disrupt barrier integrity and induce inflammation in mouse and human skin

Rinaldi AO, Li M, Barletta E, D'Avino P, Yazici D, Pat Y, Ward S, Burla D, Tan G, Askary N, Larsson R, Bost J, Babayev H, Dhir R, Gaudenzio N, Akdis M, Nadeau K, Akdis CA, Mitamura Y. Allergy. 2024 Jan;79(1):128-141.

To demonstrate the effect of laundry detergents on human skin, back skin of C57BL/6 mice was treated with two household laundry detergents at several dilutions. Barrier function was assessed by electric impedance spectroscopy (EIS) and transepidermal water loss (TEWL) measurements after the 4 h of treatments with detergents. RNA sequencing (RNA-seq) and targeted multiplex proteomics analyses in skin biopsy samples were performed. The 6-h treatment effect of laundry detergent and sodium dodecyl sulfate (SDS) was investigated on ex vivo human skin. Detergent-treated skin showed a significant EIS reduction and TEWL increase compared to untreated skin, with a relatively higher sensitivity and dose-response in EIS. The RNA-seq showed the reduction of the expression of several genes essential for skin barrier integrity, such as tight junctions and adherens junction proteins. In contrast, keratinization, lipid metabolic processes, and epidermal cell differentiation were upregulated. Proteomics analysis showed that the detergents treatment generally downregulated cell adhesion-related proteins, such as epithelial cell adhesion molecule and contactin-1, and upregulated proinflammatory proteins, such as interleukin 6 and interleukin 1 beta. Both detergent and SDS led to a significant decrease in EIS values in the ex vivo human skin model. This study demonstrated that laundry detergents and its main component, SDS impaired the epidermal barrier in vivo and ex vivo human skin. Daily detergent exposure may cause skin barrier disruption and may contribute to the development of atopic diseases.

Electrical impedance spectroscopy detects skin barrier dysfunction in childhood atopic dermatitis

Sasaki M, Sundberg M, Frei R, Ferstl R, Heye KN, Willems EP, Akdis CA, Lauener R; CK-CARE Study Group; Roduit C. Allergy. 2024 Jan;79(1):142-152.

Laundry detergents and surfactants-induced eosinophilic airway inflammation by increasing IL-33 expression and activating ILC2s.

Saito K, Orimo K, Kubo T, Tamari M, Yamada A, Motomura K, Sugiyama H, Matsuoka R, Nagano N, Hayashi Y, Arae K, Hara M, Ikutani M, Fukuie T, Sudo K, Matsuda A, Ohya Y, Fujieda S, Saito H, Nakae S, Matsumoto K, Akdis CA, Morita H. Allergy. 2023 Jul;78(7):1878-1892.

Epidemiological studies demonstrated that exposure to detergents and frequent use of cleaning products are risk factors for asthma. Laundry detergents have been reported to have epithelial barrier-opening effects. Whether laundry detergents directly induce airway inflammation and its mechanisms in vivo are focused in this study. Two commercial laundry detergents and two commonly used surfactants for cleaning and cosmetics (sodium lauryl sulfate and sodium dodecyl benzene sulfonate) were intranasally administered to mice. Lungs were analyzed using flow cytometry, histology, ELISA, and quantitative PCR. Human bronchial epithelial cells were stimulated with laundry detergents and analyzed using quantitative PCR and western blotting. Involvement of oxidative stress was assessed using an antioxidant. Dust samples from homes were analyzed to determine their detergent content by measuring their critical micelle concentration (CMC). The administered laundry detergents and surfactants-induced eosinophilic airway inflammation accompanied by increased IL-33 expression and activation of group 2 innate lymphoid cells (ILC2s). Detergent-induced eosinophilic airway inflammation was significantly attenuated in Rag2-/- Il2rg-/- , Il33-/- mice, and also in wild-type mice treated with antioxidant N-acetyl cysteine. Detergent-induced IL-33 expression in airways was attenuated by NAC treatment, both in vivo and in vitro. CMCs were found in all of the tested dust extracts, and they differed significantly

among the homes. In conclusion, the laundry detergents and surfactants-induced eosinophilic airway inflammation in vivo through epithelial cell and ILC2 activation. They induced IL-33 expression in airway epithelial cells through oxidative stress. Furthermore, detergent residues were present in house dust and are presumably inhaled into the airway in daily life.

Disrupted epithelial permeability as a predictor of severe COVID-19 development

Yazici D, Cagan E, Tan G, Li M, Do E, Kucukkase OC, Simsek A, Kizmaz MA, Bozkurt T, Aydin T, Heider A, Rückert B, Brüggen MC, Dhir R, O'Mahony L, Akdis M, Nadeau KC, Budak F, Akdis CA, Ogulur I. Allergy. 2023 Oct;78(10):2644-2658.

We assessed the potential of biomarkers of epithelial barrier dysfunction as predictive of severe COVID-19. Levels of bacterial DNA and zonulin family peptides (ZFP) as markers of bacterial translocation and intestinal permeability and a total of 180 immune and inflammatory proteins were analyzed from the sera of 328 COVID-19 patients and 49 healthy controls. Significantly high levels of circulating bacterial DNA were detected in severe COVID-19 cases. In mild COVID-19 cases, serum bacterial DNA levels were significantly lower than in healthy controls suggesting epithelial barrier tightness as a predictor of a mild disease course. COVID-19 patients were characterized by significantly elevated levels of circulating ZFP. We identified 36 proteins as potential early biomarkers of COVID-19, and six of them (AREG, AXIN1, CLEC4C, CXCL10, CXCL11, and TRANCE) correlated strongly with bacterial translocation and can be used to predict and discriminate severe cases from healthy controls and mild cases (area under the curve (AUC): 1 and 0.88, respectively). Proteomic analysis of the serum of 21 patients with moderate disease at admission which progressed to severe disease revealed 10 proteins associated with disease progression and mortality (AUC: 0.88), including CLEC7A, EIF4EBP1, TRANCE, CXCL10, HGF, KRT19, LAMP3, CKAP4, CXADR, and ITGB6. In conclusion, our results demonstrate that biomarkers of intact or defective epithelial barriers are associated with disease severity and can provide early information on the prediction at the time of hospital admission.

A Major Change in the Nomenclature of Allergic Diseases

Nomenclature of allergic diseases and hypersensitivity reactions: Adapted to modern needs: An EAACI position paper.

Jutel M, Agache I, Zemelka-Wiacek M, Akdis M, Chivato T, Del Giacco S, Gajdanowicz P, Gracia IE, Klimek L, Lauerma A, Ollert M, O'Mahony L, Schwarze J, Shamji MH, Skypala I, Palomares O, Pfaar O, Torres MJ, Bernstein JA, Cruz AA, Durham SR, Galli SJ, Gómez RM, Guttman-Yassky E, Haahtela T, Holgate ST, Izuhara K, Kabashima K, Larenas-Linnemann DE, von Mutius E, Nadeau KC, Pawankar R, Platts-Mills TAE, Sicherer SH, Park HS, Vieths S, Wong G, Zhang L, Bilò MB, Akdis CA. Allergy. 2023 Nov;78(11):2851-2874.

The exponential growth of precision diagnostic tools, including omic technologies, molecular diagnostics, sophisticated genetic and epigenetic editing, imaging and nano-technologies and patient access to extensive health care, has resulted in vast amounts of unbiased data enabling in-depth disease characterization. New disease endotypes have been identified for various allergic diseases and triggered the gradual transition from a disease description focused on symptoms to identifying biomarkers and intricate pathogenetic and metabolic pathways. Consequently, the current disease taxonomy has to be revised for better categorization. This European Academy of Allergy and Clinical Immunology Position Paper responds to this challenge and provides a modern nomenclature for allergic diseases, which respects the earlier classifications back to the early 20th century. Hypersensitivity reactions originally described by Gell and Coombs have been extended into nine different types comprising antibody- (I-III), cell-mediated (IVa-c), tissue-driven mechanisms (V-VI) and direct response to chemicals (VII). Types I-III are linked to classical and newly described clinical conditions. Type IVa-c are specified and detailed according to the current understanding of T1, T2 and T3 responses. Types V-VI involve epithelial barrier defects and metabolic-induced immune dysregulation, while direct cellular and inflammatory responses to chemicals are covered in type VII. It is notable that several combinations of mixed types may appear in the clinical setting. The clinical relevance of the current approach for allergy practice will be conferred in another article that will follow this year, aiming at showing the relevance in clinical practice where various endotypes can overlap and evolve over the lifetime.

Spatial transcriptomics combined with single-cell RNA-sequencing unravels the complex inflammatory cell network in atopic dermatitis

Mitamura Y, Reiger M, Kim J, Xiao Y, Zhakparov D, Tan G, Rückert B, Rinaldi AO, Baerenfaller K, Akdis M, Brüggen MC, Nadeau KC, Brunner PM, Roqueiro D, Traidl-Hoffmann C, Akdis CA. Allergy. 2023 Aug;78(8):2215-2231.

Skin tissues examined for spatial gene expression were derived from the upper arm of 6 healthy control (HC) donors and 7 AD patients (lesion and nonlesion). We performed spatial transcriptomics sequencing to characterize the cellular infiltrate in lesional skin. For single-cell analysis, we analyzed the single-cell data from suction blister material from AD lesions and HC skin at the antecubital fossa skin (4 ADs and 5 HCs) and full-thickness skin biopsies (4 ADs and 2 HCs). The multiple proximity extension assays were performed in the serum samples from 36 AD patients and 28 HCs. The single-cell analysis identified unique clusters of fibroblasts, dendritic cells, and macrophages in the lesional AD skin. Spatial transcriptomics analysis showed the upregulation of COL6A5, COL4A1, TNC, and CCL19 in COL18A1-expressing fibroblasts in the leukocyte-infiltrated areas in AD skin. CCR7-expressing dendritic cells (DCs) showed a similar distribution in the lesions. Additionally, M2 macrophages expressed CCL13 and CCL18 in this area. Ligand-receptor interaction analysis of the spatial transcriptome identified neighboring infiltration and interaction between activated COL18A1-expressing fibroblasts, CCL13- and CCL18-expressing M2 macrophages, CCR7- and LAMP3-expressing DCs, and T cells. As observed in skin lesions, serum levels of TNC and CCL18 were significantly elevated in AD, and correlated with clinical disease severity. In this study, we show the unknown cellular crosstalk in leukocyte-infiltrated area in lesional skin. Our findings provide a comprehensive in-depth knowledge of the nature of AD skin lesions to guide the development of better treatments.

Davos, May 2024

Prof. Dr. Mübeccel Akdis, MD, PhD

Role of Allergen-specific B cell during the establishment of immune tolerance

The prevalence of food allergy has been increasing in recent decades and it currently affects an estimated 10% of the global population. Despites that cow's milk allergy (CMA) is common in infants and children, it shows a high rate of spontaneous resolution from early childhood until adolescence. CMA can result in anaphylactic reactions, therefore, clinicians recommend avoidance of all cow's milk products in daily life as the standard procedure. However, recently as an alternative, oral allergen-specific immunotherapy (OIT) has shown to be an effective treatment, inducing clinical and immunologic tolerance to milk allergens in allergic patients. OIT can induce desensitization, which is defined as an increased allergic reaction threshold while undergoing therapy. Some patients show clinical remission, a state of non-responsiveness after discontinuation of immunotherapy. During the past years, the term remission has been used to better describe this non-responsive state after completion of immunotherapy. Understanding immune tolerance mechanisms to food allergens is crucial for further improving existing treatments and for the discovery of novel strategies to prevent and treat food allergies.

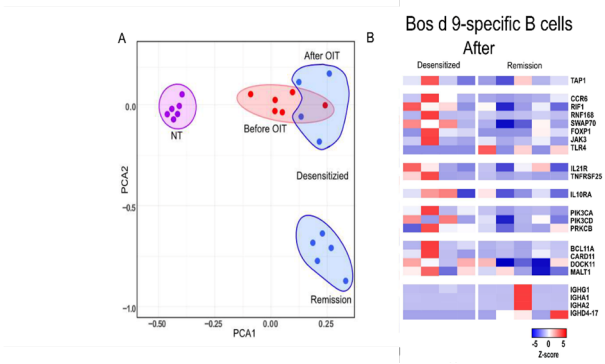


Figure 1. DGEs signatures in Bos d 9-specific B cells from after OIT (desensitized vs remission).
(A) PCA plot of 200 DGEs separating allergic groups: before OIT vs after OIT (desensitized and remission) vs NT groups. (B) Heatmap of the most significant DEGs of Bos d 9-specific B cells after OIT; desensitized VS remission, nbefore OIT=6 and nNT= 6

There are two major mechanisms by which allergic reactions to cow's milk and other food allergens can proceed, namely immunoglobulin E (IgE)-mediated and non-IgE-mediated. The development of IgE-mediated CMA is regulated by B cells through the production of allergen-specific IgE antibodies. Mechanisms driving B cell responses during allergy and the development of tolerance are not fully understood. Hence, there is a current need to further understanding of the B cell responses in food-allergic patients during OIT (Figure 1) and in individuals who outgrow food allergy (Figure 2) due to natural immune tolerance to clarify mechanisms of induction and maintenance of food allergen tolerance or remission.

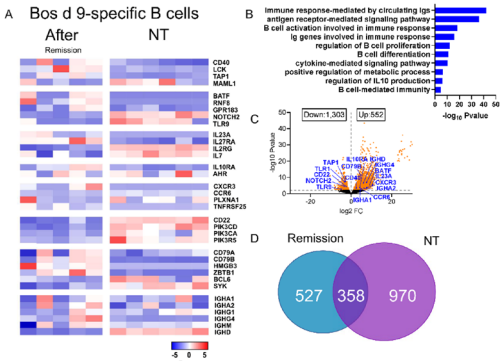


Figure 2. DGEs signatures in Bos d 9-specific B cells from after OIT (remission) vs NT.
(A) Heatmap of the top significant DEGs of Bos d 9-specific B cells from after OIT (remission) vs NT, nafter OIT (remission)=5, nNT OIT=6, (B) Top B cell-related pathways analysis (C) Volcano plot shows differentially expressed genes with top 20 significant genes (p-value <0.05). (D) Venn-diagram of differentially expressed genes from remission vs NT groups (p-value <0.05).

Natural outgrowth of food allergies represents a valuable model for studying mechanisms of immune tolerance to food allergens. So far, there are limited well-designed studies regarding the natural development of tolerance to food allergens. Reported rates of resolution (natural outgrowth) vary widely, likely attributable to methodological differences and study populations. Some food allergens are difficult to avoid and fortunately have a high tendency of natural outgrowth, such as cow's milk and egg allergens. Safely introducing cow's milk and eggs in a child's diet has important nutritional and quality-of-life benefits. It was demonstrated that tolerant children, who outgrew their allergy developed higher frequencies of circulating CD4+CD25+ Treg cells and decreased in vitro proliferative responses to bovine beta-lactoglobulin compared to children, who maintained clinically active allergy. Other food allergen sources, particularly peanuts and tree nuts, exhibit a much lower spontaneous resolution rate and therefore require an efficient OIT approach.

Molecular mechanisms of spontaneous outgrowth of food allergies have not been studied in detail and to the best of our knowledge there are no reports on the role of allergen-specific B cells in natural tolerance. Hoh et al. investigated B cell responses in peanut allergy and demonstrated that local class-switch recombination (CSR) to IgE in the gut directly has a major impact on the development of food allergen-specific IgE antibodies. Circulating IgE+ B cells mostly display an immature plasmablast phenotype. Increased numbers of circulating IgE+ memory B cells and IgE+ plasmablasts

are correlated with the presence of food allergy and may contribute to pathogenesis. To address these questions, we have performed an in-depth characterization of B cells specific for Bos d 9 (Bos taurus Domestic 9 or αS1-casein), the major allergen in cow's milk, to analyse antigen-specific B cell changes related to the development of remission to cow's milk allergy. We identified an increased frequency of allergen-specific B cells in OIT induced-remission to cow's milk and natural outgrowth-related immune tolerant individuals. Gene expression signatures associated with allergen-specific B cells were mostly downregulated after OIT. After OIT, desensitization and induced remission clustered separately showing distinct characteristic genes (Figure 1 A-B). Allergen-specific B cells decreased their expression of 1456 genes involved in B cell activation and inflammation. Notably, secreted protein profiles of specific B cells were similar after OIT and NT, suggesting common but not identical mechanisms of food allergen tolerance (Figure 2 A-D).

Role of ILC during the ascaris infection

Ascaris lumbricoides infection is one of the most prevalent and neglected tropical parasitosis worldwide (global prevalence around 11.9%). In addition, several studies have shown that sensitization to its components is associated with indicators of poorly hygienic conditions and asthma risk.

Similar to allergy, helminth infection induces a strong type-2 (T2) response that is orchestrated by alarmins, cytokines, and cells from innate and adaptive systems.

Innate lymphoid cells (ILCs) are mainly tissue-resident lymphocytes that do not express antigen recognition receptors. They are known to produce cytokines essential for the maintenance of tissue homeostasis and the communication between innate and adaptive immune system. However, several clinical studies have associated circulating-ILCs in the bloodstream with different phenotypes, stages or even therapy of immunological disorders. Recent studies have elucidated the importance of ILCs and alarmins (ex. IL-25, IL-33) in the promotion of type 2 immunity and inflammation following helminth exposure or allergen challenge. ILC2 were discovered in a mouse models of helminth infection and have been reported as an evolutionary mechanism of the response to helminths, which are essential for Th2-differentiation and worm-expulsion due to their role in the production of IL-4 and IL-13, respectively. Observations in human studies of helminth infection demonstrate that ILC frequencies fluctuate according to the infection status, its associated with antibody response and are affected by anti-helminth treatment, in its frequency due to infection and restored post-treatment (Figure 3). However, all these findings are heterogeneous due to it has been reported in different helminth species.

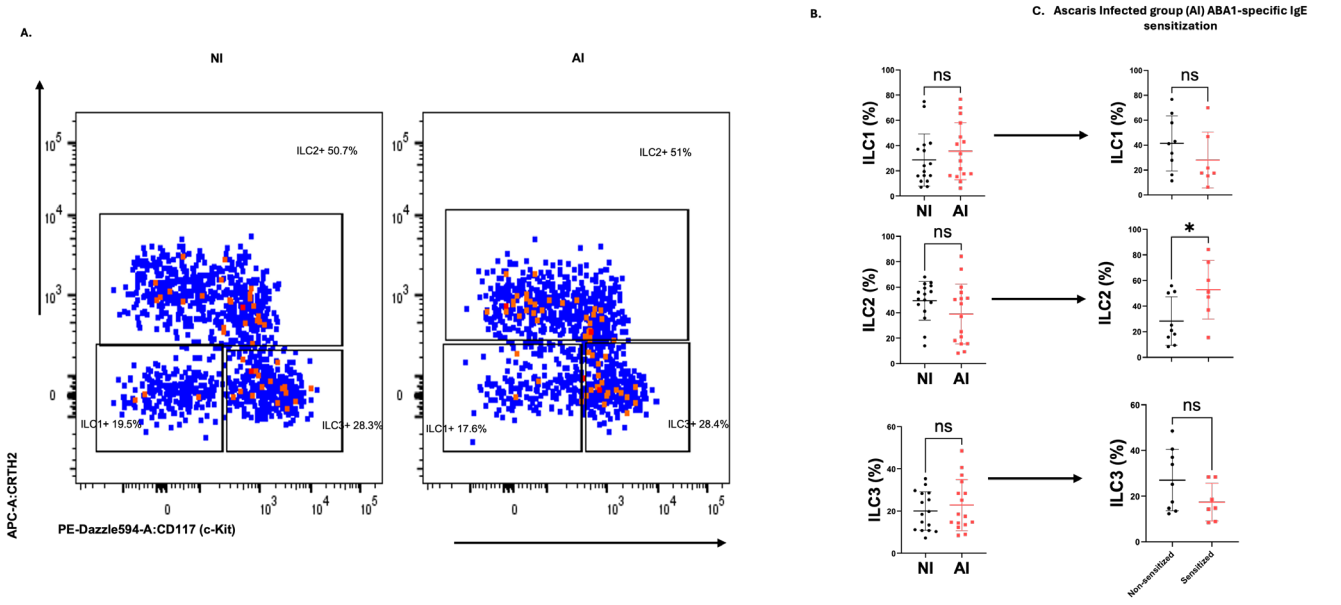


Figure 3. Higher ILC2 frequency is associated to anti-ABA-1 IgE sensitization status. (A) Representative plot of ILC subsets according to infection status. (B) ABA-1 IgE sensitization is associated to higher ILC2 frequency in AI group. Comparisons were made using unpaired T-test

Due to the strong promoting effect of Ascaris on type 2 responses, it is hypothesized that this infection may induce ILC2 development and activation (global lymphoid cell activation represented by markers like CD69 and CD25, or specific type 2 activation through TSLP receptor) (Figure 4), as observed with other helminth species. However, as the genus Ascaris does not complete its life cycle in the mouse, there is no evidence that this parasite may induce changes in ILCs. Understanding how helminths shape the immune system provides the opportunity to gain insight into natural type 2 responses and how it might be regulated. Additionally, exploration of helminth targets in the immune system may help to elucidate the mechanisms by which potential vaccine candidates do not provide sustained immunity. Hence, in this study we aimed to investigate and characterize specifically the influence of helminth infection by Ascaris lumbricoides on circulating ILCs from subjects endemically exposed.

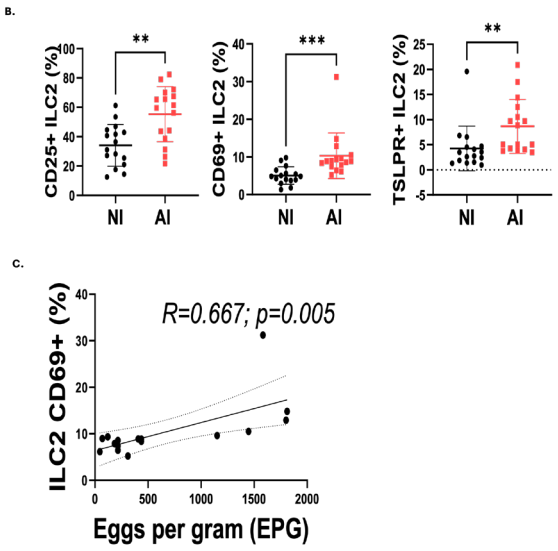


Figure 4. Activated-ILC2 numbers are associated to Ascaris infection and correlate with egg burden. (B) Frequencies of different activation markers in ILC2s according to Ascaris infection status (C) Correlation plot between CD69+ILC2 and egg burden. Comparisons were made using Mann–Whitney test and correlation analysis correspond to Spearman coefficient (Rho).

Distinct and mutually exclusive Ca++ flux- and adenyl cyclase-inducing gene expression profiles of G-Protein-Coupled Receptors on human antigen-specific B cells

(Iris Chang, Abhinav Kaushik et al. Allergy 2023 Nov;78(11):3016-3019. doi: 10.1111/all.15858.)

B cells play an essential role in allergies by producing allergen-specific IgE, which is a prerequisite for allergen-induced degranulation of mast cells (MCs) and basophils. MCs, basophils, dendritic cells and bacteria are capable of releasing inflammatory mediators including histamine. Histamine is a bioactive amine that exerts its function through binding to histamine receptors (HRs), which are 7-transmembrane G-protein-coupled receptors (GPCRs). There are four types of HRs (HR1-4), wherein HR1 ligation triggers Ca2+ mobilization, HR2 stimulates and increases cAMP concentrations, and HR3 and HR4 inhibit cAMP accumulation. We hypothesized that the expression profile of HRs (HR1+ vs HR2+ B cell clones) is associated with significant changes in the expression profile of other GPCRs that govern the downstream cascade of pathways associated with cAMP signaling or Ca2+ mobilization.

B cells: The many facets of B cells in allergic diseases

(Satitsuksanoa P, Iwasaki S, Boersma J, Imam MB, Schneider SR, Chang I, van de Veen W, Akdis M. J Allergy Clin Immunol. 2023 Sep;152(3):567-581. doi: 10.1016/j.jaci.2023.05.011.)

B cells play a key role in our immune system through their ability to produce antibodies, suppress a proinflammatory state, and contribute to central immune tolerance. We aim to provide an in-depth knowledge of the molecular biology of B cells, including their origin, developmental process, types and subsets, and functions. In allergic diseases, B cells are well known to induce and maintain immune tolerance through the production of suppressor cytokines such as IL-10. Similarly, B cells protect against viral infections such as severe acute respiratory syndrome coronavirus 2 that caused the recent coronavirus disease 2019 pandemic. Considering the unique and multifaceted functions of B cells, we hereby provide a comprehensive overview of the current knowledge of B-cell biology and its clinical applications in allergic diseases, organ transplantation, and cancer.

Mechanisms of allergen-specific B cell in cow's milk-oral immunotherapy induced desensitization, remission, and natural outgrowth

(Pattraporn Satitsuksanoa et al. Submitted)

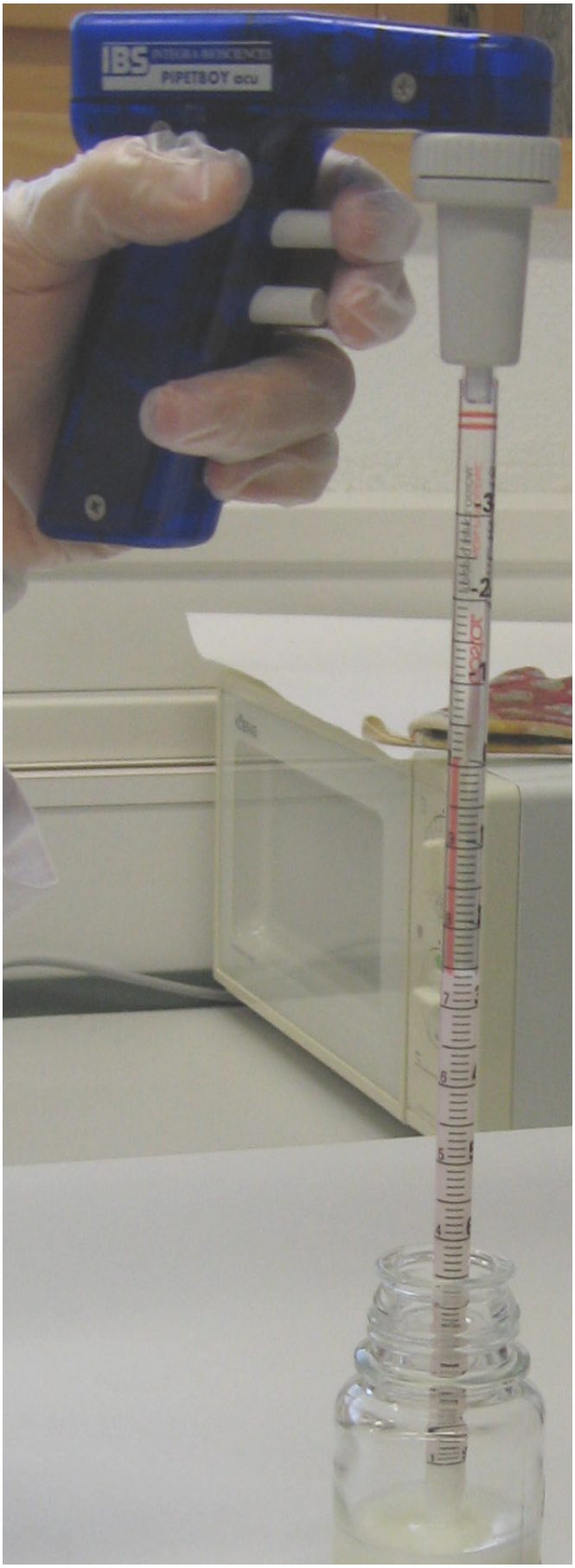
Antigen-specific memory B cells play a key role in the induction of desensitization and remission to food allergens in oral immunotherapy and in the development of natural tolerance (NT). Here, we characterized the role of milk allergen αS1-casein-specific B cells in desensitization and remission induced by oral allergen-specific immunotherapy (OIT) and in children spontaneously outgrowing cow's milk allergy due to natural tolerance. Increased frequency of circulating milk allergen αS1-casein -specific B cells was observed after OIT and NT. Milk desensitized subjects showed partial acquisition of phenotypic features of remission, suggesting that desensitization is an earlier stage of remission. Within these most significantly expressed genes, IL10RA and TGFB3 were highly expressed in desensitized OIT patients. In both the remission and desensitized groups, B cell activation-, Breg cells-, BCR signaling and differentiation-related genes are activated. In NT, pathways associated with innate immunity characteristics, development of marginal zone B cells and a more established suppressor function of B cells prevail that may play a role in long-term tolerance. The analyses of immunoglobulin heavy chain genes in specific B cells demonstrated that IgG2 in desensitization, IgG1, IgA1, IgA2, IgG4 and IgD in remission, and IgD in NT were predominating. Secreted proteins from allergen-specific B cells revealed higher levels of regulatory cytokines, IL-10 and TGF-β after OIT and NT. Taken together, allergen-specific B cells are essential elements in regulating food allergy towards remission in OIT-received and naturally resolved individuals.

Active human ascariasis increases frequencies of circulating activated type-2 peripheral blood innate lymphoid cells and tryptase AB1 levels.

(Juan-Felipe Lopez, Josefina Zakzuk, Pattraporn Satitsuksanoa, Ana Lozano, Laura Buergi, Anja Heider, Juan Alvarado2, Huseyn Babayev, Cezmi Akdis, Willem van de Veen, Luis Caraballo, Mübeccel Akdis, under submission)

Ascaris lumbricoides infection is one of the most common soil-transmitted helminthiases. IgE response to this helminth may increase the risk of asthma, bronchial hyperreactivity, and atopy. There is evidence showing the role of type-2 innate lymphoid cells (ILC2) in the pathogenesis of helminth infection and allergy. However, research on human Ascaris infection is scarce. The aim of the study to investigate and characterize the influence of helminth infection by Ascaris lumbricoides on circulating ILCs from subjects endemically exposed. Non-infected (NI; n=16) and Ascaris-infected (AI; n=16) subjects from an endemic area were included. Two consecutive stool samples from each subject were examined by Kato-Katz to define parasite infection. Antibodies to ABA-1 (an antigen from Ascaris) and Ascaris extract were measured by ELISA. Frozen PBMCs were received and ILCs, together with activation markers (CD25, CD69, thymic stromal lymphopoietin receptor (TSLPR) and NKp44), were evaluated by flow cytometry. Proximity extension assay (PEA) was performed to explore proteins associated with the infection. No significant differences in the relative frequency of total ILCs, ILC1, ILC2 and ILC3 were observed regarding to infection status. However, within AI group, ABA-1-IgE-sensitized subjects had higher frequencies of ILC2 ($p<0.05$). Frequencies of activated ILC2 (CD25+, CD69+, and TSLPR+) were higher in AI compared to the NI ($p<0.01$). Additionally, egg burden was positively correlated with CD69+ ILC2 frequencies ($r=0.67$; $p=0.005$). Tryptase alpha/beta 1 (TPSAB1), and several proteins associated with granulocyte chemotaxis were highly expressed in the AI group ($p<0.05$). Interestingly, TPSAB1 levels were positively correlated with activated-ILC2 frequencies and IgE levels against Ascaris extract. Ascaris infection is associated with increased activation of ILC2 and TPSAB1 and these factors could contribute to its type-2 response boosting effect.

Davos, May 2024



Prof. Dr. Christoph Messner, PhD

Background

Proteins are the functional building blocks of life, and their levels are defined by both genetic and environmental factors. The precise regulation of proteins is fundamental in all biological processes and alterations of the proteome are associated with diseases. Thus, studying proteins and its association with the phenotype is key for cell biology, understanding disease mechanisms, and ultimately improving patient care.

At the Precision Proteomics Center, we develop mass spectrometry-based proteomics workflows with a specific focus on enhancing their robustness and efficiency for clinical applications. In addition to measuring protein abundances, we focus on developing workflows that utilize peptide-level information and analyze post-translational modifications, particularly glycosylations. We apply these technologies in biomarker discovery studies of large cohorts, as well as in functional studies in various disease areas, with a particular focus on allergies, skin diseases, and oncology.

Improving lymphoma diagnostics and treatment through large-scale proteomcis

As part of a project funded by LOOP Zurich, we are establihing a platform that integrates lymphoma proteomes into a biomedical informatics platform. We are currently measuring the proteomes of more than 2,500 tissue and liquid biopsy samples from the biobank at the University Hospital Zurich, encompassing a broad range of diagnoses and subtypes. With this, we are creating the largest and most comprehensive proteomics dataset of lymphoma to date, with the goal of improving the diagnosis and treatment of lymphoma patients. Ultimately, we aim to incorporate this pipeline into the diagnostic routine at the University Hospital Zurich.

Mass spectrometry-based high-throughput proteomics and its role in biomedical studies and systems biology

Messner CB, Demichev V, Wang Z, Hartl J, Kustatscher G, Mülleder M, Ralser M. Proteomics. 2023 Apr;23(7-8):2200013.

There are multiple reasons why the next generation of biological and medical studies require increasing numbers of samples. Biological systems are dynamic, and the effect of a perturbation depends on the genetic background and environment. As a consequence, many conditions need to be considered to reach generalizable conclusions. Moreover, human population and clinical studies only reach sufficient statistical power if conducted at scale and with precise measurement methods. Finally, many proteins remain without sufficient functional annotations, because they have not been systematically studied under a broad range of conditions. In this review, we discuss the latest technical developments in mass spectrometry (MS)-based proteomics that facilitate large-scale studies by fast and efficient chromatography, fast scanning mass spectrometers, data-independent acquisition (DIA), and new software. We further highlight recent studies which demonstrate how high-throughput (HT) proteomics can be applied to capture biological diversity, to annotate gene functions or to generate predictive and prognostic models for human diseases.

Serum proteomics identifies patient subgroups and predicts survival in PDAC patients receiving immunotherapy combined with chemotherapy

Tognetti M, Chatterjee L, Beaton N, Sklodowski K, Bruderer R, Reiter L, Messner CB (submitted)

Immunotherapy has revolutionized cancer treatment. However, it is generally ineffective in pancreatic ductal adenocarcinoma (PDAC) patients. A recent study has shown that a subgroup of patients benefits from combined immunotherapy (CD40 agonistic antibody / anti-PD-1) and chemotherapy treatment. Here, we conducted deep serum proteome analysis to investigate the protein profiles of PDAC patients and changes during this combinatorial treatment. Utilizing an advanced serum workflow, we quantified 1,000 proteins across 211 samples from 62 patients, each providing up to four longitudinal samples. We identified patient subgroups based on their serum proteome profile, which differed in survival outcome. Furthermore, our analysis revealed that survival in anti-PD-1-treated patients could be predicted. Notably, we identified prognostic markers specific to anti-PD-1 treatment, predictive of one-year survival. Overall, our data offers insights into therapeutic responses and could potentially guide patient selection for treatment through minimally invasive serum protein biomarker measurements.

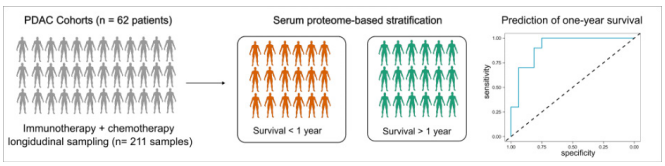


Figure: Serum proteomics identifies patient subgroups and predicts survival in PDAC patients receiving immunotherapy combined with chemotherapy

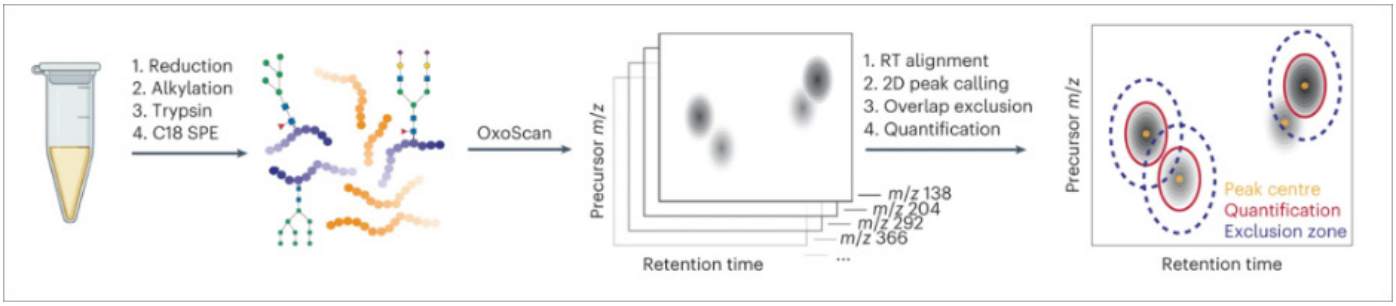


Figure: Oxonium ion scanning enables the quantification of glycopeptides across large-scale cohorts

Oxonium ion scanning mass spectrometry for large-scale plasma glycoproteomics

White ME, Sinn LR, Jones DM, de Folter J, Aulakh SK, Wang Z, Flynn HR, Krüger L, Tober-Lau P, Demichev V, Kurth F, Mülleder M, Blanchard V, Messner CB*, Ralser M*. Nature Biomedical Engineering. 2023 Jul 20:1-5. *These Authors contributed equally.

Research Briefing: Messner CB, Ralser M. Nature Biomedical Engineering. 2024 Mar 1;8(3):212-3.

Protein glycosylation, a complex and heterogeneous post-translational modification that is frequently dysregulated in disease, has been difficult to analyse at scale. Here we report a data-independent acquisition technique for the large-scale mass-spectrometric quantification of glycopeptides in plasma samples. The technique, which we named 'OxoScan-MS', identifies oxonium ions as glycopeptide fragments and exploits a sliding-quadrupole dimension to generate comprehensive and untargeted oxonium ion maps of precursor masses assigned to fragment ions from non-enriched plasma samples. By applying OxoScan-MS to quantify 1,002 glycopeptide features in the plasma glycoproteomes from patients with COVID-19 and healthy controls, we found that severe COVID-19 induces differential glycosylation in IgA, haptoglobin, transferrin and other disease-relevant plasma glycoproteins. OxoScan-MS may allow for the quantitative mapping of glycoproteomes at the scale of hundreds to thousands of samples.

Persistent complement dysregulation with signs of thromboinflammation in active Long Covid

Cervia-Hasler C, Brüningk SC, Hoch T, Fan B, Muzio G, Thompson RC, Ceglarek L, Meledin R, Westermann P, Emmenegger M, Taeschler P., Zurbuchen Y, Pons M, Menges D, Ballouz T, Cervia-Hasler S, Adamo S, Merad M, Charney AW, Puhan M, Brodin P, Nilsson J, Aguzzi A, Raeber M, Messner CB, Beckmann ND, Borgwardt K, Boyman O Science. 2024 Jan 19;383(6680):eadg7942.

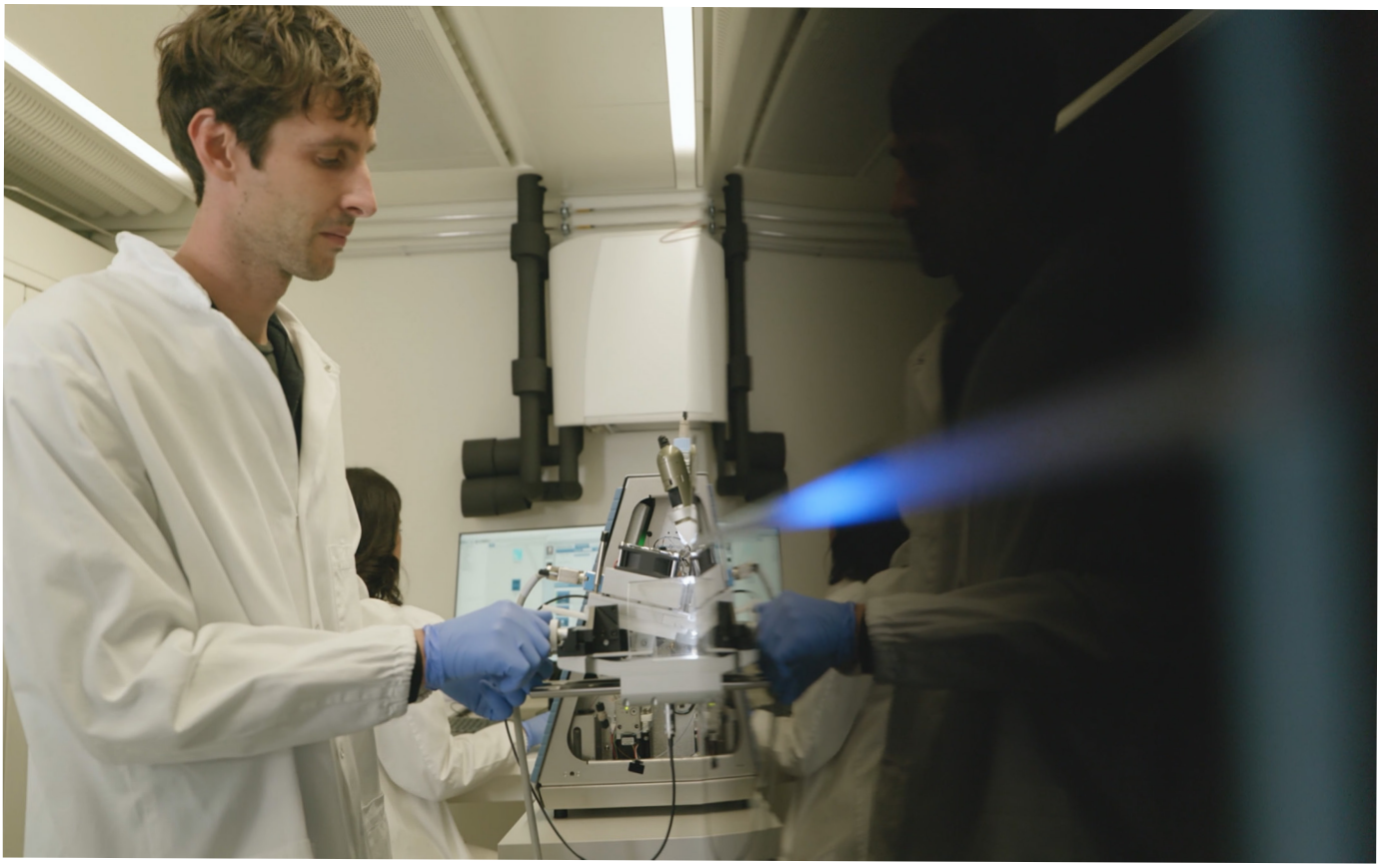
Long Covid is a debilitating condition of unknown etiology. We performed multimodal proteomics analyses of blood serum from COVID-19 patients followed up to 12 months after confirmed severe acute respiratory syndrome coronavirus 2 infection. Analysis of >6500 proteins in 268 longitudinal samples revealed dysregulated activation of the complement system, an innate immune protection and homeostasis mechanism, in individuals experiencing Long Covid. Thus, active Long Covid was characterized by terminal complement system dysregulation and ongoing activation of the alternative and classical complement pathways, the latter associated with increased antibody titers against several herpesviruses possibly stimulating this pathway. Moreover, markers of hemolysis, tissue injury, platelet activation, and monocyte–platelet aggregates were increased in Long Covid. Machine learning confirmed complement and thromboinflammatory proteins as top biomarkers, warranting diagnostic and therapeutic interrogation of these systems.

The Proteomic Landscape of Genome-Wide Genetic Perturbations.

Messner CB, Demichev V, Muenzner J, Aulakh SK, Barthel N, Röhl A, Herrera-Domínguez L, Egger AS, Kamrad S, Hou J, Tan G, Lemke O, Calvani E, Szyrwiel L, Mülleder M, Lilley KS, Kustatscher G, Ralser M (2023). Cell, 186(9), 2018-2034

Understanding the functions of genes and proteins is a major focus of life science research, as it is essential for understanding diseases and developing new therapies. However, many genes remain poorly understood, and their molecular properties are rarely annotated. To address this issue, we systematically turned off each gene in the model organism yeast and measured the resulting effect on proteins, which are the functional units of life. This approach enabled us to reveal functional annotations for many understudied genes. Functional genomic strategies have become fundamental for annotating gene function and regulatory networks. Here, we combined functional genomics with proteomics by quantifying protein abundances in a genome-scale knockout library in Saccharomyces cerevisiae, using data-independent acquisition mass spectrometry. We find that global protein expression is driven by a complex interplay of (1) general biological properties, including translation rate, protein turnover, the formation of protein complexes, growth rate, and genome architecture, followed by (2) functional properties, such as the connectivity of a protein in genetic, metabolic, and physical interaction networks. Moreover, we show that functional proteomics complements current gene annotation strategies through the assessment of proteome profile similarity, protein covariation, and reverse proteome profiling. Thus, our study reveals principles that govern protein expression and provides a genome-spanning resource for functional annotation.

Figure: Proteome Map. How do various genes and processes interact in protein production? Which potentially unknown genes are involved? The graphic illustrates the influences of non-essential genes on the proteome of yeast strains. Each line represents a different biological process and connects a gene removed from the genome with the corresponding functionally known genes.



Davos, May 2024

Molecular Allergology

PD Dr. Katja Bärenfaller, PhD

Molecular Allergology
PD Dr. Katja Baerenfaller

The molecular profile of Th cell differentiation and activation

As a conclusion to Jana Koch's PhD project that was funded by "Stiftung vormals Bündner Heilstätte Arosa" and by the Center for Precision Proteomics, we focused on challenging the current view on protein prenylation in T helper cells using experimental data and information on protein 3D structures (Figure 1).

Prenylation is a post-translational modification in which an isoprenoid, either a farnesyl or a geranylgeranyl moiety, is added to a cysteine residue, affecting the localization and function of the modified proteins. In cells, the farnesyl and geranylgeranyl moieties are products of the mevalonate pathway, which is targeted by widely prescribed lipid-lowering drugs called statins. Statins therefore possibly also inhibit protein prenylation.

The process of protein prenylation is known to be vital for the differentiation and activation of various T helper (Th) cell populations, but the involved proteins have not been characterized yet. To better understand the role of protein prenylation in Th1 cells, we therefore first identified geranylgeranylated and farnesylated proteins by adding azide-coupled geranylgeranyl (GG-Az) or farnesyl (F-Az) to ex vivo differentiated and activated Th1 cells treated or not with statins to metabolically label newly prenylated proteins followed by their enrichment and identification with mass spectrometry. This resulted in the identification of known prenylated proteins, and in the detection of proteins not yet annotated as prenylated. These findings were further investigated and validated using both bioinformatics and experimental approaches.

In the Master thesis project of Alessandra Ruggia at the University of Applied Sciences of the Grisons (FHGR), we focused on identifying the potential sites and motifs of protein prenylation. According to the current consensus, proteins are often prenylated at the cysteine in a CAAX, CXC or CC motif at the C-terminus of proteins followed by cleavage of the C-terminal peptide.

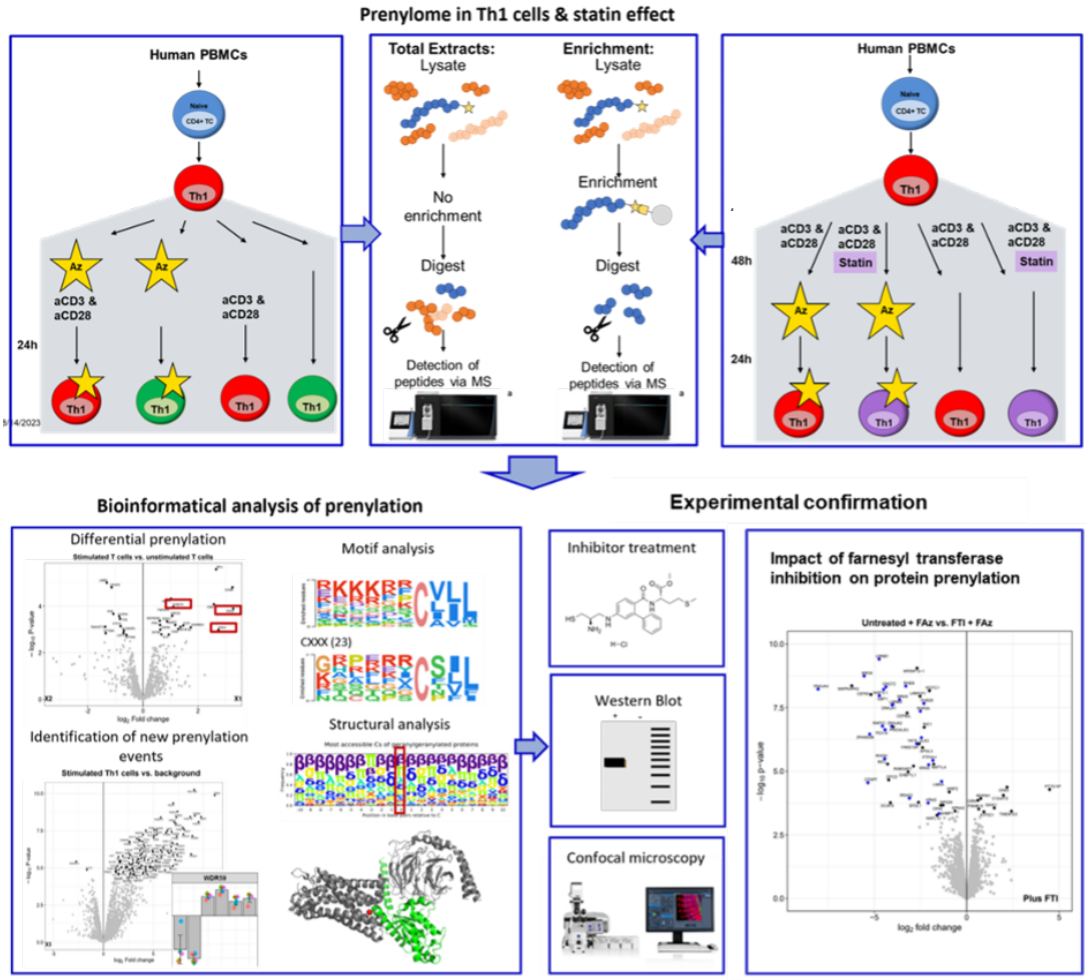


Figure 1: Workflow to investigate protein prenylation in T helper cells using experimental data and information on protein 3D structures

Inspecting our experimentally identified farnesylated and geranylgeranylated proteins, we found additional sites of prenylation. The newly identified C-terminal prenylation motifs consist of cysteines at positions -5 (CXXXX), -3 (CXX), and -2 (CX). Additionally, we identified a number of proteins that lacked cysteines at their C-terminus, suggesting prenylation at cysteines located internally within the protein sequence. For these internally prenylated proteins containing several cysteines, we next addressed the question of the most probable site of prenylation. Assuming that protein prenylation can only occur at accessible cysteines, we employed the approach reported by Bludau et al. (2022) to determine the 3D proximity of the cysteines using available protein structures. In the ETH Studio Davos project led by Irina Wipf, we further applied the FoldSeek algorithm to evaluate the structural context of the cysteines and their adjacent amino acids. The experimental confirmation of the prenylation events was addressed in the Master thesis project of Carina Beha at the Albert-Ludwigs-Universität Freiburg, Germany. In her work, prenylation of selected proteins, including KRAS, was confirmed by the presence of characteristic double bands on Western blots. Assessing the impact of treating activated Th1 cells with a farnesyl transferase inhibitor on protein prenylation nicely confirmed farnesylation of some proteins that were not previously known to be prenylated (Koch, Ruggia, Wipf, et al., *manuscript in preparation*).

Assessing Different Feature Selection Methods Applied to a Bulk RNA Sequencing Dataset with regard to Biomedical Relevance

Zhakparov D, Moriarty K, Lunjani N, Schmid M, Hlela C, Levin M, Mankahla A, SOS-ALL Consortium, Akdis C, O'Mahony L, Baerenfaller K#, Roqueiro DS# (2023) Assessing Different Feature Selection Methods Applied to a Bulk RNA Sequencing Dataset with regard to Biomedical Relevance. 2023 In: Machine Learning and Principles and Practice of Knowledge Discovery in Databases. ECML PKDD 2022. Communications in Computer and Information Science, vol 1753. Springer, Cham, DOI: 10.1007/978-3-031-23633-4_18

In the context of the MLM-SOS-ALL project in the Center for Data Analysis, Visualizsation and Simulation (DAViS), we have developed the GeneSelectR workflow. This workflow combines the machine learning (ML) capabilities of the sklearn Python package with the functionalities of bioinformatics R libraries to identify significant features that separate healthy children from children that have atopic dermatitis in a large and complex RNA sequencing dataset (Zhakparov et al., 2023b). The original workflow developed in the project has since been developed into an R package (Figure 2).

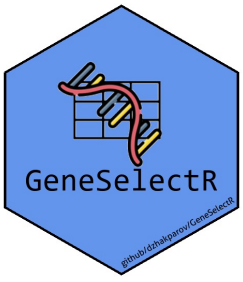


Figure 2: Hexagon logo for the GeneSelectR R package

The core functionalities of the GeneSelectR R package allow to use ML in a classification problem to select the most significant features, and then to assess the biological relevance of different ML-selected feature lists. The best-performing list can therefore be selected based on a high ML performance, a high overlap coefficient between lists, a high number of biologically relevant Gene Ontology (GO) terms that are enriched in the different lists, in these enriched GO terms, a high number of GO child terms of parent terms of interest, and finally a high number of enriched GO terms that are associated with a relevant cluster in the semantic similarity analysis (Figure 3). GeneSelectR therefore offers a robust feature selection workflow that both optimizes ML performance and ensures biological relevance through functional enrichment and semantic similarity analyses.

Following the successful completion of the necessary requirements and passing various tests, the GeneSelectR package has become available on CRAN on 13 December 2023. To make the GeneSelectR feature selection process user-friendly, the ML capabilities of Python were implemented in R, and the package was containerized with Docker so that it can be run in an isolated environment to avoid dependency conflicts and to minimize the need for frequent intermediate outputs and data transfers. More detailed information on the package was published as a preprint (Zhakparov et al. (bioRxiv, 2024), and is provided in the vignette and on GitHub.

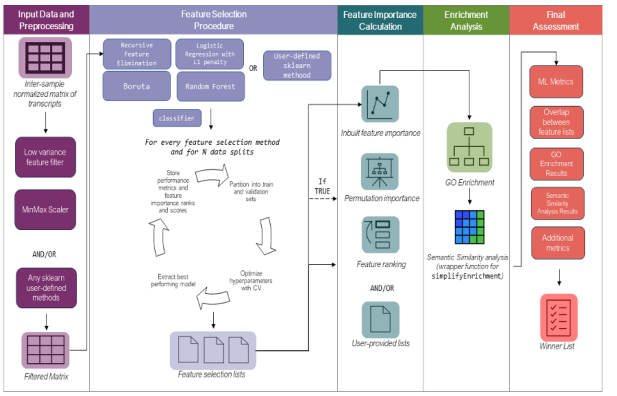


Figure 3: Figure 1 from Zhakparov et al. (bioRxiv, 2024) with the schematic representation of the GeneSelectR workflow

Sequencing of SARS-CoV-2 RNA Fragments in Wastewater Detects the Spread of New Variants during Major Events.

Zhakparov D, Quirin Y, Xiao Y, Battaglia N, Holzer M, Bühler M, Kistler W, Engel D, Zumthor JP, Caduff A#, Baerenfaller K#*. 2023, Microorganisms, 11(11), 2660, DOI: 10.3390/microorganisms11112660

In another project of the cantonal Center for Data Analysis, Visualization and Simulation (DAViS) in collaboration with several cantonal offices, we continued the wastewater-based epidemiological monitoring of the spread of different SARS-CoV-2 variants in Davos and in S-chanf during the World Economic Forum (WEF) in January 2023. As previously, the wastewater was collected and sent to the cantonal laboratory in Chur, where the RNA was extracted

and sent to the Functional Genomics Center Zurich for amplicon sequencing. The sequencing reads were then mapped to SARS-CoV-2 variant sequences using the V-Pipe pipeline to estimate the relative prevalence of the different circulating variants in the population. The results revealed a considerable shift in variant prevalence during WEF in Davos, with Omicron variant BA.2.75 arriving and soon afterwards becoming the dominant variant (Figure 4a). In contrast, XBB.1.5 and XBB remained the dominant variants in S-chanf (Figure 4b). This spread of a new variant in the host region of a major event corresponds with our previous observations during the sports events in December 2021 when Omicron BA.1 arrived in Davos and S-chanf. We can therefore conclude that major international events promote the spread of new variants in the respective host region.

According to CoVariants (https://covariants.org/), Omicron variant BA.2.75 was predominantly observed in Asia, Australia, and New Zealand before the WEF. In the clinical sample sequencing data, with a 90% reduction in testing volume compared to the previous year, 2 out of 36 sequenced samples were found to be BA.2.75 between 2 and 16 January 2023. As limited clinical sample sequencing is likely to introduce a notable bias for more severe cases, the arrival of new variants might therefore go unnoticed. This highlights the importance of wastewater-based epidemiological monitoring, which will continue in our case during WEF 2024.

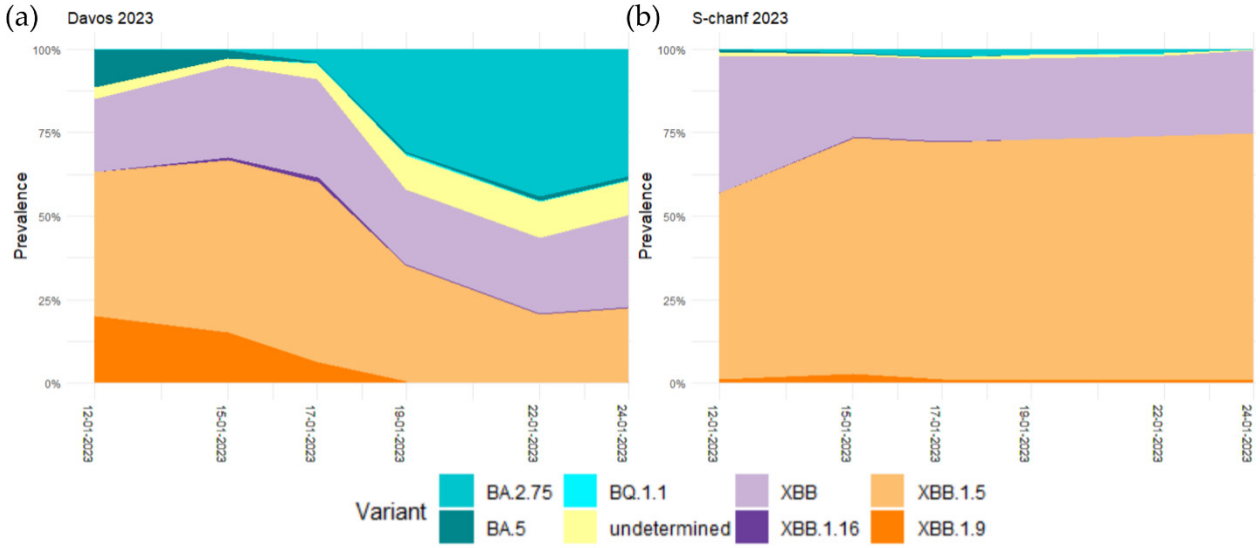


Figure 4: Figure 4 from Zhakparov et al. (2023a) with smoothed regression curves of the relative prevalence of the SARS-CoV-2 Omicron variants BA.2.75, BA.5, BQ.1.1, XBB, XBB.1.16, XBB.1.15, XBB.1.19 in January 2023 in (a) Davos and (b) S-chanf.

Additional publication:

Spatial transcriptomics combined with single-cell RNA-sequencing unravels the complex inflammatory cell network in atopic dermatitis. Mitamura Y*, Reiger M, Kim J, Xiao Y, Zhakparov D, Tan G, Rückert B, Rinaldi AO, Baerenfaller K, Akdis M, Brüggen MC, Nadeau KC, Brunner PM, Roqueiro D, Traidl-Hoffmann C, Akdis CA. 2023, Allergy, 00:1-17, DOI: 10.1111/all.15781

Davos, May 2024

Dr. Claudio Rhyner, PhD

Vaccine Development
Dr. Claudio Rhyner

Topic: Veterinary allergology

Severe equine asthma (SEA) is a common, chronic respiratory disease of horses characterized by hyperreactivity to hay dust which has many similarities to severe neutrophilic asthma in humans. SEA-provoking antigens have not been comprehensively characterized, but molds and mites have been suggested as relevant sources. Here, we identified relevant antigen candidates using immunoproteomics with IgG isotype-binding analyses. Ig binding differences were detected in 30 spots from the chromatography. Pan-Ig binding was higher with asthmatics compared to healthy horses' sera on four spots, and IgG3/5 binding was higher on 18 spots. Small IgG4/7 binding differences were detected on 10 spots with higher binding with asthmatics' sera on four but higher binding with healthy horses' sera on six spots. Proteins from the spots with group differences including mite and yeast proteins were identified by liquid chromatography mass spectrometry. The latter likely originated from the feeding substrate of the Der p culture. Prioritized antigen candidates amongst the proteins identified were Der p 1, Der p 11, group 15 allergens, myosin heavy chain, and uncharacterized Der p proteins. Additionally, yeast enolases, alcohol dehydrogenase (ADH), phosphoglycerate kinase (PGK), glyceraldehyde-3-phosphate dehydrogenase, and heat shock proteins were prioritized. Eleven antigen candidates were tested for confirmation by ELISAs using the respective proteins separately. Differences in asthmatics vs. healthy horses' serum Ig binding to Der p 1, Der p 18, and three yeast enzymes (enolase, ADH, and PGK) confirmed these as promising antigens of immune responses in SEA. Antigens with relevance in SEA were newly identified by immunoproteomics, and yeast antigens were considered for SEA for the first time. Serum IgG3/5 binding to relevant antigens was increased in SEA and is a novel feature that points to increased type-2 responses in SEA but requires confirmation of the corresponding cellular responses. (Schnabel et. al. Front Immunol. 2023 Dec 15;14:1293684)

Topic: Atopic dermatitis

Atopic dermatitis (AD) has long been regarded as a primarily pediatric disease. However, there is growing evidence for a high rate of adult-onset AD. We aimed to characterize factors associated with adult-onset versus childhood-onset AD and controls. We analyzed cross-sectional data of the CK-CARE-ProRaD cohorts Bonn, Augsburg, Davos, Zürich of 736 adult patients stratified by age of AD onset (childhood-onset <18 years: 76.4% (subsets: 0 to 2; ≥2 to 6; ≥7 to 11; ≥12 to 18); adult-onset ≥18 years: 23.6% (subsets: ≥18 to 40; ≥41 to 60; ≥61) and 167 controls (91 atopic, 76 non-atopic)). We identified active smoking to be associated with adult-onset AD versus controls (adjusted Odds Ratio (aOR) = 5.54 [95% Confidence Interval: 1.06-29.01] vs. controlsnon-atopic , aOR = 4.03 [1.20-13.45] vs. controlsatopic). Conjunctivitis showed a negative association versus controlsatopic (aOR = 0.36 [0.14-0.91]). Food allergy (aOR = 2.93 [1.44-5.96]), maternal food allergy (aOR = 9.43 [1.10-80.95]), palmar hyperlinearity (aOR = 2.11 [1.05-4.25]), and academic background (aOR = 2.14 [1.00-4.54]) increased the odds of childhood-onset AD versus controlsatopic . Shared AD-associated factors were maternal AD (4-34x), increased IgE (2-20x), atopic stigmata (2-3x) with varying effect sizes depending on AD onset and control group. Patients with adult-compared to childhood-onset had doubled odds of allergic rhinitis (aOR = 2.15 [1.12-4.13]), but reduced odds to feature multiple (3-4) atopic comorbidities (aOR = 0.34 [0.14-0.84]). Adult-onset AD, particularly onset ≥61 years, grouped mainly in clusters with low contributions of personal and familial atopy and high frequencies of physical inactivity, childhood-onset AD, particularly infant-onset, mainly in "high-atopic"-clusters. The identified associated factors suggest partly varying endo- and exogeneous mechanisms underlying adult-onset versus childhood-onset AD. Our findings might contribute to better assessment of the individual risk to develop AD throughout life and encourage prevention by non-smoking and physical activity as modifiable lifestyle factors. (Maintz et. al. Allergy. 2023 Aug;78(8):2181-2201).

Davos, May 2024

Immune Metabolism

PD Dr. Milena Sokolowska, MD, PhD

Changes in environmental conditions and lifestyle choices have contributed to an increase in allergies, respiratory viral infections, and bacterial illnesses. The COVID-19 pandemic, along with its aftermath, has starkly highlighted this trend. The underlying reasons why certain substances trigger allergic reactions in some individuals while others remain unaffected remain elusive. Similarly, the factors determining susceptibility to viral infections, the development of severe respiratory illnesses, or long-lasting consequences such as long-COVID, remain poorly understood. Various factors can contribute to this susceptibility, including inadequate early-life microbiome development, recurrent viral infections, exposure to environmental pollutants, imbalanced diets, and metabolic disorders like obesity. In recent years, concerted efforts have focused on unraveling the susceptibility to viral infections in individuals with asthma and allergies, as well as the role of allergens and allergic inflammation in these dynamics. Our research group has focused on how the above-mentioned factors can disrupt the intricate communication between airway epithelial cells and $CD4^+$T cells, impacting cellular responses at a metabolic and molecular level. Immune cells must undergo numerous energetically demanding processes to react to external stimuli such as allergens, viruses, or bacteria. These processes involve gene expression alterations, protein translation, lipid synthesis, activation of signaling pathways, cytoskeletal modifications, and the production of cytokines, lipid mediators, as well as cell proliferation or migration. Cellular energy metabolism in the form of glycolysis, the tricarboxylic acid cycle, oxidative phosphorylation, and beta-oxidation needs to sustain the changing needs of immune cells during homeostasis and inflammation or infection in the processes called metabolic reprogramming. To understand the complex interplay between immune and metabolic reprogramming at mucosal barriers in the pathogenesis of allergic, respiratory, skin and autoimmune diseases, our research group employs several advanced techniques. We analyze patients' blood, lung, and skin samples using single-cell and bulk sequencing, spatial transcriptomics, proteomics, and metabolomics, coupled with comprehensive bioinformatic approaches. We also combine these with gene editing, multi-color flow cytometry, confocal microscopy, and live-cell metabolic assays such as single-cell energy metabolism profiling to understand mechanisms of observed pathologic phenomena. Our overarching goal is to decipher immune and metabolic crosstalk, identify new biomarkers, and uncover potential targets for prevention and treatment across various respiratory viral diseases, microbial dysbiosis, allergy, immune tolerance, and asthma phenotypes.

1. Understanding immunology of viral infections and their long-term consequences

Immune Mechanisms Underpinning Long COVID: Collegium Internationale Allergologicum Update 2024

Untersmayr E, Venter C, Smith P, Rohrhofer J, Ndwandwe C, Schwarze J, Shannon E, Sokolowska M, Sadlier C, O'Mahony L. Int Arch Allergy Immunol. 2024 Jan 22:1-14. doi: 10.1159/000535736.

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection can result in a prolonged multisystem disorder termed long COVID, which may affect up to 10% of people following coronavirus disease 2019 (COVID-19). It is currently unclear why certain individuals do not fully recover following SARS-CoV-2 infection. In this review, we examine immunological mechanisms that may underpin the pathophysiology of long COVID. These mechanisms include an inappropriate immune response to acute SARS-CoV-2 infection, immune cell exhaustion, immune cell metabolic reprogramming, a persistent SARS-CoV-2 reservoir, reactivation of other viruses, inflammatory responses impacting the central nervous system, autoimmunity, microbiome dysbiosis, and dietary factors. Unfortunately, the currently available diagnostic and treatment options for long COVID are inadequate, and more clinical trials are needed that match experimental interventions to underlying immunological mechanisms.

Rhinovirus-induced epithelial RIG-I inflammasome suppresses antiviral immunity and promotes inflammation in asthma and COVID-19

Radzikowska U, Eljaszewicz A, Tan G, Stocker N, Heider A, Westermann P, Steiner S, Dreher A, Wawrzyniak P, Rückert B, Rodriguez-Coira J, Zhakparov D, Huang M, Jakiela B, Sanak M Moniuszko M, O`Mahony L, Jutel M., Kebadze T, Jackson DJ, Edwards MR, Thiel V, Johnston SL, Akdis CA*, Sokolowska M*. *Last co-authors. Nature Communications 2023 Apr 22;14(1):2329. doi: 10.1038/s41467-023-37470-4.

Rhinoviruses and allergens, such as house dust mite are major agents responsible for asthma exacerbations. The influence of pre-existing airway inflammation on the infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is largely unknown. We analyse mechanisms of response to viral infection in experimental in vivo rhinovirus infection in healthy controls and patients with asthma, and in in vitro experiments with house dust mite, rhinovirus and SARS-CoV-2 in human primary airway epithelium. Here, we show that rhinovirus infection in patients with asthma leads to an excessive RIG-I inflammasome activation, which diminishes its accessibility for type I/III interferon responses, leading to their early functional impairment, delayed resolution, prolonged viral clearance and unresolved inflammation in vitro and in vivo. Pre-exposure to house dust mite augments this phenomenon by inflammasome priming and auxiliary inhibition of early type I/III interferon responses. Prior infection with rhinovirus followed by SARS-CoV-2

infection augments RIG-I inflammasome activation and epithelial inflammation. Timely inhibition of the epithelial RIG-I inflammasome may lead to more efficient viral clearance and lower the burden of rhinovirus and SARS-CoV-2 infections.

Regulation of angiotensin-converting enzyme 2 isoforms by type 2 inflammation and viral infection in human airway epithelium

Stocker N, Radzikowska U, Huang M, Ding M, Wawrzyniak P, Tan G, Akdis CA, Sokolowska M. Mucosal Immunology 2023 Feb;16(1):5-16. doi: 10.1016/j.mucimm.2022.12.001.

SARS-CoV-2 enters human cells through its main receptor, angiotensin-converting enzyme 2 (ACE2), which constitutes a limiting factor of infection. Recent findings demonstrating novel ACE2 isoforms implicate that this receptor is regulated in a more complex way than previously anticipated. However, it remains unknown how various inflammatory conditions influence the abundance of these ACE2 variants. Hence, we studied expression of ACE2 messenger RNA (mRNA) and protein isoforms, together with its glycosylation and spatial localization in primary human airway epithelium upon allergic inflammation and viral infection. We found that interleukin-13, the main type 2 cytokine, decreased expression of long ACE2 mRNA and reduced glycosylation of full-length ACE2 protein via alteration of N-linked glycosylation process, limiting its availability on the apical side of ciliated cells. House dust mite allergen did not affect the expression of ACE2 (Fig. 1). Rhinovirus infection increased short ACE2 mRNA, but it did not influence its protein expression. In addition, by screening other SARS-CoV-2 related host molecules, we found that interleukin-13 and rhinovirus significantly regulated mRNA, but not protein of transmembrane serine protease 2 and neuropilin 1. Regulation of ACE2 and other host proteins was comparable in healthy and asthmatic epithelium, underlining the lack of intrinsic differences but dependence on the inflammatory milieu in the airways.

Machine Learning Successfully Detects Patients with COVID-19 Prior to PCR Results and Predicts Their Survival Based on Standard Laboratory Parameters in an Observational Study

Styrzynski F, Zhakparov D, Schmid M, Roqueiro D, Lukasik Z, Solek J, Nowicki J, Dobrogowski M, Makowska J*, Sokolowska M*, Baerenfaller K*. * Last-co-authors. Infectious Diseases and Therapy 2023 Jan;12(1):111-129. doi: 10.1007/s40121-022-00707-8.

In the current COVID-19 pandemic, clinicians require a manageable set of decisive parameters that can be used to (i) rapidly identify SARS-CoV-2 positive patients, (ii) identify patients with a high risk of a fatal outcome on hospital admission, and (iii) recognize longitudinal warning signs of a possible fatal outcome. Here, we identified a set of eight on-admission parameters: white blood cells, antibody-synthesizing lymphocytes, ratios of basophils/lymphocytes, platelets/neutrophils, and monocytes/lymphocytes, procalcitonin, creatinine, and C-reactive protein. The medical decision tree built using these parameters differentiated between SARS-CoV-2 positive and negative patients with up to 90-100% accuracy. Patients with COVID-19 who on hospital admission were older, had higher procalcitonin, C-reactive protein, and troponin I levels together with lower hemoglobin and platelets/neutrophils ratio were found to be at highest risk of death from COVID-19. Furthermore, we identified longitudinal patterns in C-reactive protein, white blood cells, and D dimer that predicted the disease outcome. Our study provides sets of easily obtainable parameters that allow one to assess the status of a patient with SARS-CoV-2 infection, and the risk of a fatal disease outcome on hospital admission and during the course of the disease.

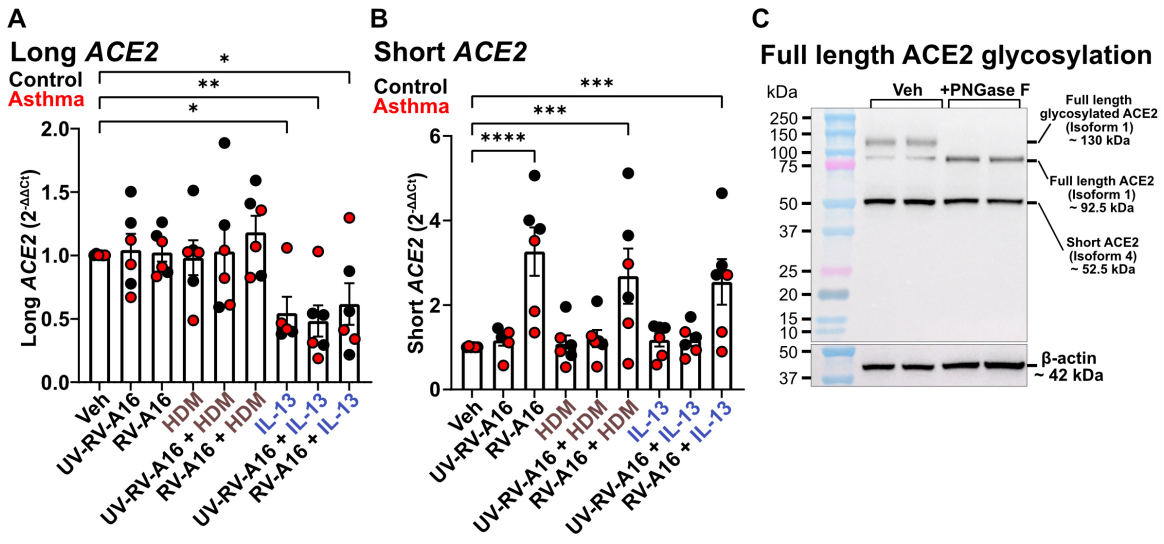


Figure 1. ACE2 isoforms are differentially regulated in human bronchial epithelium. A) mRNA of Long ACE2 is downregulated upon interleukin 13 (IL-13) exposure, B) mRNA of Short ACE2 is upregulated after rhinovirus infection. C) Full length ACE2 protein is the only isoform undergoing glycosylation

How Can Allergen Immunotherapy Protect against COVID-19?
Sokolowska M, Radzikowska U. Am J Respir Crit Care Med. 2023 May 15;207(10):1408-1410. doi: 10.1164/rccm.202302-0317LE.
Here we summarised the results of the recent double blind, placebo controlled VITAL clinical trial, which revealed the increased expression of the main antiviral molecules in the airways of patients with asthma treated with house dust mite allergen immunotherapy (HDM-AIT) in light of our own data on the role of interactions between HDM and viral infections. We also provided an overview of all the potential mechanisms in which AIT might contribute to the decreased frequencies of viral-induced asthma exacerbations in patients receiving AIT.

Pathogenesis, immunology, and immune-targeted management of the multisystem inflammatory syndrome in children (MIS-C) or pediatric inflammatory multisystem syndrome (PIMS): EAACI Position Paper
Feleszko W, Okarska-Napierała M, Buddingh EP, Bloomfield M, Sediva A, Bautista-Rodriguez C, Brough HA, Eigenmann PA, Eiwegger T, Eljaszewicz A, Eyerich S, Gomez-Casado C, Fraisse A, Janda J, Jiménez-Saiz R, Kallinich T, Krohn IK, Mortz CG, Riggioni C, Sastre J, Sokolowska M, Strzelczyk Z, Untersmayr E, Tramper-Stranders G; Immunology Section and Working Group Infections of the EAACI. Pediatr Allergy Immunol. 2023 Jan;34(1):e13900. doi: 10.1111/pai.13900.
Multisystem inflammatory syndrome in children (MIS-C) is a rare, but severe complication of coronavirus disease 2019 (COVID-19). It develops approximately 4 weeks after severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection and involves hyperinflammation with multisystem injury, commonly progressing to shock. The exact pathomechanism of MIS-C is not known, but immunological dysregulation leading to cytokine storm plays a central role. In response to the emergence of MIS-C, the European Academy of Allergy and Clinical Immunology (EAACI) established a task force (TF) within the Immunology Section in May 2021. With the use of an online Delphi process, TF formulated clinical statements regarding immunological background of MIS-C, diagnosis, treatment, follow-up, and the role of COVID-19 vaccinations. MIS-C case definition is broad, and diagnosis is made based on clinical presentation. The immunological mechanism leading to MIS-C is unclear and depends on activating multiple pathways leading to hyperinflammation. Current management of MIS-C relies on supportive care in combination with immunosuppressive and/or immunomodulatory agents. The most frequently used agents are systemic steroids and intravenous immunoglobulin. Despite good overall short-term outcome, MIS-C patients should be followed-up at regular intervals after discharge, focusing on cardiac disease, organ damage, and inflammatory activity. COVID-19 vaccination is a safe and effective measure to prevent MIS-C. In anticipation of further research, we propose a convenient and clinically practical algorithm for managing MIS-C developed by the Immunology Section of the EAACI.

2. Understanding immunometabolism in viral infections, immune tolerance, allergy and asthma

Immunometabolic reprogramming of bronchial epithelium in asthma and during viral infection
Radzikowska U*, Jardón Parages I *et al and Sokolowska M. * equally contributed. In preparation
Human rhinovirus (RV) exacerbates asthma in both children and adults, yet little is known about the immunometabolic changes occurring in airway epithelium in response to RV infection. Our study aims to elucidate abnormalities in mitochondria, oxidative phosphorylation (OXPHOS), beta-oxidation, and glycolysis in asthmatic airway epithelium, both at baseline and post-RV infection. We employed a multidimensional approach encompassing RNA-seq, qPCR, untargeted and targeted proteomics (LC-MS and OLINK), immunoassays, microscopy, and Seahorse real-time cell metabolic analysis to examine in vitro cultures of human primary bronchial epithelial cells (HBECs), as well as bronchial biopsies from healthy controls and asthma patients, including experimental in vivo infection with RV in humans (Fig. 2). Our results demonstrate that bronchial epithelium in asthma, both in vitro and in vivo, exhibits defective OXPHOS energy generation at baseline and after RV infection, coupled with an increased reliance on glycolysis. This metabolic shift is functionally linked to abnormal mitochondrial dynamics and function, as well as enhanced early RIG-I inflammasome activation, culminating in an inefficient antiviral response and unresolved airway inflammation. Transcriptomic analyses further revealed dysregulation of OXPHOS and glycolysis genes in asthma post-infection, potentially contributing to impaired viral clearance and ATP regulation. Moreover, proteomic assessments highlighted alterations in metabolism-related proteins, particularly those involved in OXPHOS, emphasizing the significance of epithelial metabolic rewiring in asthma exacerbations induced by RV-A16. Our findings underscore the importance of epithelial metabolic rewiring in asthma exacerbations induced by RV-A16, suggesting it as a potential target for therapeutic interventions aiming to prevent and treat viral exacerbations of asthma.

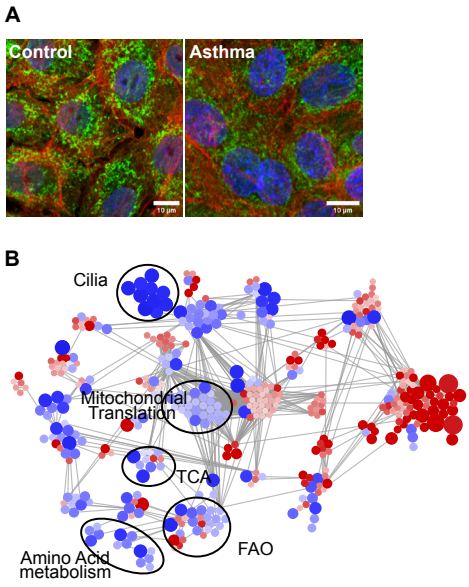


Figure 2. Mitochondrial dysfunction in bronchial epithelium in asthma. A) Representative confocal microscopy image of TOMM20, visualising mitochondria in healthy controls and patients with asthma. B) Network analysis of differentially expressed proteins in bronchial epithelial cells from patients with asthma (n=5) compared to healthy

controls (n=4). TCA-tricarboxylic acid cycle, FAO-fatty acid oxidation.

Immunoregulatory role of L-Phenylalanine in Th2 cells

Kulkarni AJ*, Rodriguez-Coira J*, Stocker N, Radzikowska U, García-Cívico AJ, I Delgado Dolset MI, Contreras N, Jardon Parages I, Saiz Sanchez J, Serrano P, Izquierdo E, Gomez-Casado C, Sanchez-Solares J, Pablo Torres C, Obeso D, Ruiz-Leon B, Espinazo M, Eljaszewicz A, Koch J, Baerenfaller K, Heider A, Tan G, Escribese M, Moreno-Aguilar C, Akdis CA, Arguello RJ, Barber D, Villasenor A**, Sokolowska M**. * First co-authors, ** Last co-authors. Under revision.

Following the completion of a primary immune response and elimination of antigenic challenge, circulating memory CD4+T effector (Teff) and T regulatory (Treg) cells are established aiding recall responses. However, in allergic and autoimmune diseases, these populations are impaired ultimately facilitating inflammation but remain poorly studied. In this study, we have assessed these key subsets by high-resolution mass spectrometry and observed complete separation of these cell types based on their metabolic profiles which were also enriched in amino acids.

By combining functional, knockdown, and energy metabolism assessment, we have determined that elevated intracellular L-phenylalanine (Phe) specifically promotes glycolysis while simultaneously limiting OXPHOS and proliferation in memory CD4+T cells in an IL4I1-dependent manner. In Th2 cells, Phe exhibited similar effects on energy metabolism along with significantly decreasing expression of key type 2 associated factors involved in Th2 cell function, development, and pathogenicity at mRNA and protein levels. Finally, by incorporating RNA-Sequencing, metabolomics, flow cytometry and proteomics analysis of multiple patient cohorts, along with in vitro verification and exploratory assessment we have identified that inefficient import of Phe, due to LAT1 (SLC7A5) dysregulation, and potentially faster intracellular turnover results in a deficit which leads to uncontrolled activation and expansion commonly observed in allergic diseases. Hence, L-phenylalanine plays a critical immunoregulatory role in CD4+T cell, particularly Th2 cell, biology. (Fig. 3).

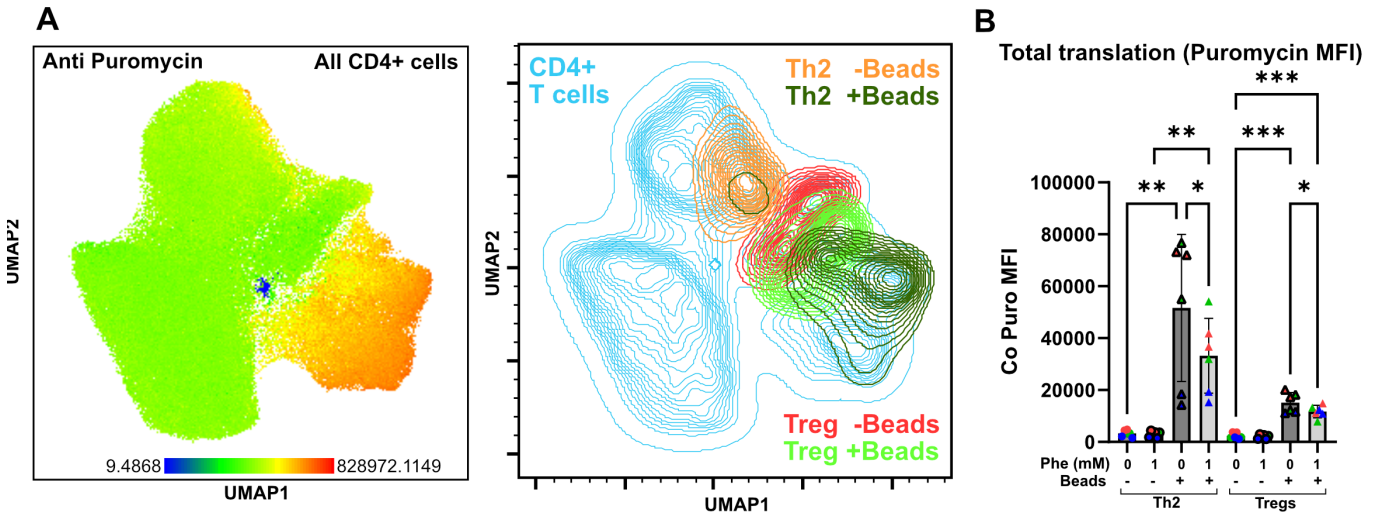


Figure 3. Single-cell energetic metabolism by profiling translation inhibition (SCENITH) of CD4+T cells. A) Uniform Manifold Approximation and Projection (UMAP) plots demonstrating metabolic activity of CD4+T cells (left) with marked Th2 cells and Treg cells upon TCR activation (right). B) Total translation levels of Th2 and Treg cells upon activation and phenylalanine supplementation

Immunometabolism of allergen-specific CD4+ T cells in allergy and immune tolerance

Sokolowska M, Boonpiyathad T et al. In preparation.

Allergic immune response in T cells is characterized, among others, by increased secretion of pro-inflammatory mediators by Th2 effector cells. The main suppressors of this response are allergen-specific regulatory T cells (Tregs) as demonstrated in the steady state and in allergen-specific immunotherapy (AIT). Little is known about the metabolic requirements of allergen-specific and non-specific effector T cells and Tregs to carry out their functions in vivo. The aim of our studies is to identify essential metabolic pathways for regulatory and effector populations of allergen-specific and non-specific memory T cells in vivo in humans, their potential alterations in allergic disease, as well as their changes during allergen-specific immunotherapy. Allergen-specific T and Treg cells in allergic patients display profound gene and protein downregulation of immune response and cell activation pathways except type 2 immunity, TCR signaling, fatty acid and prostaglandin metabolism. Plasma and nasal untargeted and targeted proteome reflect specific cellular signature with upregulation of proteins leading to lymphocyte proliferation, T cell differentiation and fatty acid metabolism and downregulation of several anti-inflammatory pathways. Remarkably, AIT induces significant changes in previously dysregulated immune and metabolic pathways and leads to induction of tolerance programs in allergen-specific CD4+ T cells and Treg cells. However, allergen-specific Treg cells in non-responders to AIT still displayed aberrant type 2 gene, protein and metabolic profiles, coupled with

the corresponding plasma and nasal inflammatory milieu, in parallel to functional impairment of their suppressive capacities. Altogether, our data suggest that in allergy there is a systemic and local aberration of immune and metabolic signaling, leading to dysfunctional metabolic reprogramming and subsequent functional impairment of allergen-specific effector and regulatory T cells.

Interleukin-13 and interleukin-22 differentially regulate glycolysis in keratinocytes of patients with atopic dermatitis

Mitamura Y*, Duphey S* et al and Sokolowska M. * equally contributed. In preparation.

Atopic dermatitis (AD) is a chronic skin disease. Interleukin-13 (IL-13) and interleukin-22 (IL-22) play the central role in the pathogenesis of AD. However, the influence of these cytokines on the keratinocytes metabolism and metabolic control of epithelial barrier remains unknown. Recently, an enhanced glycolysis pathway has been reported in AD. We aim to investigate the roles of IL-13 and IL-22 on the metabolic change in keratinocytes and their subsequent influence on barrier function. Data of bulk RNA sequencing and spatial RNA sequencing of lesional and non-lesional skin of AD patients in comparison to healthy skin from our previous cohort were analysed. In addition, we performed bulk RNA sequencing of IL-13-stimulated-reconstructed human skin (Episkin®). Next, we analysed real time glycolysis utilization by proliferating and differentiating keratinocytes in response to IL-13 and IL-22 in the seahorse glycolysis stress test. Finally, we performed qPCR and confocal microscopy experiments in air-liquid interphase cultured keratinocytes to investigate gene and protein expression of barrier- and glycolysis-related molecules. The expression of glycolysis-related genes was significantly upregulated especially in the epidermis in the lesional skin of AD patients and in the IL-13-treated Episkin, whereas the expression of several barrier molecules was downregulated. In the seahorse experiments, IL-13 significantly increased, whereas IL-22 decreased the early glycolytic capacity of basal proliferating and differentiating keratinocytes. We further demonstrated that functional blocking of glycolysis by 2-deoxy-d-glucose (2-DG) influenced the expression of some of the keratinocyte-specific molecules. Our data suggest that IL-13 and IL-22 may take the balance to regulate the glycolytic capacity of keratinocytes, which might further affect the skin proliferation, differentiation, and barrier regulation in AD.

Metabolic pathways in immune senescence and inflammaging: Novel therapeutic strategy for chronic inflammatory lung diseases. An EAACI position paper from the Task Force for Immunopharmacology

Roth-Walter F, Adcock IM, Benito-Villalvilla C, Bianchini R, Bjermer L, Caramori G, Cari L, Chung KF, Diamant Z, Eguiluz-Gracia I, Knol EF, Jesenak M, Levi-Schaffer F, Nocentini G, O'Mahony L, Palomares O, Redegeld F, Sokolowska M, Van Esch BCAM, Stellato C. Allergy. 2023 Dec 18. doi: 10.1111/all.15977.

The accumulation of senescent cells drives inflammaging and increases morbidity of chronic inflammatory lung diseases. Immune responses are built upon dynamic changes in cell metabolism that supply energy and substrates for cell proliferation, differentiation, and activation. Metabolic changes imposed by environmental stress and inflammation on immune cells and tissue microenvironment are thus chiefly involved in the pathophysiology of allergic and other immune-driven diseases. Altered cell metabolism is also a hallmark of cell senescence, a condition characterized by loss of proliferative activity in cells that remain metabolically active. Accelerated senescence can be triggered by acute or chronic stress and inflammatory responses. In contrast, replicative senescence occurs as part of the physiological aging process and has protective roles in cancer surveillance and wound healing. Importantly, cell senescence can also change or hamper response to diverse therapeutic treatments. Understanding the metabolic pathways of senescence in immune and structural cells is therefore critical to detect, prevent, or revert detrimental aspects of senescence-related immunopathology, by developing specific diagnostics and targeted therapies. In this paper, we review the main changes and metabolic alterations occurring in senescent immune cells (macrophages, B cells, T cells). Subsequently, we present the metabolic footprints described in translational studies in patients with chronic asthma and chronic obstructive pulmonary disease (COPD), and review the ongoing preclinical studies and clinical trials of therapeutic approaches aiming at targeting metabolic pathways to antagonize pathological senescence. Because this is a recently emerging field in allergy and clinical immunology, a better understanding of the metabolic profile of the complex landscape of cell senescence is needed. The progress achieved so far is already providing opportunities for new therapies, as well as for strategies aimed at disease prevention and supporting healthy aging.

A cross talk between microbial metabolites and host immunity: Its relevance for allergic diseases

Losol P, Wolska M, Wypych TP, Yao L, O'Mahony L, Sokolowska M. Clin Transl Allergy. 2024 Feb;14(2):e12339. doi: 10.1002/clt2.12339.

Background: Allergic diseases, including respiratory and food allergies, as well as allergic skin conditions have surged in prevalence in recent decades. In allergic diseases, the gut microbiome is dysbiotic, with reduced diversity of beneficial bacteria and increased abundance of potential pathogens. Research findings suggest that the microbiome, which is highly influenced by environmental and dietary factors, plays a central role in the development, progression, and severity of allergic diseases. The microbiome generates metabolites, which can regulate many of the host's cellular metabolic processes and host immune responses. Aims and methods: Our goal is to provide a narrative and comprehensive literature review of the mechanisms through which microbial metabolites regulate host immune function and immune metabolism both in homeostasis and in the context of allergic diseases. Results and discussion: We describe key microbial metabolites such as short-chain fatty acids, amino acids, bile acids and polyamines, elucidating their mechanisms of action, cellular targets and their roles in regulating metabolism within innate and adaptive immune cells. Furthermore, we characterize the role of bacterial metabolites in the pathogenesis of allergic diseases including allergic asthma, atopic dermatitis and food allergy. Conclusion: Future research efforts should focus on investigating the physiological functions of microbiota-derived metabolites to help develop new diagnostic and therapeutic interventions for allergic diseases.

3. Understanding mechanisms of asthma and novel avenues for biomarkers, prevention and treatment

A survey study on antibiotic prescription practices for acute asthma exacerbations: An European academy of allergy and clinical immunology task force report.

Redel AL, Feleszko W, Arcolaci A, Cefaloni F, Atanaskovic-Markovic M, Braunstahl GJ, Boccabella C, Bonini M, Karavelia A, Louwers E, Mülleneisen N, O'Mahony L, Pini L, Rapiejko A, Shehu E, Sokolowska M, Untersmayr E, Tramper-Stranders G; EAACI Task Force on Conscious and Rational use of Antibiotics in Allergic Diseases. Clin Transl Allergy. 2024 Mar;14(3):e12345. doi: 10.1002/clt2.12345.

Guidelines recommend treating asthma exacerbations (AAEs) with bronchodilators combined with inhaled and/or systemic corticosteroids. Indications for antibiotic prescriptions for AAEs are usually not incorporated although the literature shows antibiotics are frequently prescribed. Aim: To investigate the antibiotic prescription rates in AAEs and explore the possible determining factors of those practices. A digital survey was created to determine the antibiotic prescription rates in AAEs and the influencing factors for the prescription practices. The survey was distributed among European academy of allergy and clinical immunology (EAACI) members by mass emailing and through regional/national societies in the Netherlands, Italy, Greece, and Poland. Furthermore, we retrieved local antibiotic prescription rates. In total, 252 participants completed the survey. Respondents stated that there is a lack of guidelines to prescribe antibiotics in AAEs. The median antibiotic prescription rate in this study was 19% [IQR: 0%-40%] and was significantly different between 4 professions: paediatrics 0% [IQR: 0%-37%], pulmonologists 25% [IQR: 10%-50%], general practitioners 25% [IQR: 0%-50%], and allergologists 17% [IQR: 0%-33%]) ($p = 0.046$). Additional diagnostic tests were performed in 71.4% of patients before prescription and the most common antibiotic classes prescribed were macrolides (46.0%) and penicillin (42.9%). Important clinical factors for health care providers to prescribe antibiotics were colorised/purulent sputum, abnormal lung sounds during auscultation, fever, and presence of comorbidities. In 19% of patients with AAEs, antibiotics were prescribed in various classes with a broad range among different subspecialities. This study stresses the urgency to compose evidence-based guidelines to aim for more rational antibiotic prescriptions for AAE.

Novel candidate biomarkers of the efficacy of allergen immunotherapy

Van Elst D*, Agache I*, Ram I et al and Sokolowska M. * equally contributed. In preparation.

Allergen immunotherapy (AIT) is the only curative treatment for patients suffering from allergic diseases such as allergic rhinitis (AR) and allergic asthma by inducing allergen-specific immune tolerance. To find potential biomarkers of efficacy of AIT we implemented an untargeted proteomics comparison of serum obtained 2 years after the start of AIT against house dust mite, grass pollen or cat antigens, from adults and children suffering from AR and allergic asthma. The control group included age- and gender-matched healthy controls. Serum proteomics data, obtained by mass spectrometry in a data-independent mode were compared between non-responders (NR) and responders to the therapy (R), and between NR and controls. Biomarker assessment and network association analyses were performed to investigate activated pathways and protein interactions. We detected 166 serum proteins in adults and 223 in children. In adults, six proteins were differentially expressed in NR as compared to R. No differentially expressed proteins were detected between NR and R in children. Western blot (WB) analysis of some of these candidate proteins validated these findings. When comparing enriched process networks in NR versus R, several inflammation, metabolic and the immune response related processes were significantly enriched. nterestingly, we found that distinctly identified biomarker candidates contribute to these processes. Identified potential biomarkers in the present study could provide an important step in understanding the long-term effects of AIT and in implementing a personalised medicine approach allowing selection of responders to AIT.

AllergoOncology: Biomarkers and refined classification for research in the allergy and glioma nexus—A joint EAACI-EANO position paper

Turner MC, Radzikowska U et al and Poli A. Allergy. 2024; 00: 1-21. doi:10.1111/all.15994.

This collaborative European Academy of Allergy and Clinical Immunology (EAACI) and European Association of Neuro-Oncology (EANO) Position Paper summarizes recent advances and emerging biomarkers for refined allergy and adult-type diffuse glioma classification to inform future epidemiological and clinical studies.

Sex hormones and asthma: The role of estrogen in asthma development and severity

Radzikowska U, Golebski K. Allergy. 2024. 78: 620-622. https://doi.org/10.1111/all.15548.

In this Editorial, authors summarize the study by Vijeyakumaran et al. investigating the association between type 2 inflammation and estrogen receptor signaling on Th2 cells in severe asthma.

Davos, May 2024

B Cell Immunology

Dr. Willem van de Veen, PhD

B cell immunology

B cells have a crucial role in IgE-mediated allergies due to their distinctive capability to generate allergen-specific IgE antibodies that bind to high-affinity IgE receptors (FcεRI) on mast cells and basophils, sensitizing them to allergens. Upon subsequent allergen exposure, the crosslinking of FcεRI-bound IgE initiates the release of pro-inflammatory mediators, leading to type I hypersensitivity reactions. In addition to their pro-inflammatory role, B cells, including regulatory B (Breg) cells, can also produce anti-inflammatory cytokines, providing immune regulatory functions. Serological mechanisms of immune regulation by B cells include the increase of IgG4 antibodies in patients undergoing allergen-specific immunotherapy, leading to immune tolerance. Thus, B cells are involved in the development of allergies as well as the development of tolerance to allergens. Our laboratory is interested in investigating various aspects of B cell immunology related to allergies and other immune disorders.

1. Development and maintenance of allergen-specific immune memory

Long lived immune memory and food allergy

Kelly Bruton,*, Manal Bel imam,*, Joshua F.E. Koenig, Ramona Hoh, Paula H. Ruiz de Azcarate, Sarita U. Patil, Manel Jordana, Willem van de Veen**, and Rodrigo Jimenez-Saiz**

* /** Authors contributed equally

Book chapter in 'reference collection in food science', Elsevier, 2023

The persistence of allergies can be attributed to a deeply embedded immunological memory that operates beyond the ephemeral lifespan of IgE antibodies. At the heart of this enduring allergic response are the interactions between, memory B cells, and CD4+ T cells, which together create a persistent allergic state.

In this book chapter we explore the intricate mechanisms underlying immune memory in the context of food allergies, emphasizing the dual perspectives of humoral and cellular memory. We outline how food allergies originate from type 2 immune responses to harmless environmental proteins, which in many cases, result in lifelong sensitization to specific allergens despite avoidance. This persistent sensitization suggests the existence of a robust allergen-specific immune memory, comprised of memory B cells, various types of antibody-secreting cells (including both short-lived and long-lived plasma cells), and CD4+ memory T cells (such as Th2, Th2a, and TFh cells). Focusing on humoral memory, we delve into the characteristics, differentiation, survival, and tissue localization of IgE+ plasma cells in the context of food allergies. We discuss the possible mechanisms involved in maintaining IgE levels despite the generally short-lived nature of IgE+ plasma cells and examine the potential role of long-lived plasma cells residing in the bone marrow in sustaining long-term IgE production.

Moreover, we examine the contributions of B-cell and T-cell memory to food allergies. It discusses the mechanisms of class-switch recombination that lead to the formation of IgE-switched B cells (Figure 1) and explores the diverse roles of CD4+ T cell subsets in maintaining immune memory related to food allergies.

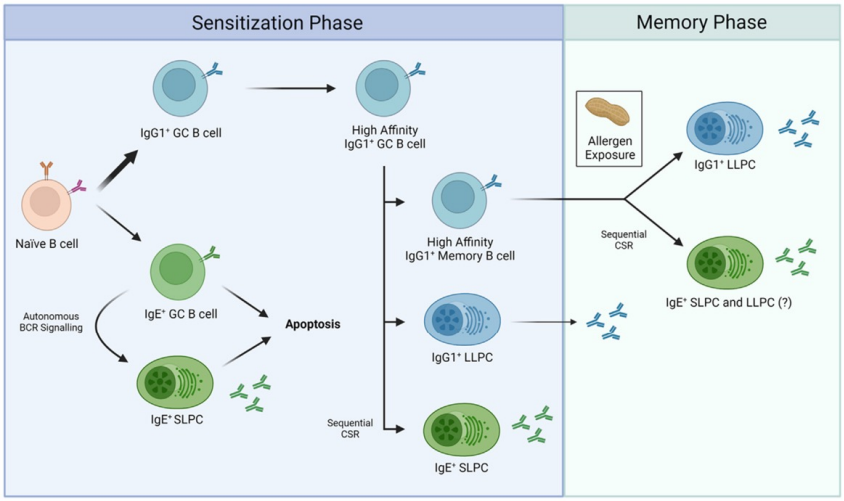


Figure 1. Cellular pathways of sequential class switch recombination during development of B cell memory. Left: The majority of activated allergen-specific naïve B cells switch to IgG1 and enter the GC. A small number of cells directly switch to IgE and enter the GC, though these are constrained by autonomous BCR signaling and rapidly differentiate into SLPCs. Both IgE+ SLPCs and GC B cells have a predisposition to apoptosis. IgG1+ GC B cells persist in the GC, accumulate high affinity mutations, and exit the GC as IgG1+ memory B cells or LLPCs. IgG1+ GC B cells can undergo sequential CSR to IgE and export as IgE+ SLPCs. Right: Upon allergen exposure, high affinity IgG1+ memory B cells differentiate into IgG1+ PCs and undergo sequential CSR to generate IgE+ SLPC which maintain IgE titers. IgE+ LLPCs may be generated in chronic allergen exposure conditions. BCR, B-cell receptor; CSR, class-switch recombination; GC, germinal center; Ig, immunoglobulin; LLPCs, long-lived plasma cells; SLPCs: short-lived plasma cells

In vivo dynamics of the allergen-specific B cell repertoire in a human model of high-dose allergen exposure

Willem van de Veen*, Ramona A. Hoh*, Ji-Yeun Lee, David Mirer, Monique Daanje, Mirelle Kleuskens, Hergen Spits, Scott D. Boyd**, Mübeccel Akdis**. * /** Authors contributed equally. In preparation

Understanding the mechanisms underlying the development and maintenance of allergen-specific B-cell memory is of paramount importance for devising targeted therapies to treat allergic diseases. To elucidate these mechanisms, we utilized three human in vivo models of high dose allergen exposure: long-term beekeepers, novice beekeepers, and allergic patients undergoing immunotherapy.

Methods: We tracked the development of B-cells and antibodies specific for the bee venom allergen PLA in long-term beekeepers for up to 20 years, in novice beekeepers for a period of one year, and in allergic patients before and after 3 months of venom immunotherapy. Blood was collected and PLA-specific B-cells were, purified, immortalized and subjected to BCR repertoire analysis. PLA-specific IgG1-4 and IgE antibodies were quantified using ELISA.

During the beekeeping season, PLA-specific B-cell frequencies increased, whereas PLA-specific antibodies remained stable over time in long-term beekeepers and did not vary between seasons. Novice beekeepers experienced a temporary increase in specific B-cells and antibodies following their initial bee stings. In allergic patients, immunotherapy resulted in significantly increased sIgG1 and sIgG4, but specific B-cells did not significantly increase. Most long-term beekeepers had PLA-specific clones that were found at different time points spanning a period of up to 20 years. PLA-specific clone frequencies varied between individuals but demonstrated remarkable stability over time in the same person. Clonal lineages exhibited multiple immunoglobulin heavy chain isotypes, including IgE, IgG1, IgG2, IgG3, and IgG4. Additionally, public antibody clonotypes against PLA were identified in different individuals.

Non-allergic individuals who are highly exposed to bee venom have allergen-specific clonal lineages that persist for many years, and these lineages exhibit clonal expansion and a significant level of diversity. Stability of PLA-specific antibodies indicates the presence of plasma cells that continuously provide a continuous supply of antibodies independent of persistent exposure. This may require long-term high dose exposure, as novice beekeepers do not display stable levels of specific antibodies. Long-term intrapersonal stability of PLA-specific clone frequencies indicates that a set number of clones dominate the allergen-specific B cell response and persist over many years. Presence of public clonotypes may aid in the development of targeted therapies.

Optimizing Flow Cytometric Analyses of B-Cell Receptor Immunoglobulin Heavy Chain Isotypes: A Comprehensive Evaluation of Fc Receptor Blocking Strategies and Their Impact on Detection Accuracy

Ozge Ardicli, Juan F. Lopez, Margot E. Starrenburg, Laura Buergi, K. Tayfun Carli, Cezmi A. Akdis, Mübeccel Akdis, Willem van de Veen. In preparation

Accurate identification of B cells expressing B cell receptors (BCR) of various immunoglobulin heavy chain isotypes using flow cytometry is a valuable tool for studying B cell responses. FcR blocking reagents, commonly used to prevent off-target antibody binding, often contain human IgG. Antibodies targeting different immunoglobulin isotypes, such as IgG and IgA, are employed to label BCR isotypes. However, the presence of human serum components, such as IgG in FcR blocking reagents, may affect staining accuracy. This study aims to assess the impact of FcR blocking reagents on detection of BCR heavy chain isotypes IgM, IgD, IgA1-2, and IgG1-4.

Peripheral blood mononuclear cells (PBMCs) were treated with FcR blocking reagents prior to staining with a B cell immunoglobulin heavy chain isotype phenotyping panel. Five FcR blocking reagents were tested: normal mouse serum, human AB serum and three commercial FcR blocking reagents.

While normal mouse serum did not affect the detection of any BCR heavy chain isotype, all three commercial FcR blocking reagents negatively impacted IgG1-4+ B cell detection. Human AB serum interfered with detection of IgM+, IgA1-2+, and IgG1-4+ B cells. Washing the blocking reagent away prior to staining partially restored the detection of B cells expressing IgG subclasses. Moreover, washing after incubation with human AB serum completely recovered detection of IgA1-2+ B cells.Evaluation of FcR blocking conditions on non-specific background staining revealed that mouse IgG2aκ binds non-specifically to FcR in monocytes. Washing the FcR blocking region before staining could potentially result in higher non-specific background, indicating that washing cells before staining adversely affects the blocking effect.

This study provides practical solutions to the inevitable challenges that may arise when utilizing FcR blocking reagents in cytometry panels for the analysis of B cells.

2. Regulatory B cells

Human Ascaris infection is associated with higher frequencies of IL-10 producing B cells

Zakzuk J, Lopez JF, Akdis C, Caraballo L, Akdis M and van de Veen W. Submitted

Ascaris lumbricoides has dual effects on the immune system of infected hosts. The IgE response to this parasite has been thoroughly studied, but little is known about cellular responses induced by infection. In this study, we explored the interplay between the parasite Ascaris lumbricoides infection and B cell responses in a helminth-endemic town in Colombia. We observed that infected individuals have higher frequencies of regulatory B cells, particularly in severe cases, suggesting an immunosuppressive response mediated by Bregs. Additionally, A. lumbricoides infection correlated with reduced levels of circulating ABA-1-specific IgG1 and IgE, indicating a modulation of antibody responses. Our findings suggest that A. lumbricoides infection mediates a dose-dependent immunosuppressive response characterized by an increase in Breg cells and concomitant suppression of ABA-1-specific humoral responses.

Observational study of changes in B cells, Breg cells and amoxicillin-specific immunoglobulins after a type-I hypersensitivity reaction in allergic patients to amoxicillin.

Ruben Fernandez-Santamaria, Maria Salas, Gador Bogas, Cristobalina Mayorga, Mübeccel Akdis, Cezmi Akdis, Maria Jose Torres and Willem van de Veen. In preparation

Immediate drug hypersensitivity reactions (IDHRs) to betalactams, notably triggered by amoxicillin, are on the rise. This study examines the humoral and cellular B cell responses in amoxicillin-allergic patients at various times post-reaction. Using samples from 20 allergic patients and 10 controls, we measured serum levels of specific immunoglobulin E (sIgE) and other immunoglobulins through tests like RAST and ImmunoCAP, alongside analyzing B cell and B regulatory (Breg) cell frequencies via flow cytometry. Findings reveal early post-reaction phases show high sIgE, indicative of the acute phase, with a notable decrease after six months. Contrarily, specific immunoglobulin G (sIgG) levels drop in the first 12 months then increase, highlighting a potential protective role. Notably, IgG2 and IgG4 levels varied significantly over time, suggesting differential immune responses. The study also found a decrease in certain B cell subsets and regulatory cells immediately following the reaction, with a gradual increase over time. This suggests a complex interplay of humoral and cellular mechanisms in IDHRs to amoxicillin, highlighting the dynamic nature of the immune response over time following an allergic reaction to the drug.

3. Food allergy and Eosinophilic esophagitis

Outcomes reported in randomized controlled trials for mixed and non-IgE mediated food allergy: a systematic review

Manal Bel imam*, Charalampos-Vlasios Stikas*, Payal Guha, Bo L Chawes, Derek Chu, Matthew Greenhawt, Ekaterina Khaleva, Daniel Munblit, Nikita Nekliudov, Willem van de Veen, Ann-Marie M Schoos on behalf of Core Outcome Measures for Food Allergy (COMFA) consortium. Clin Exp Allergy. 2023 May;53(5):526-535. doi: 10.1111/cea.14304.

Mixed and non-IgE-mediated food allergies can greatly impact patients and their families, necessitating reliable outcome measures for clinical trials. To address this, the Core Outcome Measures for Food Allergy (COMFA) project analyzed outcomes reported in randomized clinical trials (RCTs) investigating treatments for food protein-induced enterocolitis syndrome, food protein-induced allergic proctocolitis, food protein-induced enteropathy, and eosinophilic gastrointestinal disorders. We reviewed 26 eligible studies published until October 14th, 2022, with 23 focused on eosinophilic esophagitis (EoE). Most interventions were corticosteroids or monoclonal antibodies, and patient-reported dysphagia was frequently assessed using non-validated questionnaires. Peak tissue eosinophil count was the primary outcome in most EoE studies, often using non-validated assessment methods. Only 3 RCTs examined other forms of food allergy, reporting on fecal immunological markers and patient-reported outcomes. Heterogeneity and lack of validation in outcome measures were prevalent in these trials. Core outcomes for EoE exist and should be implemented in future trials, while the development of core outcomes for other mixed or non-IgE-mediated food allergies is needed to facilitate effective treatment development.

Circulating food allergen-specific antibodies are elevated in eosinophilic esophagitis patients.

Manal Bel Imam, Sayuri Iwasaki, Sophieke Lems, Philipp Schreiner, Mübeccel Akdis, Luc Biedermann, Alex Straumann, Willem van de Veen. In preparation

Eosinophilic esophagitis (EoE) is a chronic, immune-mediated inflammatory condition with an incompletely understood etiology. Studies have suggested the involvement of Th2 cytokines and antibody production, along with food ingestion as a potential trigger. However, several observations suggest that EoE is not an IgE-mediated food allergy. Instead, it has been noted that patients with EoE exhibit elevated levels of IgG4 in esophageal biopsies and circulating food antigen-specific IgG4. This project aims to uncover the basic mechanisms underlying EoE, particularly focusing on antigen-specific B cell responses.

Blood samples from patients with inactive, moderately active, and highly active EoE were collected at the Swiss EoE Clinics at the University Hospital Zurich. Plasma levels of IgG and IgG4 against casein, whey, wheat, egg extracts, and individual cow's milk allergens were measured using enzyme-linked immunosorbent assay (ELISA). Additionally, the levels of IgG1, IgG2, IgG3, IgA1, and IgA2 against individual casein and whey components were assessed. For selected patients with high levels of food allergen-specific antibodies, the frequency of alpha s1-casein- and beta-lactoglobulin-specific B cells was determined using flow cytometry.

Our study identified patients with varying levels of food-specific antibody isotypes, including highly positive, intermediate, and low levels. Notably, differences in casein- and whey-derived allergens were observed not only between healthy controls and EoE samples but also between the active and inactive EoE subgroups. The attempt to isolate food allergen-specific B cells was unsuccessful, indicating that antibody production in EoE might be local rather than systemic.

Through our analysis, we were able to identify patients with elevated levels of food antigen-specific antibodies. Moving forward, we will isolate and characterize antigen-specific B cells and conduct a B cell receptor (BCR) repertoire analysis in a subset of patients. Additionally, tissue biopsies will be examined using confocal microscopy to assess the presence of food antigens, specifically those derived from cow's milk, and the presence of B cells.

Core Outcome Set for IgE-mediated food allergy clinical trials and observational studies of interventions: International Delphi consensus study 'COMFA'.

Demidova A, Drewitz KP, Kimkool P, Banjanin N, Barzylovich V, Botjes E, Capper I, Castor MAR, Comberiati P, Cook EE, Costa J, Chu DK, Epstein MM, Galvin AD, Giovannini M, Girard F, Golding MA, Greenhawt M, Ierodiakonou D, Jones CJ, Khaleva E, Knibb RC, Macit-Çelebi MS, Mack DP, Mafra I, Marchisotto MJ, Mijakoski D, Nekliudov N, Özdemir C, Patel N, Pazukhina E, Protudjer JLP, Rodríguez Del Rio P, Roomet J, Sammut P, Schoos AM, Schopfer AF, Schultz F,

Seylanova N, Skypala I, Sørensen M, Stoleski S, Stylianou E, Upton J, van de Veen W, Genuneit J, Boyle RJ, Apfelbacher C, Munblit D; COMFA Consortium. Allergy. 2024 Mar 3. doi: 10.1111/all.16023.

The Core Outcome Measures for Food Allergy (COMFA) initiative

sought to create a standardized set of outcomes for evaluating food allergy (FA) treatments due to the inconsistencies in outcomes reported across studies. Through a review of literature and a two-round Delphi process complemented by a hybrid consensus meeting, initial outcomes were narrowed down. Despite starting with 39 potential outcomes, the iterative process, involving 778 participants from 52 countries, concluded with 'allergic symptoms' and 'quality of life' being chosen as core outcomes for FA clinical trials and observational studies. This decision underscores the importance of consistent outcome reporting in FA research, aiming to enhance study comparisons and improve treatment evaluations. Future efforts by COMFA will focus on defining the optimal methods for measuring these core outcomes, alongside the mandatory reporting of adverse events.

4. B cell responses and infections

The effect of measles on allergic sensitization in children

Tan Nguyen, Renske Schappin, Suzanne Pasmans, Marco Schreurs, Rik de Swart, Willem van de Veen. Pediatric Allergy and Immunology. 2023 Oct 10;34;10: e14033.

Measles virus (MV) is a highly infectious and potentially fatal virus that is clinically characterized by fever, cough, and a maculopapular skin rash, and immunologically infects both memory B and T lymphocytes and plasma cells expressing CD150.

As the immune system restricts viral replication and clears MV-infected memory cells, it results in transient functional immune amnesia, but at the same time, an MV infection also elicits a strong immunologic response, conferring life-long immunity. This contradiction is also known as the measles paradox.

Such immune amnesia is considered harmful in most cases because of the loss of protective immune memory against pathogens. However, in the context of allergies, a loss of allergen-specific type-II immune memory has the potential to result in desensitization, as measles could result in the depletion of allergen-specific B and T-lymphocytes, plasma cells, and IgE antibodies

A retrospective cohort study was conducted to investigate whether measles virus infection was associated with changes in allergic sensitization. The study analyzed previously collected paired plasma samples from children who were not vaccinated against measles before and after measles. Total and allergen-specific IgE antibody levels in these samples were analyzed before and after measles infection to establish a possible link between MV infections and allergic sensitization

We observed a decrease in total IgE and specific IgE levels. However, it should be noted that a similar reduction in IgE levels was observed in paired plasma samples from children who had not experienced measles during the study period. This suggests the possibility that these changes were related to seasonal or environmental factors rather than MV infection. Therefore, a larger longitudinal observational cohort study with more frequent sampling time points, including the day of MV infection, during the infection, and post-infection, is warranted.

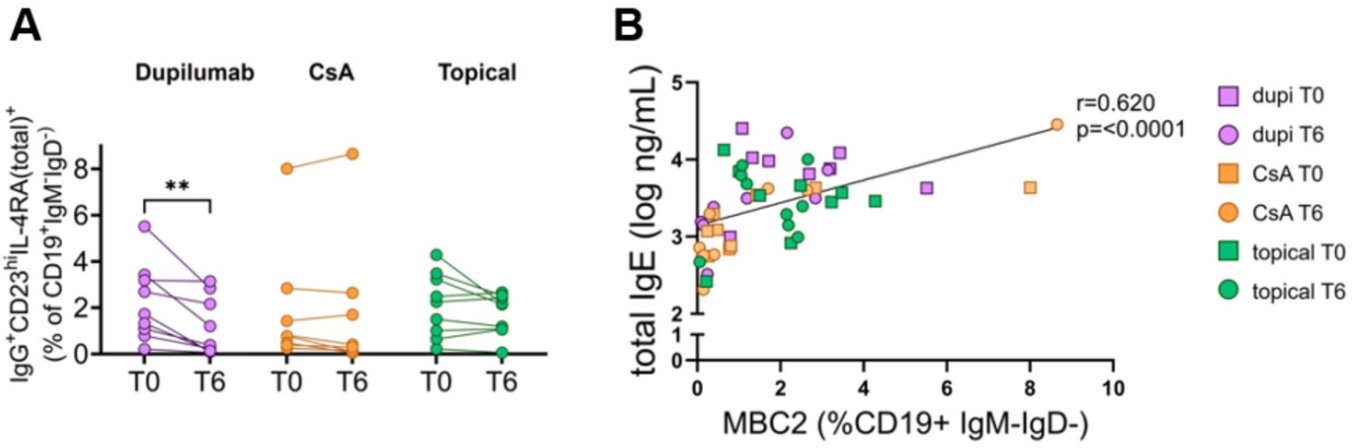


Figure 2. MBC2 frequencies are decreased after dupilumab treatment and correlate with circulating total IgE levels. (A) Frequencies of MBC2 cells before and after treatment. (B) Correlation of MBC2 frequency in CD19+IgM-IgD- switched B-cells (x-axis) and total IgE plasma levels (y-axis, log scale). Graph depicts N=8 in the dupilumab group and N=9 in the CsA and topical therapy groups (total N=26). A Spearman correlation coefficient, statistically tested: r=0.620, p<0.0001.

5. Using biologics to study human in vivo immune responses with a focus on B cells.

Dupilumab Treatment Decreases MBC2s, Correlating with Reduced IgE Levels in Pediatric AD

Margot Elise Starrenburg, Laura Buergi, N. Tan Nguyen, Juan F. Lopez-Crespo, Anouk Nouwen, Manal Bel Imam, Nicolette J. T. Arends, Peter J. Caspers, Mübeccel Akdis, Suzanne G. M. A. Pasmans, Willem van de Veen. Submitted

In this study we investigated the effects of dupilumab treatment compared to alternative therapies on the frequency of the recently identified Type 2–polarized memory B (MBC2) and their correlation to total IgE levels in pediatric patients with atopic dermatitis (AD). Type 2 immunity, characterized by increased IgE production, is central to AD pathogenesis. Dupilumab inhibits IL-4 and IL-13 signaling, crucial cytokines involved in IgE class switch recombination. Recent research identifies MBC2 as IgE-producing B-cell precursors, linked to total IgE serum levels in atopic patients. Total IgE levels decrease during dupilumab treatment.

Pediatric AD patients in an ongoing trial were randomized into three treatment groups: dupilumab, cyclosporine, or topical treatment. Blood samples were collected at baseline (T0) and after 6 months (T6). Flow cytometry and ELISA were used for phenotyping and assessing total IgE levels, respectively.

Results from 36 patient samples revealed a significant reduction in MBC2 frequency and total IgE levels in dupilumab-treated patients (Figure 2). Additionally, a significant correlation was found between MBC2s and total IgE levels. The reduction in MBC2s and total IgE levels was not observed with cyclosporine or topical treatment. Dupilumab binds to IL-4RA, inhibiting IL-4 and IL-13 signaling, leading to decreased MBC2 cells and total IgE levels. The study confirms the role of IL-4 signaling in MBC2 differentiation or survival, revealing a novel mechanism of dupilumab's impact on the atopic signature.

Clinical implications include the potential of MBC2 as precursors of IgE-producing B-cells, with their frequency correlating with total IgE levels. This suggests MBC2 and total IgE levels are IL-4 signaling dependent, as both decrease during dupilumab treatment in pediatric AD patients. Key findings indicate that dupilumab treatment reduces MBC2 cells and total IgE levels, highlighting its effectiveness in managing AD. This study contributes to understanding the immunological mechanisms underlying AD and the therapeutic effects of dupilumab.

In conclusion, the study demonstrates that inhibition of IL-4RA leads to decreased MBC2 cells and total IgE levels in pediatric AD patients, providing insights into the pathogenesis of AD and the mechanism of action of dupilumab. These findings have implications for the development of targeted therapies for AD and related atopic diseases.

Characterization of B cell responses during immune checkpoint inhibitor treatment in metastatic melanoma

Lacin Cevhertas, Mirjam Fassler , Fiamma Berner , Mübeccel Akdis, Lukas Flatz, Willem van de Veen. In preparation

Immune checkpoint inhibitor (ICI) therapies have gained approval for treating malignant melanoma, yet the response to these treatments varies among patients. This variability underscores the urgent need to discover new biomarkers that can predict how patients will react to ICI therapy and determine their suitability for it. By examining the phenotypes of B cells via surface markers, we can deepen our understanding of B cell immunity in melanoma and how ICIs influence B cells. To this end, we analyzed circulating B cells in healthy individuals and a cohort of 25 metastatic melanoma patients, both before and after they received anti-PD1 and/or anti-CTLA4 monoclonal antibodies, at both early and late stages of their response to the treatment. We found that patients who did not respond to the treatment (n=12) exhibited significant changes in the frequencies of naïve B cells, switched B cells, and IgA+ B cells during their therapy. Notably, B cells from patients who responded to the treatment showed higher expression of the BAFF receptor compared to those from non-responders, right from the baseline and into the early response stage. Furthermore, non-responders had significantly elevated serum levels of BAFF compared to responders at the outset. Our research thus indicates that ICI treatment impacts B cell attributes through the modulation of BAFF receptor expression, and that the soluble protein BAFF might serve as a valuable biomarker for predicting the response of metastatic melanoma patients to ICI therapy.

Exclusion of Ranitidine From Premedication Regimens During Paclitaxel Treatment

Daan W. Huntjens, Joost W. Vanhommerig, Willem van de Veen, Mirjam Crul, PhD. JAMA Oncol. 2024;10(1):131-132. doi:10.1001/jamaoncol.2023.4821

In this study we examined the impact of excluding ranitidine, a histamine-2 receptor antagonist, from paclitaxel chemotherapy premedication due to its 2019 market withdrawal over contamination concerns. Conducted at Amsterdam University Medical Center, we retrospectively analyzed 2503 paclitaxel administrations between 2016 and 2020 to evaluate hypersensitivity reaction (HSR) incidences pre- and post-ranitidine exclusion. Findings from logistic regression showed no significant difference in HSR incidence between cohorts with or without ranitidine, suggesting age, sex, and allergy history as more significant HSR predictors. This largest, seasonally inclusive study implies ranitidine's exclusion from premedication does not affect HSR rates, challenging adherence to initial drug registration recommendations.

Davos, May 2024


WIR
WIR


STANDARD BIOTOOLS
Advancing spatial biology assays with rapid, high-plex whole slide imaging

PUBLICATIONS

Akdis M, Akdis CA. Legends of allergy and immunology: Kurt Blaser and major contributions to deciphering the role of T cells in allergic disease. Allergy. 2023 May;78(5):1393-1394. doi: 10.1111/all.15648. Epub 2023 Jan 31. PMID: 36718675, IPF: 12.4.

Bayram H, Rastgeldi Dogan T, Şahin ÜA, Akdis CA., Environmental and health hazards by massive earthquakes., Allergy. 2023 Aug;78(8):2081-2084. doi: 10.1111/all.15736. Epub 2023 Jun 14., PMID: 37026989, IPF: 12.4.

Bousquet J, Melén E, Haahtela T, Koppelman GH, Togias A, Valenta R, Akdis CA, Czarlewski W, Rothenberg M, Valiulis A, Wickman M, Akdis M, Aguilar D, Bedbrook A, Bindslev-Jensen C, Bosnic-Anticevich S, Boulet LP, Brightling CE, Brussino L, Burte E, Bustamante M, Canonica GW, Cecchi L, Celedon JC, Chaves Loureiro C, Costa E, Cruz AA, Erhola M, Gemicioglu B, Fokkens WJ, Garcia-Aymerich J, Guerra S, Heinrich J, Ivancevich JC, Keil T, Klimek L, Kuna P, Kupczyk M, Kvedariene V, Larenas-Linnemann DE, Lemonnier N, Lodrup Carlsen KC, Louis R, Makela M, Makris M, Maurer M, Momas I, Morais-Almeida M, Mullol J, Naclerio RN, Nadeau K, Nadif R, Niedoszytko M, Okamoto Y, Ollert M, Papadopoulos NG, Passalacqua G, Patella V, Pawankar R, Pham-Thi N, Pfaar O, Regateiro FS, Ring J, Rouadi PW, Samolinski B, Sastre J, Savouré M, Scichilone N, Shamji MH, Sheikh A, Siroux V, Sousa-Pinto B, Standl M, Sunyer J, Taborda-Barata L, Toppila-Salmi S, Torres MJ, Tsiligianni I, Valovirta E, Vandenplas O, Ventura MT, Weiss S, Yorgancioglu A, Zhang L, Abdul Latiff AH, Aberer W, Agache I, Al-Ahmad M, Alobid I, Ansotegui IJ, Arshad SH, Asayag E, Barbara C, Baharudin A, Battur L, Bennoor KS, Berghea EC, Bergmann KC, D Bernstein, M Bewick, H Blain, M Bonini, F Braido, R Buhl, R S Bumbacea, A Bush, M Calderon, M Calvo-Gil, P Camargos, L Caraballo,…, I Ogulur, K Ohta, …, J M Anto. Allergy. 2023 May;78(5):1169-1203. doi: 10.1111/all.15679. IPF: 12.4

Cabanillas B, Murdaca G, Guemari A, Torres MJ, Azkur AK, Aksoy E, Vitte J, de Las Vecillas L, Giovannini M, Fernández-Santamaria R, Castagnoli R, Orsi A, Amato R, Giberti I, Català A, Ambrozej D, Schaub B, Tramper-Stranders GA, Novak N, Nadeau KC, Agache I, Akdis M, Akdis CA. A compilation answering 50 questions on Monkeypox virus and the current Monkeypox outbreak. Allergy. 2023 Jan 1. doi: 10.1111/all.15633. Online ahead of print.PMID: 36587287. IPF: 12.4.

Chang I, Kaushik A, Satitsuksanoa P, Yang M, Buergi L, Schneider SR, Babayev H, Akdis CA, Nadeau K, van de Veen W, Akdis M. Distinct and mutually exclusive Ca²⁺ flux- and adenylyl cyclase-inducing gene expression profiles of G-protein-coupled receptors on human antigen-specific B cells. Allergy. 2023 Nov;78(11):3016-3019. doi: 10.1111/all.15858. Epub 2023 Aug 24. PMID: 37615338. IPF: 12.4.

Jutel M, Agache I, Zemelka-Wiacek M, Akdis M, Chivato T, Del Giacco S, Gajdanowicz P, Gracia IE, Klimek L, Lauerma A, Ollert M, O'Mahony L, Schwarze J, Shamji MH, Skypala I, Palomares O, Pfaar O, Torres MJ, Bernstein JA, Cruz AA, Durham SR, Galli SJ, Gómez RM, Guttman-Yassky E, Haahtela T, Holgate ST, Izuhara K, Kabashima K, Larenas-Linnemann DE, von Mutius E, Nadeau KC, Pawankar R, Platts-Mills TAE, Sicherer SH, Park HS, Vieths S, Wong G, Zhang L, Bilò MB, Akdis CA. Nomenclature of allergic diseases and hypersensitivity reactions: Adapted to modern needs: An EAACI position paper. Allergy. 2023 Nov;78(11):2851-2874. doi: 10.1111/all.15889. Epub 2023 Oct 10. PMID: 37814905. IPF: 12.4.

Jutel M, Zemelka-Wiacek M, Ordak M, Pfaar O, Eiwegger T, Rechenmacher M, Akdis CA., The artificial intelligence (AI) revolution: How important for scientific work and its reliable sharing., Allergy. 2023 Aug;78(8):2085-2088. doi: 10.1111/all.15778. Epub 2023 Jun 5., PMID: 37278131. IPF: 12.4.

Kortekaas Krohn I, Badloe FMS, Herrmann N, Maintz L, De Vriese S, Ring J; CK-CARE Study Group; Bieber T, Gutermuth J., Immunoglobulin E autoantibodies in atopic dermatitis associate with Type-2 comorbidities and the atopic march., Allergy. 2023 Dec;78(12):3178-3192. doi: 10.1111/all.15822. Epub 2023 Jul 24., PMID: 37489049. IPF: 12.4.

Kwasniewski M, Korotko U, Chwialkowska K, Niemira M, Jaroszewicz J, Sobala-Szczygiel B, Puzanowska B, Moniuszko-Malinowska A, Pancewicz S, Parfieniuk-Kowerda A, Martonik D, Zarebska-Michaluk D, Simon K, Pazgan-Simon M, Mozer-Lisewska I, Bura M, Adamek A, Tomasiewicz K, Pawłowska M, Piekarska A, Berkan-Kawinska A, Horban A, Kowalska J, Podlasin R, Wasilewski P, Azzadin A, Czuczwar M, Borys M, Piwowarczyk P, Czaban S, Bogocz J, Ochab M, Kruk A, Uszok S, Bielska A, Szałkowska A, Raczkowska J, Sokołowska G, Chorostowska-Wynimko J, Jezela-Stanek A, Rozy A, Lechowicz U, Połowianiuk U, Tycinska A, Grubczak K, Starosz A, Izdebska W, Krzemiński TF, Bousqet J, Franchini G, Hadlock J, Kretowski A, Akdis M, Akdis CA, Sokolowska M, Eljaszewicz A, Flisiak R, Moniuszko M. Implementation of the web-based calculator estimating odds ratio of severe COVID-19 for unvaccinated individuals in a country with high coronavirus-related death toll. Allergy. 2023 Jan;78(1):311-314. doi: 10.1111/all.15524. Epub 2022 Sep 29. IPF 14.71, PMID: 36129377. IPF: 12.4.

Lunjani N, Akdis CA, O'Mahony L. Importance of examining atopic dermatitis disease mechanisms in African populations. Allergy. 2023 Jan;78(1):329-330. doi: 10.1111/all.15559.PMID: 36576006. IPF: 12.4.

Maintz L, Welchowski T, Herrmann N, Brauer J, Traidl-Hoffmann C, Havenith R, Müller S, Rhyner C, Dreher A, Schmid M, Bieber T; CK-CARE study group., IL-13, periostin and dipeptidyl-peptidase-4 reveal endotype-phenotype associations in atopic dermatitis., Allergy. 2023 Jan 17. doi: 10.1111/all.15647. Online ahead of print., PMID: 36647778. IPF: 12.4.

Maintz L, Schmitz MT, Herrmann N, Müller S, Havenith R, Brauer J, Rhyner C, Dreher A, Bersuch E, Fehr D, Hammel G, Reiger M, Luschkova D, Neumann A, Lang CCV, Renner ED, Schmid-Grendelmeier P, Traidl-Hoffmann C, Akdis CA, Lauener R, Brüggen MC,

Schmid M, Bieber T., Atopic dermatitis: Correlation of distinct risk factors with age of onset in adulthood compared to childhood., Allergy. 2023 Aug;78(8):2181-2201. doi: 10.1111/all.15721. Epub 2023 Apr 16., PMID: 36946297. IPF: 12.4.

Marone G, Triggiani M, Casolaro V, Stellato C, de Paulis A, Holgate ST, Akdis CA, Galli SJ., In memoriam: Lawrence M. Lichtenstein (1934-2022). Allergy. 2023 Jan;78(1):331-332. doi: 10.1111/all.15549. Epub 2022 Oct 20. PMID: 36219503. IPF: 12.4.

Mitamura M, Reiger M, Kim J, Xiao Y, Zhakparov D, Tan G, Rückert B, Rinaldi AO, Baerenfaller K, Akdis, Brüggen MC, Nadeau KC, Brunner PM, Roqueiro D, Traidl-Hoffmann C, Akdis CA. Spatial transcriptomics combined with single-cell RNA-sequencing unravels the complex inflammatory cell network in atopic dermatitis. Allergy. 2023 June 14. doi: https://doi.org/10.1111/all.15781. IPF: 12.4.

Ogulur I, Yazici D, Pat Y, Bingöl EN, Babayev H, Ardicli S, Heider A, Rückert B, Sampath V, Dhir R, Akdis M, Nadeau K, Akdis CA. Mechanisms of gut epithelial barrier impairment caused by food emulsifiers polysorbate 20 and polysorbate 80. Allergy. 2023 Sep;78(9):2441-2455. doi: 10.1111/all.15825. Epub 2023 Aug 2. PMID: 37530764. IPF: 12.4.

Papadopoulos NG, Akdis C, Akdis M, et al. Addressing adverse synergies between chemical and biological pollutants at schools-The 'SynAir-G' hypothesis. Allergy. Published online August 31, 2023. doi:10.1111/all.15857. IPF: 12.4.

Parsons ES, Liu F, Kaushik A, Lee A, Schuetz J, Dunham D, Seastedt H, Ogulur I, Heider A, Tan G, Shah A, Cao S, Smith E, Kost L, Acharya S, Prunicki M, Rothenberg M, Sindher S, Leib R, Akdis CA, Nadeau K, Lejeune S. Detection of gut and mucosal peptides through TOMAHAQ in healthy individuals. Allergy. 2023 Jul;78(7):2052-2055. doi: 10.1111/all.15698. IPF: 12.4.

Pawankar R, Akdis CA., Climate change and the epithelial barrier theory in allergic diseases: A One Health approach to a green environment., Allergy. 2023 Nov;78(11):2829-2834. doi: 10.1111/all.15885. Epub 2023 Sep 7., PMID: 37675628. IPF: 12.4.

Rinaldi AO, Li M, Barletta E, D'Avino P, Yazici D, Pat Y, Ward S, Burla D, Tan G, Askary N, Larsson R, Bost J, Babayev H, Dhir R, Gaudenzio N, Akdis M, Nadeau K, Akdis CA, Mitamura Y. Household laundry detergents disrupt barrier integrity and induce inflammation in mouse and human skin. Allergy. 2023 Sep 27. doi: 10.1111/all.15891. Epub ahead of print. PMID: 37766519. IPF: 12.4.

Roth-Walter F, Berni Canani R, O'Mahony L, Peroni D, Sokolowska M, Vassilopoulou E, Venter C. Nutrition in chronic inflammatory conditions: Bypassing the mucosal block for micronutrients. Allergy. 2023 Dec 12. doi: 10.1111/all.15972. Online ahead of print. PMID 38084827. IPF 12.4.

Roth-Walter F, Adcock IM, Benito-Villalvilla C, Bianchini R, Bjermer L, Caramori G, Cari L, Chung KF, Diamant Z, Eguiluz-Gracia I, Knol EF, Jesenak M, Levi-Schaffer F, Nocentini G, O'Mahony L, Palomares O, Redegeld F, Sokolowska M, Van Esch BCAM, Stellato C. Metabolic pathways in immune senescence and inflammaging: Novel therapeutic strategy for chronic inflammatory lung diseases. An EAACI position paper from the Task Force for Immunopharmacology. Allergy. 2023 Dec 18. doi: 10.1111/all.15977. Online ahead of print. PMID: 38108546 IPF 12.4.

Rovira Rubió J, Megremis S, Pasioti M, Lakoumentas J, Constantinides B, Xepapadaki P, Bachert C, Finotto S, Jartti T, Andreakos E, Stanic B, Akdis CA, Akdis M, Papadopoulos NG. Respiratory virome profiles reflect antiviral immune responses. Allergy. 2023 Jan 3. doi: 10.1111/all.15634. Online ahead of print. PMID: 36595290. IPF: 12.4.

Shamji MH, Ollert M, Adcock IM, Bennett O, Favaro A, Sarama R, Riggioni C, Annesi-Maesano I, Custovic A, Fontanella S, Traidl-Hoffmann C, Nadeau K, Cecchi L, Zemelka-Wiacek M, Akdis CA, Jutel M, Agache I., EAACI guidelines on environmental science in allergic diseases and asthma - Leveraging artificial intelligence and machine learning to develop a causality model in exposomics., Allergy. 2023 Jul;78(7):1742-1757. doi: 10.1111/all.15667. Epub 2023 Feb 15.
PMID: 36740916. IPF: 12.4.

Yazici D, Pat Y, Mitamura Y, Akdis CA, Ogulur I. Detergent-induced eosinophilic inflammation in the esophagus: A key evidence for the Epithelial Barrier Theory. Allergy. 2023 Jan 16. doi: 10.1111/all.15646. Online ahead of print.PMID: 36645729. IPF: 12.4.

Yazici D, Cagan E, Tan G, Li M, Do E, Kucukkase OC, Simsek A, Kizmaz MA, Bozkurt T, Aydin T, Heider A, Rückert B, Brüggen MC, Dhir R, O'Mahony L, Akdis M, Nadeau KC, Budak F, Akdis CA, Ogulur I. Disrupted epithelial permeability as a predictor of severe COVID-19 development. Allergy. 2023 Oct;78(10):2644-2658. doi: 10.1111/all.15800. Epub 2023 Jul 8. PMID: 37422701. IPF: 12.4.

Santos AF, Riggioni C, Agache I, Akdis CA, Akdis M, Alvarez-Perea A, Alvaro-Lozano M, Ballmer-Weber B, Barni S, Beyer K, Bindslev-Jensen C, Brough HA, Buyuktiryaki B, Chu D, Del Giacco S, Dunn-Galvin A, Eberlein B, Ebisawa M, Eigenmann P, Eiwegger T, Feeney M, Fernandez-Rivas M, Fisher HR, Fleischer DM, Giovannini M, Gray C, Hoffmann-Sommergruber K, Halken S, Hourihane JO, Jones CJ, Jutel M, Knol E, Konstantinou GN, Lack G, Lau S, Marques Mejias A, Marchisotto MJ, Meyer R, Mortz CG, Moya B, Muraro A, Nilsson C, Lopes de Oliveira LC, O'Mahony L, Papadopoulos NG, Perrett K, Peters RL, Podesta M, Poulsen LK, Roberts G, Sampson HA, Schwarze J, Smith P, Tham EH, Untersmayr E, Van Ree R, Venter C, Vickery BP, Vlieg-Boerstra B, Werfel T, Worm M, Du Toit G, Skypala I. EAACI guidelines on the diagnosis of IgE-mediated food allergy. Allergy. 2023 Dec;78(12):3057-3076. doi: 10.1111/all.15902. Epub 2023 Oct 10. PMID: 37815205. IPF: 12.4.

Santos AF, Riggioni C, Halken S, Muraro A, Akdis CA, Roberts G, Du Toit G, Skypala I., Executive summary of the EAACI guidelines on diagnosis of IgE-mediated food allergy., Allergy. 2023

Dec;78(12):3053-3056. doi: 10.1111/all.15906. Epub 2023 Oct 10., PMID: 37815198. IPF: 12.4.

Sasaki M, Sundberg M, Frei R, Ferstl R, Heye KN, Willems EP, Akdis CA, Lauener R; CK-CARE Study Group; Roduit C., Electrical impedance spectroscopy detects skin barrier dysfunction in childhood atopic dermatitis. , Allergy. 2024 Jan;79(1):142-152. doi: 10.1111/all.15895. Epub 2023 Sep 27., PMID: 37753955. IPF: 12.4.

Zemelka-Wiacek M, Agache I, Akdis CA, Akdis M, Casale TB, Dramburg S, Jahnz-Różyk K, Kosowska A, Matricardi PM, Pfaar O, Shamji MH, Jutel M. Hot topics in allergen immunotherapy, 2023: Current status and future perspective. Allergy. 2023 Nov 20. doi: 10.1111/all.15945. Online ahead of print. PMID: 37984449. IPF: 12.4.

Zhang HP, Sun YL, Wang YF, Yazici D, Azkur D, Ogulur I, Azkur AK, Yang ZW, Chen XX, Zhang AZ, Hu JQ, Liu GH, Akdis M, Akdis CA, Gao YD. Recent developments in the immunopathology of COVID-19. Allergy. 2023 Feb;78(2):369-388. doi: 10.1111/all.15593. Epub 2022 Dec 5. PMID: 36420736; PMCID: PMC10108124. IPF: 12.4.

Zhang L, Akdis CA., Resolving the etiology and treatments of allergic diseases., Allergy. 2023 Jun;78(6):1419-1421. doi: 10.1111/all.15727., PMID: 36965003 . IPF: 12.4.

Losol P, Sokolowska M, Hwang Y-K, Ogulur I, Mitamura Y, Yazici D, Pat Y, Radzikowska U, Ardicli S, Yoon J-E, et al. Epithelial Barrier Theory: The Role of Exposome, Microbiome, and Barrier Function in Allergic Diseases. Allergy Asthma Immunol Res. 2023 Nov;15(6):705-724. DOI: 10.4168/aair.2023.15.6.705. IPF: 5.026.

Sokolowska M, Radzikowska U. How can allergen immunotherapy protect against COVID-19? American Journal of Respiratory and Critical Care Medicine, 2023, online, ahead of print: https://doi.org/10.1164/rccm.202302-0317LE. IPF 24.7.

Ozdemir C, Kucuksezer UC, Ogulur I, Pat Y, Yazici D, Agache I, Jutel M, Nadeau KC, Akdis M, Akdis CA. How does global warming contribute to disorders originating from an impaired epithelial barrier? Ann Allergy Asthma Immunol. 2023 Dec;131(6):703-712. doi: 10.1016/j.anai.2023.08.010. Epub 2023 Aug 22. PMID: 37619777. IPF: 6.47.

Kucuksezer UC, Ozdemir C, Yazici D, Pat Y, Mitamura Y, Li M, Sun N, D'Avino P, Bu X, Zhu X, Akdis M, Nadeau K, Ogulur I, Akdis CA. The epithelial barrier theory: Development and exacerbation of allergic and other chronic inflammatory diseases. Asia Pac Allergy. 2023 Mar;13(1):28-39. doi: 10.5415/apallergy.0000000000000005. Epub 2023 Apr 28. PMID: 37389096; PMCID: PMC10166244. IPF: 2.0

Ragamin A, Schappin R, de Graaf M, Tupker RA, Fieten KB, van Mierlo MMF, Bronner MB, Romeijn GLE, Sloot MM, Boesjes CM, van der Rijst L, Arents BWM, Rustemeyer T, Schuttelaar MLA, Pasmans SGMA. The effectiveness of antibacterial therapeutic clothing compared with non-antibacterial therapeutic clothing in patients with moderate-to-severe atopic dermatitis: A randomized controlled, observer-blind pragmatic trial (ABC trial). Br J Dermatol. 2023 Nov 4:ljad437. PMID: 37936331. IPF:11.1.

Correia-Melo C., Kamrad S., Tengölics R., Messner C. B., Trebulle P., Townsend S., Varma S. J., Freiwald A., Heineke B. M., Campbell K., Herrera-Dominguez L., Aulakh S. K., Szyrwiel L., Yu J. S. L., Zelezniak A., Demichev V., Mülleder M., Balazs P., Alam M. T. & Ralser M. (2023). Cell-cell metabolite exchange creates a pro-survival metabolic environment that extends lifespan. Cell, 186(1), 63-79. IPF: 64. https://doi.org/10.1016/j.cell.2022.12.007. IPF: 64

Messner C. B., Demichev V., Muenzner J., Aulakh S. K., Barthel N., Röhl A., Herrera-Dominguez L., Egger A., Kamrad S., Hou J., Tan G., Lemke O., Calvani E., Szyrwiel L., Mülleder M., Lilley K. S., Boone C., Kustatscher G., & Ralser M. (2023). The proteomic landscape of genome-wide genetic perturbations. Cell, 186(9), 2018-2034. https://doi.org/10.1016/j.cell.2023.03.026. IPF: 64

Bel imam M*, Stikas CV*, Guha P, Chawes BL, Chu D, Greenhawt M, Khaleva E, Munblit D, Nekliudov N, van de Veen W, Schoos AM. Outcomes reported in randomized controlled trials for mixed and non-IgE-mediated food allergy: Systematic review. Clinical and experimental allergy: journal of the British Society for Allergy and Clinical Immunology. 2023. DOI: 10.1111/cea.14304. IPF: 5.018.

Hurme P, Sahla R, Rückert B, Vahlberg T, Turunen R, Vuorinen T, Akdis M, Söderlund-Venermo M, Akdis C, Jartti T. Human bocavirus 1 coinfection is associated with decreased cytokine expression in the rhinovirus-induced first wheezing episode in children. Clin Transl Allergy. 2023 Nov;13(11):e12311. doi: 10.1002/clt2.12311. PMID: 38006383 Free PMC article. IPF: 5.018.

Molitor N, Hofer D, Çimen T, Gasperetti A, Akdis D, Costa S, Jenni R, Breitenstein A, Wolber T, Winnik S, Fokstuen S, Fu G, Medeiros-Domingo A, Ruschitzka F, Brunckhorst C, Duru F, Saguner AM., Evolution and triggers of defibrillator shocks in patients with arrhythmogenic right ventricular cardiomyopathy, Heart. 2023 Jul 12;109(15):1146-1152. doi: 0.1136/heartjnl-2022-321739., PMID: 36889907, IPF: 5.7.

Styrzynski F, Zhakparov D, Schmid M, Roqueiro D, Lukasik Z, Solek J, Nowicki J, Dobrogowski M, Makowska J, Sokolowska M, Baerenfaller K. Machine Learning Successfully Detects Patients with COVID-19 Prior to PCR Results and Predicts Their Survival Based on Standard Laboratory Parameters in an Observational Study. Infect Dis Ther. 2023 Jan;12(1):111-129. doi: 10.1007/s40121-022-00707-8. Epub 2022 Nov 4. PMID 36333475, IPF 5.4.

Wise SK, Damask C, Roland LT, Ebert C, Levy JM, Lin S, Luong A, Rodriguez K, Sedaghat AR, Toskala E, Villwock J, Abdullah B, Akdis C, Alt JA, Ansotegui IJ, Azar A, Baroody F, Benninger MS, Bernstein J, Brook C, Campbell R, Casale T, Chaaban MR, Chew FT, Chambliss J, Cianferoni A, Custovic A, Davis EM, DelGaudio JM, Ellis AK, Flanagan C, Fokkens WJ, Franzese C, Greenhawt M, Gill A, Halderman A, Hohlfeld JM, Incorvaia C, Joe SA, Joshi S,

Kuruvilla ME, Kim J, Klein AM, Krouse HJ, Kuan EC, Lang D, Larenas-Linnemann D, Laury AM, Lechner M, Lee SE, Lee VS, Loftus P, Marcus S, Marzouk H, Mattos J, McCoul E, Melen E, Mims JW, Mullol J, Nayak JV, Oppenheimer J, Orlandi RR, Phillips K, Platt M, Ramanathan M Jr, Raymond M, Rhee CS, Reitsma S, Ryan M, Sastre J, Schlosser RJ, Schuman TA, Shaker MS, Sheikh A, Smith KA, Soyka MB, Takashima M, Tang M, Tantilipikorn P, Taw MB, Tversky J, Tyler MA, Veling MC, Wallace D, Wang Y, White A, Zhang L., International consensus statement on allergy and rhinology: Allergic rhinitis - 2023., Int Forum Allergy Rhinol. 2023 Apr;13(4):293-859. doi: 10.1002/alr.23090. Epub 2023 Mar 6., PMID: 36878860. IPF: 6.4.

Saguner AM, Lunk D, Mohsen M, Knecht S, Akdis D, Costa S, Gasperetti A, Duru F, Rossi VA, Brunckhorst CB., Electroanatomical voltage mapping with contact force sensing for diagnosis of arrhythmogenic right ventricular cardiomyopathy., Int J Cardiol. 2023 Dec 1;392:131289. doi: 10.1016/j.ijcard.2023.131289. Epub 2023 Aug 22.,PMID: 37619879. IPF: 4.039.

Huntjens DW, Vanhommerig JW, van de Veen W, Crul M. Exclusion of Ranitidine From Premedication Regimens During Paclitaxel Treatment. JAMA Oncol. 2023 Nov 2:e234821. doi: 10.1001/jamaoncol.2023.4821. Epub ahead of print. PMID:37917074; PMCID: PMC10623296. IPF: 33.012. IPF: 33.012.

Agache I, Shamji MH, Kermani NZ, Vecchi G, Favaro A, Layhadi JA, Heider A, Akbas DS, Filipaviciute P, Wu LYD, Cojanu C, Laculiceanu A, Akdis CA, Adcock IM., Multidimensional endotyping using nasal proteomics predicts molecular phenotypes in the asthmatic airways. J Allergy Clin Immunol. 2023 Jan;151(1):128-137. doi: 10.1016/j.jaci.2022.06.028. Epub 2022 Sep 22. PMID: 36154846. IPF: 14.2

Satitsuksanoa P, Iwasaki S, Boersma J, Bel Imam M, Schneider SR, Chang I, van de Veen W, Akdis M. B cells: The many facets of B cells in allergic diseases. Journal of Allergy and Clinical Immunology. 2023 May. DOI:10.1016/j.jaci.2023.05.011. IPF: 14.2

Aguilera J, Kaushik A, Cauwenberghs N, Heider A, Ogulur I, Yazici D, Smith E, Alkotob S, Prunicki M, Akdis CA, Nadeau KC. Granzymes, IL-16, and poly(ADP-ribose) polymerase 1 increase during wildfire smoke exposure. J Allergy Clin Immunol Glob. 2023 May;2(2):100093. doi: 10.1016/j.jacig.2023.100093. Epub 2023 Mar 21. PMID: 37539354; PMCID: PMC10399148. IPF: 14.2.

Bendien SA, Kroes JA, van Hal LHG, Braunstahl GJ, Broeders MEAC, Oud KTM, Patberg KW, Smeenk FWJM, van Veen IHPAA, Weersink EJM, Fieten KB, Hashimoto S, van Veen A, Sont JK, van Huisstede A, van de Ven MJT, Langeveld B, Maitland-van der Zee AH, Ten Brinke A; Registry of Adult Patients With Severe Asthma for Optimal Disease Management Team. Real-World Effectiveness of IL-5/5Ra Targeted Biologics in Severe Eosinophilic Asthma With Comorbid Bronchiectasis. J Allergy Clin Immunol Pract. 2023 Sep;11(9):2724-2731.e2. PMID: 37295671. IPF: 14.2.

Ogulur I, Pat Y, Aydin T, Yazici D, Rückert B, Peng Y, Kim J, Radzikowska U, Westermann P, Sokolowska M, Dhir R, Akdis M, Nadeou K, Akdis CA. Gut epithelial barrier damage caused by dishwasher detergents and rinse aids. Journal of Allergy and Clinical Immunology 151, 469-484 (2023). DOI: 10.1016/j.jaci.2022.10.020. IPF: 14.2.

Ten Have L, Visser E, Meulmeester FL, Bendien SA, Braunstahl GJ, Broeders MEAC, Fieten KB, Hashimoto S, van Huisstede A, Langeveld B, Oud KTM, Patberg KW, Smeenk FWJM, van Veen A, van Veen IH, van de Ven MJT, Weersink EJM, de Jong K, Sont JK, Kroes JA, Ten Brinke A. Long-Term Weight Changes After Starting Anti-IL-5/5Ra Biologics in Severe Asthma: The Role of Oral Corticosteroids. J Allergy Clin Immunol Pract. 2023 Sep;11(9):2748-2756.e3. PMID: 37399945. IPF: 14.2.

van der Valk JPM, Hekking PP, Rauh SP, Patberg KW, van Veen IA, Van Huisstede A, Smeenk FWJM, van de Ven MJT, Broeders MEAC, Hilvering B, van Exsel J, Oud KTM, Langeveld B, Fieten KB, van Veen A, Hashimoto S, Sont JK, Ten Brinke A, Braunstahl GJ; RAPSODI Team. Anti-IL-5/5Ra biologics improve work productivity and activity in severe asthma: a RAPSODI registry-based cohort study. J Asthma. 2023 Oct;60(10):1869-1876. PMID: 36976568. IPF: 2.5.

Ost DE, Feller-Kopman DJ, Gonzalez AV, Grosu HB, Herth F, Mazzone P, Park JES, Porcel JM, Shojaee S, Tsiligianni I, Vachani A, Bernstein J, Branson R, Flume PA, Akdis CA, Kolb M, Portela EB, Smyth A., Reporting Standards for Diagnostic Testing: Guidance for Authors From Editors of Respiratory, Sleep, and Critical Care Journals., J Bronchology Interv Pulmonol. 2023 Jul 1;30(3):207-222. doi: 10.1097/LBR.0000000000000920., PMID: 37070780. IPF: 11.7.

Niechcial A, Schwarzfischer M, Wawrzyniak M, Atrott K, Laimbacher A, Morsy Y, Katkeviciute E, Häfliger J, Westermann P, Akdis CA, Scharl M, Spalinger MR., Spermidine Ameliorates Colitis via Induction of Anti-Inflammatory Macrophages and Prevention of Intestinal Dysbiosis., J Crohns Colitis. 2023 Oct 20;17(9):1489-1503. doi: 10.1093/ecco-jcc/jjad058., PMID: 36995738. IPF: 8.0

Çimen T, Medeiros-Domingo A, Kolios A, Akdiş D, Anwer S, Tanner FC, Brunckhorst C, Duru F, Saguner AM., A Novel Heterozygous Desmoplakin Variant Causes Cardiocutaneous Syndrome with Arrhythmogenic Cardiomyopathy and Palmoplantar Keratosis., J Clin Med. 2023 Jan 24;12(3):913. doi: 10.3390/jcm12030913., PMID: 36769561. IPF: 3.9.

Guan F, Gass M, Berger F, Akdis D, Duru F, Wolber T., Transseptal Puncture Guided by Three-Dimensional Electroanatomical Mapping: Early Experience Using a Simplified Approach in Adults with Congenital Heart Disease., J Clin Med. 2023 Jul 5;12(13):4491. doi: 10.3390/jcm12134491., PMID: 37445531. IPF: 3.9.

Zhakparov D, Quirin Y, Xiao Y, Battaglia N, Holzer M, Bühler M, Kistler W, Engel D, Zumthor JP, Caduff A, Baerenfaller K. Sequencing of SARS-CoV-2 RNA Fragments in Wastewater Detects the Spread of New Variants during Major Events. Microorganisms 2023, 11(11), 2660; PMID: 38004672, DOI: 10.3390/microorganisms11112660.

IPF: 4.167.

Nuñez NG, Berner F, Friebel E, Unger S, Wyss N, Gomez JM, Purde MT, Niederer R, Porsch M, Lichtensteiger C, Kramer R, Erdmann M, Schmitt C, Heinzerling L, Abdou MT, Karbach J, Schadendorf D, Zimmer L, Ugurel S, Klümper N, Hölzel M, Power L, Kreutmair S, Capone M, Madonna G, Cevhertas L, Heider A, Amaral T, Hasan Ali O, Bomze D, Dimitriou F, Diem S, Ascierto PA, Dummer R, Jäger E, Driessen C, Levesque MP, van de Veen W, Joerger M, Früh M, Becher B, Flatz L. Immune signatures predict development of autoimmune toxicity in patients with cancer treated with immune checkpoint inhibitors. Med. 2023 Feb10;4(2):113-129.e7. doi: 10.1016/j.medj.2022.12.007. Epub 2023 Jan 23. PMID:36693381. IPF: 17.0

Stocker N, Radzikowska U, Wawrzyniak P, Tan G, Huang M, Ding M, Akdis CA, Sokolowska M. Regulation of ACE2 isoforms by type 2 inflammation and viral infection in human airway epithelium. Mucosal Immunology, (2023). DOI: 10.1016/j.mucimm.2022.12.001. IPF: 8.000.

Kolkhir P, Akdis CA, Akdis M, Bachert C, Bieber T, Canonica GW, Guttman-Yassky E, Metz M, Mullol J, Palomares O, Renz H, Ständer S, Zuberbier T, Maurer M. Type 2 chronic inflammatory diseases: targets, therapies and unmet needs. Nat Rev Drug Discov. 2023 Sep;22(9):743-767. doi: 10.1038/s41573-023-00750-1. Epub 2023 Aug 1. PMID: 37528191. IPF: 100.7.

White M. E., Sinn L. R., Jones D. M., de Folter J., Aulakh S. K., Wang Z., Flynn H. R., Krüger L., Tober-Lau P., Demichev V., Kurth F., Mülleder M., Blanchard V., Messner C. B. & Ralser M. (2023). Oxonium ion scanning mass spectrometry for large-scale plasma glycoproteomics. Nature Biomedical Engineering, 1-15. IPF: 29, https://doi.org/10.1038/s41551-023-01067-5.

Radzikowska U, Eljaszewicz A, Tan G, Stocker N, Heider A, Westermann P, Steiner S, Dreher A, Wawrzyniak P, Rückert B, Rodriguez-Coira J, Zhakparov D, Huang M, Jakiela B, Sanak M, Moniuszko M, O'Mahony L, Jutel M, Kebadze T, Jackson DJ, Edwards MR, Thiel V, Johnston SL, Akdis CA, Sokolowska M., Rhinorivus-induced epithelial RIG-I inflammasome suppresses antiviral immunity and promotes inflammation in asthma and COVID-19. Nat Commun 14, 2329 (2023)., doi.org/10.1038/s41467-023-37470-4. IPF 16.6.

Kayhan M, Vouillamoz J, Rodriguez DG, Bugarski M, Mitamura Y, Gschwend J, Schneider C, Hall A, Legouis D, Akdis CA, Peter L, Rehrauer H, Gewin L, Wenger RH, Khodo SN., Intrinsic TGF-β signaling attenuates proximal tubule mitochondrial injury and inflammation in chronic kidney disease., Nat Commun. 2023 Jun 3;14(1):3236. doi: 10.1038/s41467-023-39050-y., PMID: 37270534. IPF 16.6.

Feleszko W, Okarska-Napierała M, Buddingh EP, Bloomfield M, Sediva A, Bautista-Rodriguez C, Brough H, Eigenmann P, Eiwegger T, Eljaszewicz A, Eyerich S, Gomez-Casado C, Fraisse A, Janda J, Jiménez-Saiz R, Kallinich T, Kortekaas Krohn I, Mortz C, Riggioni C, Sastre J, Sokolowska M, Strzelczyk Z, Untersmayr E, Tramper-Stranders G. Pathogenesis, immunology, and immune-targeted management of the multisystem inflammatory syndrome in children (MIS-C) or pediatric inflammatory multisystem syndrome (PIMS): EAACI Position Paper. Pediatric Allergy and Immunology. In Press. First Published: 04.01.2023. doi.org/10.1111/pai.13900; IPF 5.464.

Nguyen NT, Schappin R, Pasmans SGMA, Schreurs MWJ, de Swart RL, van de Veen W. Can measles attenuate previous allergic sensitization in children? Pediatr Allergy Immunol. 2023 Oct;34(10):e14033. doi: 10.1111/pai.14033. PMID: 37877848. IPF: 5.464.

Losol P, Sokolowska M, Chang YS. Interactions between microbiome and underlying mechanisms in asthma. Respir Med. 2023 Mar;208:107118. doi: 10.1016/j.rmed.2023.107118. Epub 2023 Jan 11. PMID 36641058, IPF 4.3.

Wang M, Wang C, Akdis CA, Zhang L., The highly prevalent allergic rhinitis: does new treatments move toward a cure? ,Sci Bull (Beijing). 2023 Dec 30;68(24):3094-3097. doi: 10.1016/j.scib.2023.11.028. Epub 2023 Nov 14., PMID: 37993333, IPF: 18.9.

Akdis CA, Akdis M, Boyd SD, Sampath V, Galli SJ, Nadeau KC. Allergy: Mechanistic insights into new methods of prevention and therapy. Sci Transl Med. 2023 Jan 18;15(679):eadd2563. doi: 10.1126/scitranslmed.add2563. Epub 2023 Jan 18. PMID: 36652536 Review, IPF: 17.1.

Kıykım A, Öğülür İ, Yazıcı D, Çokuğraş H, Akdiş M, Akdiş CA. Epithelial Barrier Hypothesis and Its Comparison with the Hygiene Hypothesis. Turk Arch Pediatr. 2023 Mar;58(2):122-128. doi: 10.5152/TurkArchPediatr.2023.23006. PMID: 36856348 Free PMC article.

Yazici D, Ogulur I, Pat Y, Babayev H, Barletta E, Ardicli S, Bel Imam M, Huang M, Koch J, Li M, Maurer D, Radzikowska U, Satitsuksanoa P, Schneider SR, Sun N, Traidl S, Wallimann A, Wawrocki S, Zhakparov D, Fehr D, Ziadlou R, Mitamura Y, Brüggen MC, van de Veen W, Sokolowska M, Baerenfaller K, Nadeau K, Akdis M, Akdis CA. The epithelial barrier: The gateway to allergic, autoimmune, and metabolic diseases and chronic neuropsychiatric conditions. Semin Immunol. 2023 Oct 4;70:101846. doi: 10.1016/j.smim.2023.101846. Epub ahead of print. PMID: 37801907, IPF 7.8.

Pat Y, Ogulur I, Yazici D, Mitamura Y, Cevhertas L, Küçükkase OC, Mesisser SS, Akdis M, Nadeau K, Akdis CA. Effect of altered human exposome on the skin and mucosal epithelial barrier integrity. Tissue Barriers. 2023 Oct 2;11(4):2133877. doi: 10.1080/21688370.2022.2133877. Epub 2022 Oct 19. PMID: 36262078; PMCID: PMC10606824, IPF: 3.1.

Lv X, Gao Z, Tang W, Qin J, Wang W, Liu J, Li M, Teng F, Yi L, Dong J, Wei Y., Trends of therapy in the treatment of asthma., Ther Adv Respir Dis. 2023 Jan-Dec;17:17534666231155748. doi: 10.1177/17534666231155748., PMID: 36942731, IPF: 4.8.

Fieten KB, Maya-Manzano JM, Rückert B, Candeias J, Pusch G, Buters J, Akdis CA, Traidl-Hoffmann C. Environmental exposure and sensitization patterns in a Swiss alpine pediatric cohort. World Allergy Organ J. 2023 Dec 3;16(12):100847. PMID:38075553 IPF: 7.3

BOOK CHAPTERS

Bruton K*, Bel imam M*, Koenig JFE, Hoh R, de Azcárate PHR, Patil SU, Jordana M, van de Veen W, Jiménez-Saiz R, Long lived immune memory and food allergy. In: Encyclopedia of Food Allergy. Editors: Elsevier, Date: 2023, Place of Publication: Amsterdam, Page: NA, ISBN: 9780081005965.

Zhakparov D, Moriarty K, Lunjani N, Schmid M, Hlela C, Levin M, Mankahla A, SOS-ALL Consortium, Akdis C, O'Mahony L, Baerenfaller K#, Roqueiro DS. Assessing Different Feature Selection Methods Applied to a Bulk RNA Sequencing Dataset with regard to Biomedical Relevance. In: Machine Learning and Principles and Practice of Knowledge Discovery in Databases. ECML PKDD 2022. Communications in Computer and Information Science, Editors: Koprinska I et al. Publisher: Springer, Date: 2023, Place of Publication: Cham, Volume: 1753, ISBN Print:978-3-031-23632-7, ISBN Online: 978-3-031-23633-4, DOI: 10.1007/978-3-031-23633-4_18.

ABSTRACTS

Barletta E, Westermann P, Fröhlich K, Brüggen MC, Schmid-Grendelmeier P and Bärenfaller K. Mass spectrometry-based identification of allergen proteins involved in seafood related allergic reactions. WIRM 2023, Davos, Switzerland, 5-8 July 2023.

Barletta E, Westermann P, Fröhlich K, Brüggen MC, Schmid-Grendelmeier P and Bärenfaller K. Mass spectrometry-based identification of allergen proteins involved in seafood related allergic reactions. SSAI ANNUAL CONGRESS 2023, Bern, Switzerland, 24-25 August 2023.

Barletta E, Westermann P, Fröhlich K, Brüggen MC, Schmid-Grendelmeier P and Bärenfaller K. Mass spectrometry-based identification of allergen proteins involved in seafood related allergic reactions. SIICA-SYIS JOINT SYMPOSIUM 2023, Rome, Italy, 3-4 November 2023.

Beha C, Koch J, Ruggia A, Westermann P, Kessler C, Schmelzer S, Froehlich K, Baerenfaller K. Characterisation of prenylated proteins in T helper 1 cells, WIRM, Davos, 5-8 July 2023

Bel imam M, Identification of circulating biomarkers in eosinophilic esophagitis. SYIS Second Annual Symposium, Bern, Switzerland, 23 August 2023.

Bel imam M, Identification of circulating biomarkers for the differentiation of active versus inactive eosinophilic esophagitis. WIRM 2023, Davos, Switzerland, 5-8 July 2023.

Bel imam M, Identification of blood-based biomarkers for eosinophilic esophagitis elassification. SIICA-SYIS "Multi omics approaches in immunological research" Joint Symposium, Rome, Italy, Nov 3-4 2023.

Jardón Parages I., Radzikowska U., Huang M., Stocker N., Ding M., Tan G., Heider A., Westermann P., Johnston S., Messner C., Akdis CA., Sokolowska M., Immunometabolic reprogramming of bronchial epithelium in asthma and during viral infection, WIRM, Davos, Switzerland, 5-8 July 2023.

Koch J, Marigona I, Schmelzer S, Westermann P, Heider A, Scheckel C, Fröhlich K, Baerenfaller K. Following the footprints to detect polypeptides encoded by non-coding RNA. WIRM 2023, Davos, Switzerland, 5-8 July 2023.

Koch J, Westermann P, Imeri M, Schmelzer S, Froehlich K, Heider A, Scheckel C, Baerenfaller K. Translational regulation of metabolism in T helper 1 cell differentiation. Swiss RNA meeting, Bern, 27 January 2023.

Koch J, Westermann P, Ruggia A, Beha C, Schmelzer S, Froehlich K, Baerenfaller K. Protein Prenylation in T cell activation, WIRM, Davos, 5-8 July 2023

Koch J, Westermann P, Ruggia A, Beha C, Schmelzer S, Froehlich K, Heider A, Baerenfaller K. Challenging the current view on protein prenylation in T helper cells using experimental data and information on protein 3D structures, BC2 Basel, Switzerland, 11-13 Sep 2023

Mitamura Yasutaka, Matthias Reiger, Juno Kim, Yi Xiao, Damir Zhakparov, Katja Baerenfaller, Marie-Charlotte Brüggen, Patrick M Brunner, Damian Roqueiro, Claudia Traidl-Hoffmann, and Cezmi A Akdis Spatial and single-cell transcriptomics provide insights into the complex inflammatory cell network in atopic dermatitis AAAAI Annual Meeting 2023, San Antonio, USA, 23-26 February 2023.

2023

Mitamura Yasutaka, Matthias Reiger, Juno Kim, Yi Xiao, Damir Zhakparov, Katja Baerenfaller, Marie-Sanne S. Meisser, Yasutaka Mitamura, Can Altunbulakli, Josefine Bandier, Morten S. Op-strup, Anne-Sofie Ø. Gadsbøll, Manru Li, Ge Tan, Cezmi A. Akdis, Carsten Geisler, Jeanne D. Johansen & Charlotte M. Bonefeld. Different regulation of immune-related genes in the skin from non-responders and allergic individuals exposed to p-phenylenediamine Springtime School 2023: Skin homeostasis and inflammation, Copenhagen, Denmark, 24-26 April 2023.Charlotte Brüggen, Patrick M Brunner, Damian Roqueiro, Claudia Traidl-Hoffmann, and Cezmi A Akdis Spatial transcriptomics and single-cell transcriptomics elucidates the intricate inflammatory cellular network in atopic dermatitis.ISID Annual Meeting 2023, Tokyo, JAPN, 10-13 April 2023.

Mitamura Yasutaka, Household laundry detergents cause barrier dysfunction and induce inflammation in mouse and human skin. Tight Junctions: from Structure and Development to Therapeutics, Leysin, Switzerland, 4-8 June 2023

Mitamura Yasutaka,Household laundry detergents disrupt barrier integrity and induce inflammation in mouse and human skin. EAACI congress 2023, Hamburg, Germany, 9-11 June 2023

Mitamura Yasutaka, Carbonic anhydrase: A novel potential therapeutic target in atopic dermatitis. WIRM 2023, Davos, Switzerland, 5-8 July 2023
Yasutaka Mitamura, Differential regulation of epidermal differentiation and its metabolism by interleukin-13 and interleukin-22 in atopic dermatitis. SSAI 2023, Bern, Switzerland, 24-25 August 2023

Mitamura Yasutaka, Discovery of Carbonic Anhydrase as a Novel Controller of Skin Inflammation and Barrier Strength in Atopic Dermatitis. EEAACI Summer Symposium on Epithelial Cell Biology 2023, London, England, 21-22 September 2023

Mitamura Yasutaka, PM2.5 and CO2 levels affecting epidermal barriers and subsequent allergic and immune conditions, Bern, Switzerland, 9-10 November 2023

Na S., Yazici D., Pat Y., Babayev H., Bu X., Zhu X., Ruckert B., Ogulur I., Akdis M., Akdis C. A. Food emulsifiers kappa-, lambda- and iota-carrageenan disrupt intestinal epithelial barrier integrity on a gut-on-a-chip model. World Immune Regulation Meeting XVII (WIRM XVII), Davos, Switzerland 5-8 July 2023.

Ogulur I., D. Yazici, E. Cagan, T. Aydin, OC. Kucukkase, M. Li1, E. Do, A. Simsek, MA. Kizmaz, T. Bozkurt, M. Akdis, K. Nadeau, F. Budak, CA. Akdis, Investigation of Epithelial Barrier Damaging and Healing Compounds with Gut-on-a-chip System, EAACI Hybrid Congress, Hamburg June 9-11, 2023

Ogulur I., Yazici D., Cagan E., Aydin T, Kucukkase O.C., Li M., Do E., Simsek A., Kizmaz M.A., Bozkurt T., Akdis M., Nadeau K., Budak F., Akdis C. Novel biomarkers of disrupted gut permeability in severe COVID-19 patients. EAACI Hybrids Congress, Hamburg, Germany, 7-11 June 2023.

Ogulur I., Pat Y., Aydin T., Yazici D., Rückert B., Peng Y., Kim J., Radzikowska U., Westermann P., Sokolowska M., Akdis M., Nadeau K., Akdis C. A. Gut epithelial barrier damage caused by dishwasher detergents and rinse aids. World Immune Regulation Meeting XVII (WIRM XVII), Davos, Switzerland 5-8 July 2023.

Ogulur I., Yazici D., Cagan E., Babayev H., Do E., Simsek A., Kizmaz M. A., Bozkurt T., Heider A., Rückert B., Dhir R., O'Mahony L., Akdis M., Nadeau K., Budak F., Akdis C. A. Biomarkers of epithelial barrier leakiness in healthy subjects. World Immune Regulation Meeting XVII (WIRM XVII), Davos, Switzerland 5-8 July 2023.

Ogulur I., Yazici D., Pat Y., Babayev H., Ardicli S., Heider A., Rückert B., Akdis M., Nadeau K., Akdis C. A. Recent molecular mechanisms of food emulsifiers and dishwasher detergents on epithelial barrier disruption. SSAI Annual Congress 2023, Bern, Switzerland, August 24.25 2023.

Pat Y, Rückert B, Ogulur I, Yazici D, Perez-Diego M, Küçükkase OC, Li M, Akdis CA. Differentiation of bronchial epithelial spheroids in the presence of IL-13 recapitulates characteristic features of asthmatic airway epithelia. Tight Junctions: from Structure and Development to Therapeutics. Leysin, Switzerland, 4-8 June 2023.

Pat Y., Yazici D., Ogulur I., Do E., Li M., Buyuktiryaki A.B., Sackesen C., Nadeau K., Akdis M., Akdis C.A.Investigation of epithelial barrier affecting compounds with gut-on-a-chip system. EAACI Hybrids Congress, Hamburg, Germany, 7-11 June 2023.

Pat Y., Yazici D., Ogulur I., Ardicli S., Simmons S., Almada A., Avena C., Jensen T., Do E., Li M., Mitamura Y., Babayev H., Heider A., Buyuktiryaki B., Sackesen C., Dihr R., Akdis M., Nadeau K., Akdis C.A. Regulation of gut epithelial barrier by microbiome metabolites. World Immune Regulation Meeting XVII (WIRM XVII), Davos, Switzerland 5-8 July 2023.

Pat Y., Yazici D., Ogulur I., Ardicli S., Simmons S., Almada A., Avena C., Jensen T., Do E., Li M., Mitamura Y., Babayev H., Heider A., Buyuktiryaki B., Sackesen C., Dihr R., Akdis M., Nadeau K., Akdis C.A. Regulation of gut epithelial barrier by microbiome metabolites. SSAI Annual Congress 2023, Bern, Switzerland, August 24.25 2023.

Pat Y., Yazici D., Ogulur I., Ardicli S., Simmons S., Almada A., Avena C., Jensen T., Do E., Li M., Mitamura Y., Babayev H., Heider A., Buyuktiryaki B., Sackesen C., Dihr R., Akdis M., Nadeau K., Akdis C.A. Regulation of gut epithelial barrier by microbiome metabolites. EAACI Epithelial Cell Biology Summer Symposium, London, England, 21-22 September 2023.

Radzikowska U. Rhinovirus-induced Epithelial RIG-I Inflammasome Activation Suppresses Antiviral Immunity and Promotes Inflammatory Responses in Virus-induced Asthma Exacerbations and COVID-19. Inflammation in the Lung: Friend or Foe in Viral Infections?, Snowbird, UT, United States, 23-26 April 2023.

Radzikowska U. Rhinovirus-induced epithelial RIG-I inflammasome

activation suppresses antiviral immunity and promotes inflammatory responses in virus-induced asthma exacerbations and COVID-19, European Academy of Allergy and Clinical Immunology Annual Congress 2023, Hamburg, Germany, 9-11.06.2023.

Radzikowska U. RIG-I signaling in asthma and COVID-19. XVII World Immune Regulation Meeting, Davos, Switzerland, 5-8 July 2023.

Rinaldi AO, Li M, Ward S, Burla D, Barletta E, Bost J, Askary N, Larsson R, Gaudenzio N, Akdis CA, Mitamura Y. Household laundry detergents cause barrier dysfunction and induce inflammation in mouse and human ski. World Immune Regulation Meeting-XVII, Davos, Switzerland, 5 - 8 July 2023

Rodriguez-Coira J, Kulkarni A, Stocker N, Garcia-Civico A, Radzikowska U, Jardon-Parages I, Contreras N, Saiz Sanchez V, Gomez-Casado C, Sanchez-Solares J, Pablo-Torres C, Obeso D, Ruiz- Leon B, Espinazo-Romeu M, Serrano P, Heider A, Tan G, Escribese MM, Moreno-Aguilar C, Akdis CA, Barber D, Villaseñor A, Sokolowska M. Metabolomics of circulating human memory CD4+T effector and T regulatory cells reveals that phenylalanine is a metabolic checkpoint of pathogenic Th2 cells development. World Immune Regulation Meeting - XVII, Davos, Switzerland, 5-8 July 2023.

Ruggia A, Koch J, Westermann P, Schmelzer S, Froehlich K, Mundani RP, Baerenfaller K. Challenging the current view of protein prenylation sites, WIRM, Davos, 5-8 July 2023

Schneider S, Satitsuksanoa P, van de Veen W, Chang I, Akdis CA, Nadeau K, Akdis M. Investigation of allergen specific B-cells in allergy concordant and discordant twin. EAACI winter school 2023, Davos, Switzerland, 26-29 January 2023

Schneider S, Satitsuksanoa P, van de Veen W, Chang I, Akdis CA, Nadeau K, Akdis M. Investigation of allergen specific B-cells in allergy concordant and discordant twin. World Immune Regulation Meeting (WIRM) 2023, Davos, Switzerland 5-8 July 2023

Sokolowska M. Immune metabolism of type 2 immunity in allergy and immune tolerance. XVII World Immune Regulation Meeting (WIRM), Davos, Switzerland, 5-8 July 2023

Sokolowska M. Epithelial RIG-I inflammasome and ACE2 isoforms in type 2 inflammation, asthma exacerbations and COVID-19. Swiss Society for Allergology and Immunology Annual Congress, Bern, Switzerland, 24-25 August 2023

Sokolowska M. Breathing with confidence: Interplay between Immunity and Metabolism in Asthma and COVID-19. BIO2023 Szczecin, Poland 13-16 September 2023

Sokolowska M. Metabolomics of Circulating Human Memory CD4+T Effector and T Regulatory Cells Reveals that Phenylalanine is a Metabolic Checkpoint of Pathogenic Th2 Cells Development. 33rd Symposium of the Collegium Internationale Allergologicum, Montreal, Canada, 10 - 14 October, 2023

Van de Veen W. In Vivo Monitoring of Allergen-Specific Memory B-Cells: Tracking Development and Persistence. 33rd Biennial Symposium of the Collegium Internationale Allergologicum, Montréal, Canada, 10-14 October 2023.

Yazici Duygu, Ismail Ogulur, Evan Do, Manru Li, Ozan C. Kucukkase, Betul Buyuktiryaki, Cansin Sackesen, Mubeccel Akdis, Kari Nadeau, Cezmi A. Akdis, Investigation of Epithelial Barrier Damaging, Healing and Protecting Compounds with Gut-on-a-chip System, EAACI Winter School, Davos January 26-29, 2023

Yazici Duygu, Ismail Ogulur, Evan Do, Manru Li, Betul Buyuktiryaki, Cansin Sackesen, Mubeccel Akdis, Kari Nadeau, Cezmi A. Akdis, Investigation of Epithelial Barrier Damaging and Healing Compounds with Gut-on-a-chip System, Tight Junction Symposium, Geneva June 4-8, 2023

Yazici Duygu, Yagiz Pat, Ismail Ogulur, Sena Ardicli, Sheri Simmons, Anthony Almada, Christine Avena, Tye Jensen, Evan Do, Manru Li, Yasutaka Mitamura, Huseyn Babayev, Betul Buyuktiryaki, Cansin Sackesen, Raja Dhir, Mubeccel Akdis, Kari Nadeau, Cezmi A. Akdis, Epithelitis: barrier disruption and activation of pro-inflammatory molecules in gut epithelial cells by food additives, WIRM, Davos July 5-8, 2023

Yazici Duygu, Yagiz Pat, Ismail Ogulur, Sena Ardicli, Sheri Simmons, Anthony Almada, Christine Avena, Tye Jensen, Evan Do, Manru Li, Yasutaka Mitamura, Huseyn Babayev, Anja Heider, Betul Buyuktiryaki, Cansin Sackesen, Raja Dhir, Mubeccel Akdis, Kari Nadeau, Cezmi A. Akdis, Epithelitis: barrier disruption and activation of pro-inflammatory pathways in gut epithelial cells by food additives, SSAI Annual Congress, Bern August 24-25, 2023

Yazici Duygu, Yagiz Pat, Ismail Ogulur, Sena Ardicli, Sheri Simmons, Anthony Almada, Christine Avena, Tye Jensen, Manru Li, Yasutaka Mitamura, Huseyn Babayev, Anja Heider, Raja Dhir, Mubeccel Akdis, Kari Nadeau, Cezmi A. Akdis, Epithelitis: barrier disruption and activation of pro-inflammatory pathways in gut epithelial cells by food emulsifiers, EAACI Summer Symposium on Epithelial Cell Biology, London September 21-22, 2023

Yazici D., Pat Y., Ogulur I., Simmons S., Almada A., Avena C., Jensen T., Dickson T., Do E., Li M., Mitamura Y., Babayev H., Heider A., Buyuktiryaki B., Sackesen C., Dihr R., Akdis M., Nadeau K., Akdis C.A.Epithelitis: barrier disruption and activation of pro-inflammatory molecules in gut epithelial cells by food additives. EAACI Epithelial Cell Biology Summer Symposium, London, England, 21-22 September 2023.

Zhakparov D. GeneSelectR: A Machine Learning-Based R Package for Enhanced Feature Selection and Biological Assessment in RNAseq Analysis of Complex Biological Datasets. BC2 Computational Biology Conference, Basel, Switzerland 11 - 13 September

2023.

Zhakparov D, Moriarty K, Roqueiro D, Baerenfaller K. GeneSelectR: A machine learning-based R package for feature selection and biological assessment in RNAseq analysis of complex biological datasets. World Immune Regulation Meeting (WIRM), Davos, Switzerland, 5 - 8 July 2023.

Zhakparov D, Moriarty K, Roqueiro D, Baerenfaller K. GeneSelectR: A machine learning-based R package for feature selection and biological assessment in RNAseq analysis of complex biological datasets. BiotechX Europe, Basel, Switzerland, 4 - 6 October 2023.

SEMINAR AND CONGRESS TALKS

Akdis C. Epithelial Barrier Theory and Allergic Diseases. EAACI Immunology Winter School, Davos, Switzerland 28 January 2023.

Akdis C. Epithelial Barrier Theory and Global Health Crisis. Greek Society of Allergy and Immunology, Athens, Greece, February 4, 2023

Akdis C. Online, Digging the Cytokines: The essence in advanced treatments for Atopic Dermatitis. Type 2 Inflammatory Diseases, Hong Kong, Taipei, Singapore Online. February 19, 2023.

Akdis C. An Update on Changes in the Innate Immune System During Allergen Immunotherapy, 2023 AAAAI Annual Meeting, February 24 – 27, 2023, San Antonio, USA

Akdis C. Mechanisms and Consequences of Epithelial Cell Barrier Disruption, 2023 AAAAI Annual Meeting, February 24 – 27, 2023, San Antonio, USA

Akdis C. Environmental Factors in Epithelial Barrier Dysfunction, Plenary Talk, 2023 AAAAI Annual Meeting, February 24 – 27, 2023, San Antonio, USA

Akdis C. Epithelial Barriers and Global Health Crisis. National Institute of Health, National Institute of Allergy and Infectious Diseases, March 1, 2024, Bethesda, Washington DC, USA

Akdis C. Epithelial Barriers and Global Health Crisis. AmerImmune Virginia USA, March 2, 2023.

Akdis C. University Zurich Medical Faculty, Dept of Dermatology Retreat, Epithelial barrier theory in allergic and autoimmune disease. March 17, 2023, Davos, Switzerland.

Akdis C. Online, Epithelial Barrier Theory and Global Health Crisis. Hacettepe University Students Congress March 20, 2023, Ankara, Turkey

Akdis C. Podcast Chemical Epithelial Barrier Damage, International Eczema Council, March 23, 2023, Melbourne, Australia

Akdis C. Allergic Diseases, Mechanisms, General Overview. Course Zurich University Medical Faculty, March 29, 2023, Davos, Switzerland

Akdis C. Online, Epithelial barrier theory in allergic and autoimmune disease. Acıbadem University, April 14, 2023, Istanbul, Turkey

Akdis C. Online, French Allergology Meeting, One Health Session, April, 25, 2023

Akdis C. OnLine, French Allergology Meeting, Epithelial barrier theory in allergic and autoimmune disease April 25, 2023

Akdis C. CFA, Novel Evidence on Epithelial Barrier Theory and Veterinary Involvement. April 27, 2023

Akdis C. Online, Meeting with graduate students of the KOC University, Istanbul on Epithelial Barriers and Environment. April 28, 2023, Istanbul, Turkey

Akdis C. Romanian Allergy and Immunology Meeting, Epithelial Barriers and Inflammation, Bucharest, Romania, May 4-6, 2023

Akdis C. Online, Epithelial Barrier Hypothesis, Online Faculty of Medicine of Porto University, May 17, 2023

Akdis C. Online, Meeting with graduate students of the KOC University, Istanbul on Epithelial Barriers and Environment. May 17, 2023

Akdis C. Online, Epithelial Barrier Theory and Global Health Crisis. Marmara University Students Congress May 26, 2023, Istanbul, Turkey

Akdis C. Press conference Allergy Journal, Launch of the China Issue, Highlights and Achievements, Beijing, May 31, 2023

Akdis C. Recent Evidence Supporting the Epithelial Barrier Theory, Beijing, May 31, 2023

Akdis C. Novel Findings Supporting the Epithelial Barrier Theory, Wuhan Doctors' Association and Allergy Society, Zhongnan Hospital, June 3, 2023

Akdis C. Epithelial Barrier Theory Allergy and Autoimmunity, Wuhan Tongji Hospital, June 3, 2023

Akdis C. EAACI Annual Meeting, Allergy Journal Highlights and Achievements. June 11, 2023 Hamburg, Germany

Akdis C. EAACI Annual Meeting, Allergy Journal Editorial Board Meeting, Highlights and Achievements. June 11, 2023, Hamburg, Germany

Akdis C. EAACI Annual Meeting, Allergy Journal Associate Editors' Meeting, Highlights and Achievements. June 11, 2023, Hamburg, Germany

Akdis C. Online, Uludağ University Air Pollution Meeting June 12, 2024, Bursa Turkey.

Akdis C. Epithelial Barrier Theory and Global Health Crisis. Stanford University, June 19, 2023.

Akdis C. Online, Epithelial Barrier Theory webinar – Genoskin June 30, 2023

Akdis C. World Immune Regulation Meeting, Epithelial Barrier Theory. July 5, 2023, Davos, Switzerland

Akdis C. Epithelial Barrier Theory and Global Health Crisis. Swiss Society of Allergy and Immunology, Bern, Switzerland, August 23, 2023

Akdis C. Epithelial Barrier Theory and Global Health Crisis. Paul Ehrlich Institute, Langen, Germany August 28, 2023

Akdis C. Online, New York University, Langone Hospital-Long Island Allergy/Immunology Grand Rounds on "Mechanism and Consequences of Epithelial Cell Barrier Disruption" September 15, 2023

Akdis C. EAACI Summer Symposium on Epithelial Cell Biology, Loss of tolerance due to the defect in epithelial barrier, London, September 22, 2023

Akdis C. Epithelial Barriers and Global Health Crisis. Ukranian Immunology, Allergy and Infectiology Congress. September 27-29, 2023

Akdis C. Online, Pathways to Excellence-Dermatology Awardee Session. Sanofi AG. September 22, 2023

Akdis C. Epithelial Barrier Theory, Mechanisms and Consequences. 6th International Severe Asthma Forum (ISAF), Rome, Italy, October 5, 2023.

Akdis C. Epithelial Barrier Theory, Novel Evidence, Asia Pacific Society of Allergy and Clinical Immunology Annual Meeting, Singapore October 23-26, 2023

Akdis C. How to write a first-class paper – tips and tricks" Asia Pacific Society of Allergy and Clinical Immunology Annual Meeting, Singapore October 23-26, 2023

Akdis C. Epithelial Barriers and Type 2 Response. EAACI PAAM Hybrid 2023, 2 November 2023, Porto, Portugal

Akdis C. Measuring the dysfunction of the Epithelial Barrier. EAACI PAAM Hybrid 2023, 3 November 2023, Porto, Portugal

Akdis C. International Immunology IUIS Congress. Epithelial Barriers and Immune Response. December 1, 2023, Cape Town, South Africa.

Akdis M
Mechanism of allergen tolerance: Role of B cells. MIM Introductory Course, Zurich, January 11-13, 2023

Akdis M
Mechanisms of Allergen Immunotherapy. WAO PASAAI Pan Arab Allergy Meeting. Dubai, 27, 28, and 29 January 2023

Akdis M
Biomarkers and Biologics: The promise for the Future. AAAAI (American Academy of Allergy Asthma & Immunology) San Antonio, TX. February 24-27 2023

Akdis M
B reg cells and allergen-specific B cell tolerance. LAD, DAID meeting in NIH, Bethesda, Maryland. 2 March, 2023

Akdis M
Allerjide tolerans gelisimi. 19. National Pediatric Winter congress, Uludag, Bursa, Turkey. March 12-15.2023.

Akdis M
Role of antigen-specific B cells in tolerance. (Online) Manchester University, Northwest Paediatric Network Allergy Study day. March 23,2023.

Akdis M
Regulatory B cells, where we are? European Federation for Immunogenetics (EFI) and 36th European Immunogenetics and Histocompatibility Conference, Nantes, France. April 26-29, 2023.

Akdis M
The role of allergen-specific B cells during the Food OIT. The Romanian Society of Allergology and Clinical Immunology National Congress, Buchares, Romania. May 4 - 6, 2023.

Akdis M
Allergene spesifik tolerans mekanizmaları ve B hücrelerinin rolu: Marmara Student Congress 2023 (MaSCo'23), Marmara University, Istanbul, Turkey. May 26-28, 2023.

Akdis M
Antigen-specific immune tolerance development: T and B regulatory cells. Allergic Diseases Department,
Zhongnan hospital of Wuhan University, China. June 1-5, 2023.

Akdis M
Allergen-specific B cells tolerance in food allergy. EAACI Hybrid Congress, Hamburg, Germany. June 9-11, 2023.
Akdis M
Role of Allergen-specific B cells tolerance to food allergens. Boston Focis annual meeting, Boston, USA. June 20-23,2023.

Akdis M
Novel mechanisms of induced and natural antigen-specific B cells tolerance. WIRM XVII, Davos, July 5-8, 2023.

Akdis M
Allergen-specific B cells tolerance in food allergy. SSAI, Bern, Switzerland. August 24-25, 2023.

Akdis M
The role of IgG4 in Allergic Disease. NIAID IgG4 Workshop, NIH, Rockville, MD. October 4, 2023.

Akdis M
Specific B cell responses in Allergen-specific Immunotherapy. CIA Collegium Internationale Allergologicum, 33rd Biennial Symposium, Montreal, Canada. October 10-14, 2023.

Akdis M
B-Cell Tolerance and Immunotherapy. APAAACI 2023 International Conference, Singapore. October 23-26, 2023.

2023

Akdis M
Immune tolerance induction - from bench to bedside. Pediatric Allergy and Asthma Meeting – PAAM Hybrid, Porto, Portugal, November 2-4, 2023.

Akdis M
Immune mechanisms crossing viral infection and allergy and asthma. 18th International Congress of Immunology – IUIS. Cape Town, South Africa. November 27- December 2, 2023.

Baerenfaller K, Evaluation of different RNA-Seq feature selection methods with regard to their biomedical relevance, SSS Dermatology Research Retreat 2023, Davos, Switzerland, 17-18 March 2023

Baerenfaller K, mRNAs and non-coding RNAs - Translatomics and its applications. EAACI Congress 2023, Hamburg, Germany, 9-11 June 2023.

Baerenfaller K, Using proteomics to investigate the molecular profile of allergic diseases. EAACI Congress 2023, Hamburg, Germany, 9-11 June 2023.

Baerenfaller K, Welcome from the host, PASC23 Conference, Davos, Switzerland, 26-28 June 2023.

Baerenfaller K, Following the footprints to detect peptides encoded by non-coding RNA. WIRM 2023, Davos, Switzerland, 5-8 July 2023.

Barletta E. Introduction to Proteomics. Biomedical Data Mining Blockkurs FS 2023 (BME351), Davos, Switzerland, 5-23 June 2023.

Barletta E, Westermann P, Fröhlich K, Brüggen MC, Schmid-Grendelmeier P and Bärenfaller K. Mass spectrometry-based identification of allergen proteins involved in seafood related allergic reactions. SIICA-SYIS JOINT SYMPOSIUM 2023, Rome, Italy, 3-4 November 2023.

Bel imam M, Identification of blood-based biomarkers for eosinophilic esophagitis elassification. SIICA-SYIS "Multi omics approaches in immunological research" Joint Symposium, Rome, Italy, Nov 3-4 2023.

Jardón Parages I., Immunometabolic reprogramming of bronchial epithelium in asthma and during viral infection, WIRM, Davos, Switzerland, 5-8 July 2023.

Koch J, Westermann P, Ruggia A, Beha C, Schmelzer S, Froehlich K, Baerenfaller K. Protein Prenylation in T cell activation, WIRM, Davos, 5-8 July 2023

Koch J, Westermann P, Ruggia A, Beha C, Imeri M, Schmelzer S, Froehlich K, Heider A, Scheckel C, Baerenfaller K. T helper 1 cell differentiation and activation, a multi-omics approach, SSAI Annual Congress 2023, Bern, Switzerland, 24-25 Aug 2023

Koch J, Westermann P, Ruggia A, Beha C, Schmelzer S, Froehlich K, Heider A, Baerenfaller K. Challenging the current view on protein prenylation in T helper cells using experimental data and information on protein 3D structures, BC2 Basel, Switzerland, 11-13 Sep 2023

Kulkarni A. Metabolomics of circulating human memory CD4+T effector and T regulatory cells reveals that phenylalanine is a metabolic checkpoint of pathogenic Th2 cells development. World Immune Regulation Meeting XVII 2023, Davos, Switzerland, 5-8 July 2023.

Messner C. B., Mapping Functional Associations of Proteins using Large-Scale Proteomics Datasets. HUPO Pre-Congress Training Course (Protein Interactions/Spatial Proteomics), Busan, South-Korea, 17 September 2023.

Mitamura Yasutaka, Matthias Reiger, Juno Kim, Yi Xiao, Damir Zhakparov, Katja Baerenfaller, Marie-Charlotte Brüggen, Patrick M Brunner, Damian Roqueiro, Claudia Traidl-Hoffmann, and Cezmi A Akdis Spatial and single-cell transcriptomics provide insights into the complex inflammatory cell network in atopic dermatitis AAAAI Annual Meeting 2023, San Antonio, USA, 23-26 February 2023.

Mitamura Yasutaka, Matthias Reiger, Juno Kim, Yi Xiao, Damir Zhakparov, Katja Baerenfaller, Marie-Sanne S. Meisser, Yasutaka Mitamura, Can Altunbulakli, Josefine Bandier, Morten S. Op-strup, Anne-Sofie Ø. Gadsbøll, Manru Li, Ge Tan, Cezmi A. Akdis, Carsten Geisler, Jeanne D. Johansen & Charlotte M. Bonefeld. Different regulation of immune-related genes in the skin from non-responders and allergic individuals exposed to p-phenylenediamine Springtime School 2023: Skin homeostasis and inflammation, Copenhagen, Denmark, 24-26 April 2023.Charlotte Brüggen, Patrick M Brunner, Damian Roqueiro, Claudia Traidl-Hoffmann, and Cezmi A Akdis Spatial transcriptomics and single-cell transcriptomics elucidates the intricate inflammatory cellular network in atopic dermatitis.ISID Annual Meeting 2023, Tokyo, JAPN, 10-13 April 2023.

Mitamura Yasutaka, Household laundry detergents cause barrier dysfunction and induce inflammation in mouse and human skin. Tight Junctions: from Structure and Development to Therapeutics, Leysin, Switzerland, 4-8 June 2023

Mitamura Yasutaka,Household laundry detergents disrupt barrier integrity and induce inflammation in mouse and human skin. EAACI congress 2023, Hamburg, Germany, 9-11 June 2023

Mitamura Yasutaka, Carbonic anhydrase: A novel potential therapeutic target in atopic dermatitis. WIRM 2023, Davos, Switzerland, 5-8 July 2023

Mitamura Yasutaka, Differential regulation of epidermal differentiation and its metabolism by interleukin-13 and interleukin-22 in atopic dermatitis. SSAI 2023, Bern, Switzerland, 24-25 August 2023

Mitamura Yasutaka, Discovery of Carbonic Anhydrase as a Novel Controller of Skin Inflammation and Barrier Strength in Atopic Dermatitis. EEAACI Summer Symposium on Epithelial Cell Biology 2023, London, England, 21-22 September 2023

Mitamura Yasutaka, PM2.5 and CO2 levels affecting epidermal barriers and subsequent allergic and immune conditions, Bern, Switzerland, 9-10 November 2023

Ogulur I. Recent evidence and molecular mechanisms on epithelial barrier theory. EAACI Hybrid Congress 2023, Hamburg, Germany, 9-11 June 2023.

Pat Y. Epithelial Barrier Theory: Novel evidence on mechanisms of development of allergic and autoimmune diseases.Aerobiology Symposium 2023, Bern, Switzerland, 9-10th November 2023

Radzikowska U. Epithelial RIG-I signaling in asthma exacerbations and COVID-19. Biomedicine Seminar HS 2023, University of Zurich, Zurich, Switzerland, 31.10.2023.

Radzikowska U. Omics technologies in allergy and asthma research: An EAACI position paper. Hot Topics Speaker, European Academy of Allergy and Clinical Immunology Annual Congress 2023, Hamburg, Germany, 9-11.06.2023.

Sokolowska M. Novel mechanisms controlling viral and allergic inflammation in airway epithelium 17h Introductory Course in Microbiology and Immunology, ETH Zurich, January 11-13 2023

Sokolowska M. Novel mechanisms controlling viral and allergic inflammation in airway epithelium. Institute of Environmental Medicine, University of Augsburg, Technical University Munich and the Helmholtz Zentrum München. 20th March 2023

Sokolowska M. Trained innate immunity, a new target for asthma prevention? European Respiratory Society Research Seminar. Berlin, Germany ,17-18 April 2023

Sokolowska M. Novel mechanisms controlling viral and allergic inflammation in airway epithelium. National Institutes of Health, Critical Care Medicine Department Research Seminar, Bethesda, US, 25.04.2023

Sokolowska M. Crosstalk of innate immunity and immune metabolism in allergic disease. EAACI Annual Congress, Hamburg, Germany 9-11th June 2023

Sokolowska M. New aspects of universal mechanisms of allergic diseases. Konferencja Alergia, Astma, Immunologia Kliniczna, Lodz, Poland 15-17th June 2023

Sokolowska M. Immune metabolism of type 2 immunity in allergy and immune tolerance. WORLD IMMUNE REGULATION MEETING – XVII., Davos, Switzerland, 5-8th July 2022

Sokolowska M. Breathing with confidence: Interplay between Immunity and Metabolism in Asthma and COVID-19. BIO2023 13-16, September 2023, Szczecin, Poland

Sokolowska M. Breathing with confidence: Interplay between Immunity and Metabolism in Asthma and COVID-19. University of Zurich Inaugural Lecture, 25 September 2023, Zurich, Switzerland

Sokolowska M. Microbiome and virome in asthma. EAACI International Severe Asthma Forum 6-7 October 2023, Rome, Italy

Sokolowska M. Lipid signaling in severe asthma. EAACI International Severe Asthma Forum 6-7 October 2023, Rome, Italy

Sokolowska M. Metabolomics of Circulating Human Memory CD4+T Effector and T Regulatory Cells Reveals that Phenylalanine is a Metabolic Checkpoint of Pathogenic Th2 Cells Development. Collegium Internationale Allergologicum (CIA), 10-14th October 2023, Montreal, Canada

Sokolowska M. Astma oskrzelowa i COVID-19: nowe mechanizmy zaostrzeń wywołanych wirusami i alergenami". 28 sympozjum naukowo-szkoleniowe postepy w alergologii i pneumonologii. 2-4 November 2023 Cracow, Poland

Sokolowska M. Breathing with confidence: Interplay between Immunity and Metabolism in Asthma and COVID-19. Thermo Fisher Scientific / EAACI PhARF award ceremony. 05.12.2023 Uppsala, Sweden

Van de Veen W. Long term follow up of specific memory B cells in vivo. 26th annual research meeting of the Department of Dermatology University of Zurich & University Hospital Zurich, Davos, Switzerland, 17 – 19 March 2023.

van de Veen W. What has Omics technologies brought to the allergy field? Eosinophilic diseases. EAACI Hybrid congress, Hamburg, Germany, 9-11 June 2023.

van de Veen W. Biomarkers and B cells in EoE. 1st Swiss Eosinophilic Esophagitis retreat, Rasses, Switzerland, 24-25 August 2023.

van de Veen W. Allergen-specific B cell responses in food allergy. 3rd International Conference Food Allergy Forum, Amsterdam, NL, 27-29 September 2023.

van de Veen W. In Vivo Monitoring of Allergen-Specific Memory B-Cells: Tracking Development and Persistence. 33rd Biennial Symposium of the Collegium Internationale Allergologicum, Montréal, Canada, 10-14 October 2023.

Zhakparov D, Moriarty K, Roqueiro D, Baerenfaller K. GeneSelectR: A Machine Learning-Based R Package for Enhanced Feature Selection and Biological Assessment in RNAseq Analysis of Complex Biological Datasets. BC2 Computational Biology Conference, Basel, Switzerland 11 - 13 September 2023.

Zhakparov D, Moriarty K, Roqueiro D, Baerenfaller K. GeneSelectR: A machine learning-based R package for feature selection and biological assessment in RNAseq analysis of complex biological datasets. World Immune Regulation Meeting (WIRM), Davos, Switzerland, 5 - 8 July 2023.

CHAIRS AT CONGRESSES

Akdis C. EAACI Immunology Winter School, Davos, Switzerland 26-29 January.

Akdis C. Press conference Editor-in-Chief Allergy Journal, Launch of the China Issue, Beijing, May 31, 2023

Akdis C. EAACI Annual Meeting, Allergy Journal Editorial Board Meeting, Highlights and Achievements. June 10, 2023, Hamburg, Germany

Akdis C. EAACI Annual Meeting, Allergy Journal Associate Editors' Meeting, Highlights and Achievements. June 10, 2023, Hamburg, Germany

2023

Akdis C. EAACI Annual Meeting, Plenary Session 2. June 10, 2023, Hamburg, Germany

Akdis C. World Immune Regulation Meeting, Session 1, Innate Immune Response. July 5, 2023, Davos, Switzerland

Akdis C. World Immune Regulation Meeting, Congress Chair. July 5-8, 2023, Davos, Switzerland

Akdis C. Editors' Retreat Allergy-EAACI/Wiley, Imperial College, London, September 22, 2023

Akdis C. EAACI Summer Symposium on Epithelial Cell Biology, Session 2, Imperial College,London, September 22, 2023

Akdis C. Opening Session. 6th International Severe Asthma Forum (ISAF), Rome, Italy, October 5-7, 2023.

Akdis C. Asia Pacific Society of Allergy and Clinical Immunology Annual Meeting, Singapore October 23-26, 2023

Akdis C. International Immunology IUIS Congress. New Nomenclature of Hypersensitivity Diseases. December 1, 2023, Cape Town, South Africa.

Akdis M. Symposium 16: Advances in Clinical Allergy/Immunology: Shared Decision Making. WAO PASAAI Pan Arab Allergy Meeting. Dubai, 27, 28, and 29 January 2023

Akdis M. ORAL Session: OAS 2 - Immunotherapy to food allergy Plenary Symposia: PL2 - Microbial immune interactions over the life span Year in Review Sessions: YIR 2 - Year in Review 2, EAACI Hybrid Congress, Hamburg, Germany. June 9-11, 2023.

Akdis M
Session 8 – The epithelial barrier as common denominator for other diseases. EAACI Summer Symposium on Epithelial Cell Biology, London, UK. September 21-22, 2023.

Baerenfaller K. Deepening the Understanding of Biodiversity through Genome Sequencing and Artificial Intelligence. LS2 Annual Meeting 2023, Zurich, Switzerland, 16-17 February 2023.

Baerenfaller K. Plenary Session 11: Metabolism and type 2 immunity. World Immune Regulation Meeting XVII 2023, Davos, Switzerland, 5-8 July 2023

Baerenfaller K. [BC]2 Highlights, BC2 Basel Computational Biology Conference, Basel, Switzerland, 11-13 September 2023

Baerenfaller K. Closing Session, BC2 Basel Computational Biology Conference, Basel, Switzerland, 11-13 September 2023

Barletta E. Epigenomics and transcriptomics in immune regulation. WIRM 2023, Davos, Switzerland, 5-8 July 2023

Koch J, Poster Session 4: Epigenomics and transscriptomics in immune regulation. WIRM, Davos, 5-8 July 2023
Messner CB, HUPO Pre-Congress Training Course (Protein Interactions/Spatial Proteomics), Busan, South-Korea, 17 September 2023.

Messner CB, HUPO World Congress, Interactomes/Protein Networks, Busan, South-Korea, 18 September 2023

Mitamura Yasutaka, OAS7 Biologicals in atopic dermatitis. EAACI congress 2023, Hamburg, Germany, 9 June 2023

Mitamura Yasutaka, Workshop Session 6: Epigenomics and transscriptomics in immune regulation. WIRM 2023, Davos, Switzerland, 5-8 July 2023

Ogulur I. COVID-19. EAACI Hybrid Congress 2023, Hamburg, Germany, 9-11 June 2023.

Ogulur I. Epithelial barriers and immune response. World Immune Regulation Meeting XVII (WIRM XVII), Davos, Switzerland 5-8 July 2023.

Ogulur I. Innate immunity II. World Immune Regulation Meeting XVII (WIRM XVII), Davos, Switzerland 5-8 July 2023.

Pat Y. Epithelial barriers: mechanisms of disruption. WIRM 17, Davos, Switzerland, 5-8 July 2023.

Pat Y. Strategies to foster innovation and resilience. Aerobiology Symposium 2023, Bern, Switzerland 9-10th November 2023

Radzikowska U. Inflammation in the Lung: Friend or Foe in Viral Infections?, Snowbird, UT, United States, 23-26 April 2023.

Radzikowska U. European Academy of Allergy and Asthma Research (EAACI) Annual Congress 2023im Hamburg, Germany, 09-11 June 2023.

Radzikowska U. XVII World Immune Regulation Meeting, Davos, Switzerland, 5-8 July 2023.

Sokolowska M. Microbiology and Immunology 17th introductory course, Oral Abstract Session, ETH Zurich, 11-13 January 2023.

Sokolowska M. Environment and Immunology StandUp Talks. 21st EAACI Immunology Winter School "Basic Immunology Research in Allergy and Clinical Immunology, 26-29th January 2023

Sokolowska M. Keynote lecture of Gábor Tamás Szabó "The principles and therapeutic use of mRNA technology". 21st EAACI Immunology Winter School "Basic Immunology Research in Allergy and Clinical Immunology, 26-29th January 2023

Sokolowska M. Poster Session: Asthma and airway diseases. 21st EAACI Immunology Winter School "Basic Immunology Research in Allergy and Clinical Immunology, 26-29th January 2023

Sokolowska M. Immunology treasure hunt on Environment and Immunology: Workshop session. 21st EAACI Immunology Winter School "Basic Immunology Research in Allergy and Clinical Immunology, 26-29th January 2023

Sokolowska M. Practical course at SIAF. 21st EAACI Immunology Winter School "Basic Immunology Research in Allergy and Clinical Immunology, 26-29th January 2023

Sokolowska M. Flash talks on immune-mediated diseases. EAACI Annual Congress, Hamburg, Germany 9-11th June 2023

Sokolowska M. Plenary Session: Metabolism and immunity symposium. WORLD IMMUNE REGULATION MEETING – XVII., Davos, Switzerland, 5-8th July 2022

Sokolowska M. Immunometabolism workshop. WORLD IMMUNE REGULATION MEETING – XVII., Davos, Switzerland, 5-8th July 2022

Sokolowska M. Short Communication Session II Basic Immunology II. Swiss Society for Allergology and Immunology Annual Congress, Bern, Switzerland, 24-25 August 2023

Sokolowska M. Symposium. Microbial triggers of asthma exacerbations. EAACI International Severe Asthma Forum 6-7 October 2023, Rome, Italy

Sokolowska M. Plenary Session: Biomarkery w diagnostyce, monitorowaniu skuteczności leczenia oraz ocenie progresji chorób atopowych. 28 sympozjum naukowo-szkoleniowe postepy w alergologii i pneumonologii. 2-4 November 2023 Cracow, Poland

Zhakparov D, Özge A. Poster Session 8: COVID-19 and SARS-COV-2 . World Immune Regulation Meeting (WIRM), Davos, Switzerland, 5 - 8 July 2023.

DEGREES

Baerenfaller K.
Obtained the Right to Confer a PhD at the Faculty of Science at the University of Zurich (from October 2023)

AWARDS

Akdis M
World Allergy Organisation (WAO), Special Recognition Award. WAO PASAAI Pan Arab Allergy Meeting. Dubai, 27, 28, and 29 January 2023

Akdis M
Asia Pacific Association of Allergy, Asthma and Clinical Immunology, APAAACI Women in Science Award 2023, Singapore, October 23-26, 2023.

Barletta E. Registration grant. SSAI Annual Congress 2023, Bern, Switzerland, 24-25 Aug 2023

Barletta E. EFIS-EJI Travel Grant 2023. SIICA-SYIS JOINT SYMPOSIUM 2023, Rome, Italy, 3-4 November 2023

Bel imam M. SYIS Best Poster Presentation Award. WIRM 2023 in Davos, Switzerland, 5-8 July 2023.

Koch J. BC2 poster prize. BC2, Basel, Switzerland, 11-13 Sep 2023.

Koch J. SCNAT fellowship. BC2 Basel, Switzerland, 11-13 Sep 2023.

Koch J. Registration grant. SSAI Annual Congress 2023, Bern, Switzerland, 24-25 Aug 2023

Mitamura Yasutaka. 2023 AAAAI International Travel Scholarship. AAAAI Annual Meeting 2023, San Antonio, USA, 23-26 February 2023.

Mitamura Yasutaka. 2023 Travel grant from SUND-ISIM. Springtime School 2023: Skin homeostasis and inflammation, Copenhagen, Denmark, 24-26 April 2023.

Mitamura Yasutaka.2023 SSDV travel grant. ISID Annual Meeting 2023, Tokyo, JAPN, 10-13 April 2023.
Mitamura Yasutaka. Brunello Wüthrich aha! Neurodermitis (Atopic dermatitis) Research Prize 2023. SSAI 2023, Bern, Switzerland, 24-25 August 2023

Radzikowska U., Wiley top downloaded article: DOI: 10.1111/all.15089

Radzikowska U., Scholarship for EAACI Annual Congress 2023 (Hamburg, Germany, 9-11.06.2023) awarded 03.04.2023.

Radzikowska U. Keystone Symposia Future of Science Fund Scholarship. Inflammation in the Lung: Friend or Foe in Viral Infections? in Snowbird Resort, Snowbird, UT, United States, 23-26 April 2023.

Schneider S. SIAF Science Day Award 2nd Place. SIAF science day in Davos, Switzerland, 14. December 2023

Sokolowska M. European Academy of Allergy and Clinical Immunology (EAACI)-Phadia Research Forum (PhARF) award for outstanding and independent research in allergy and Immunology

Sokolowska M. Willey top cited articles 2021-2022: DOI: 10.1111/all.14739; DOI: 10.1111/all.14657

Zhakparov D. Best Workshop Presentation Award by BioLegend. World Immune Regulation Meeting (WIRM) in Davos, Switzerland, 5 - 8 July 2023.

LECTURES

Baerenfalleer K.
Lecture in 'Advanced Block Course: Computational Biology' of the Life Science Zurich Graduate School; Topic: Large data sets: Transcriptomics and Proteomics; duration: 3 hours

Lecture in BIO390 'Indroduction to Bioinformatics'; Topic: Proteomics, duration 2 hours
BME351 Block course "Biomedical Data Mining"; duration: 3 weeks

Additional lectures 2023:
636-0704-00L Computational Biology and Bioinformatics Seminar (ETH Zurich), duration: 2 hours
CDS 303 - Data Science und Informatik in der Biologie (University of Applied Sciences of the Grisons FHGR), duration: teaching blocks

of 3 x 2 days
TecDay Bündner Kantonsschule, Modul M02 'Bananasplit – Vom Bananen-Genom zu menschlichen Allergien'
Besuch Gymnasium Lengmatta 'Das Immunsystem und Forschung am SIAF'

PUBLIC SEMINARS

24.01.2023
Dr. Ganesh Pandan Namasivayam, “Nucleic acid-based small molecule therapeutics.”

23.03.2023
Dr. Marc Emmenegger, “Cystic fibrosis and the response to peanut allergens.”

31.03.2023
Prof. Dr. med Onur Boyman, “Neutrophils and inflammation”

03.04.2023
SIAF JMA Board
Mattia Giovannini: Anaphylaxis Phenotypes in Children
Yasutaka Mitamura: Diving deep into skin immunology: Novel subsets of macrophages, dendritic cells, T cells and fibroblasts and their interactions in atopic dermatitis
Cristina Boccabella: Small Airways Disease (SAD) in severe asthma as a novel endpoint and distinct target for Mepolizumab (SASAM Study)
Urszula Radzikowska: Immune metabolism
Ilsmail Ögülür: Food emulsifiers, dish washer detergents and epithelitis
Duygu Yazici: Organochips (organ-on-a-chips) and future of the epithelial barrier research
Damir Zhakparov: Feature Selection Workflow for RNAseq Datasets with regard to Biomedical Relevance
Riccardo Castagnoli: Translational approaches to dissect microbiota-host interactions in inborn errors of immunity
Yagiz Pat: Organoids and future of epithelial barrier research
Manal Bel imam: B cells, antibodies and biomarkers in eosinophilic esophagitis
Pattraporn Satitsuksanoa: Distinct mechanisms of induced and natural immune tolerance
Rubén Fernández-Santamaría: Cellular recognition of drug antigenic determinants - New parameters to improve in vitro tests

19.04.2023
EAACI Symposium on Highlights and Novel Developments in Allergy
Prof. Maria J. Torres "Immunomodulation in LTP allergy"
Prof. Stefano del Giacco "Biologics in Asthma: more than just controller medications? The hunt for a potential disease-modifying effect"
Prof. Mohamed Shamji “Machine learning algorithms advancing novel therapeutics and biomarker discovery in allergy and asthma”
Prof. André Moreira “Targeting environmental inequality towards allergy health”

29.06.2023
Prof. Dr. med. Alex Straumann “EoE, some relevant clinical principles."
Dr. med. Andrea Kreienbühl “EoE, epidemiological aspects."
PD Dr. med. Luc Biedermann “EoE, known and hypothetical pathogenetic features."

03.10.2023
Dr. Peter Wick “What do cells and tissues inform us about novel nanomaterial-enabled health solutions?"

31.10.2023
Dr. Urszula Radzikowska, “Epithelial RIG-I signaling in asthma exacerbations and COVID-19" online

16.11.2023
SIAF Company Day
Vitaris AG
Faust Laborbedarf AG
Bucher Biotec AG, Cutting edge technologies used in life science research
BioLegend – Enabling Legendary discovery
LabForce highlights – transfection, electrophoresis, and mycoplasma prevention
Miltenyi Biotec
Chemie Brunschwig AG, Chemie Brunschwig AG is your reliable partner
Qiagen, The future of PCR is digital: QIAcuity dPCR system
RUWAG Handels AG
Axon Lab AG
Agilent Technologies
Revvity, Meet Revvity: Powering Innovation From Discovery To Cure
Beckman Coultier

22.11.2023
Prof. Wolf-Dietrich Hardt “Food components can disrupt colonization resistance against Salmonella gut infections: lessons from mice."

SIAF SCIENCE DAY

14.12.2023
Ula Radzikowska
Ula Radzikowska and immunometabolism of asthma
Ines Jardon Parages
The Magi's Chili Encounter: Christmas Season Countdown
Elena Barletta
Feathered fun and Shell surprises: bridging species to find the perfect balance
Karin Fieten
Treating patients with severe asthma in the alpine climate
Yagiz Pat
X-files
Manru Li
The big bad wolf is on the way! Quick, time to build my sturdy brick house!
Duygu Yazici
How to make a peanut butter?
Paolo D'Avino
Inglorious Scientists
Sena Ardicli
Milk N' Roses
Minglin Yang
One Piece: The Adventure of B Cells Expressing Diverse Histamine Receptors
Stephan Schneider
ARRRRNA Pirating 101
Juan Felipe Lopez
Jingle cells, jingle all D way: A Holiday Expedition into Immunoglobulin Delights!
Manal Bel imam
EoE Disclosed
Özge Ardicli
FcR blocking reagent adventures in the realm of B cell

Winner of the SIAF Science Day 2023:
Paolo D'Avino

SCIENTIFIC POSTS AND EDITORIAL ACTIVITIES

Akdis CA.
Allergy, Editor in Chief
Current Opinion in Immunology, editorial board member
Expert Opinion on Emerging Drugs, editorial board member
International Reviews of Immunology, editorial board member
Journal of Investigational Allergology and Clinical Immunology, editorial board member
American Academy of Allergy, Asthma & Immunology (AAAAI) - Eczema Atopic Dermatitis Committee Member
American Academy of Allergy, Asthma & Immunology (AAAAI) - Cells and Mediators Committee, Board Member
Christine Kuehne - Center for Allergy Research and Education (CK-CARE) – Directorium member
COST Action BM0806 - Recent advances in histamine receptor H4 research member
National Institute of Health, USA - Scientific Advisory Board, Food Allergy, Allergen-Specific Immunotherapy
European Academy of Allergy Clinical Immunology (EAACI) – Member of Biologicals Guidelines
European Academy of Allergy Clinical Immunology (EAACI) - Member of Allergen Immunotherapy Guidelines
EAACI Research and Outreach Committee (ROC) Immunology Chair
European Asthma Research and Innovation Partnership (EARIP) - Member
Global Allergy and Asthma European Network GA2LEN - Member
World Immune Regulation Meeting - Chairman
Stanford University, School of Medicine, Department of Immunology, Sean Parker Allergy Center - Scientific Advisory Board Member

Akdis M.
Principal Investigator-The Microbiology and Immunology PhD program, UZH-ETH
EAACI Research and Outreach Committee (ROC) Member
EAACI Food Allergy Guidelines member
European Academy of Allergy Clinical Immunology (EAACI) – Member of Biologicals Guidelines
Member of Scientific Board of Sean Parker Allergy Center, Stanford
Member of Scientific Board of Leo Foundation Skin Immunology Research Center
Workpackage Member of EU project CURE
Allergy, Editorial Board Member
Journal of Allergy and Clinical Immunology, Reviewer Board Member
SNF project reviewer
PAI, Reviewer Board Member
Science Foundation Ireland, Reviewer Board member
World Immune Regulation Meeting, Member of the scientific committee

Baerenfaller K.
Member of the Scientific Committee Core Team (SCCT) of the BC2 Basel Computational Biology Conference
Member of the SIB Board of Directors
Group leader of the Swiss Institute of Bioinformatics (SIB)
Member of LS2, President of the LS2 Bioinformatics intersection
Member of the European Reference Genome Atlas (ERGA)
Member of EAACI (European Academy of Allergy & Clinical Immunology)
Board member of Science City Davos
Project leader of ETH Studio Davos
Co-President of Naturforschende Gesellschaft Davos

2023

Fieten K.
Article collection 'Women in Science: Allergy Research' for Frontiers in Allergy

Messner C.
Member of the Human Proteome Organization (HUPO)
Member of Life Science Switzerland, Proteomics and Bioinformatics Section
Member of the Austrian Proteomics and Metabolomics Association (APMA)
Member of the European Academy of Allergy Clinical Immunology (EAACI)
Group leader SIB – Swiss Institute of Bioinformatics
Principal Investigator – Systems Biology PhD program (UZH/ETH)
Principal Investigator – Molecular Life Science PhD program (UZH/ETH)
Reviewer for Nature Communications Reviewer, Nature Biomedical Engineering, ACS omega, Expert review of proteomics"

Mitamura Yasutaka
Editor in Frontiers in Allergy

Rhyner C.
Allergy, member of the editorial board
JACI, Member of the reviewer board
Int Arch All, member of the editorial board
Frontiers in Allergy Therapies, Therapeutic targets and Mechanisms, Associated Editor
EAACI Interest Group „Clinical and veterinary allergology", member of the board
Member of Life Sciences Zurich Graduate School-Zurich
World Immune Regulation Meeting, Member of the scientific committee

Sokolowska M.
Principal Investigator- the Microbiology and Immunology PhD program, UZH-ETH
Chair, European Academy of Allergy and Clinical Immunology (EAACI) Basic and Clinical Immunology Section
Chair, European Academy of Allergy and Clinical Immunology (EAACI) Research and Outreach Committee (ROC), Immunology Working Group
Chair, European Academy of Allergy and Clinical Immunology (EAACI) Task Force on Immune Metabolism
Secretary, European Academy of Allergy and Clinical Immunology (EAACI) Task Force on Eicosanoids
Secretary, European Academy of Allergy and Clinical Immunology (EAACI) Task Force on Public Outreach
Member of the scientific committee, World Immune Regulation Meeting 2023
Chair, European Academy of Allergy and Clinical Immunology (EAACI) Immunology Winterschool 2023, Davos, Switzerland
Expert Reviewer for Grant agencies: Medical Research Council, UK Research and Innovation (MRC-UKRI), German Research Foundation ("Deutsche Forschungsgemeinschaft", DFG), Polish National Sceince Center (NCN), Vrije Universiteit Brussel (VUB), Sidra Medicine, Quatar
Editotial activities
Heliyon, Cell Press, Associate Editor Immunology
Scientific Reports, Editorial Board member
Allergy, Editorial Board member
Frontiers in Immunology, Editorial Board member
Clinical and Molecular Allergy, Editorial Board member
Frontiers in Pharmacology, Reviewer Board member
Frontiers in Allergy, Reviewer Board member

van de Veen W.
Member College of Expert Reviewers - European Science Foundation (ESF).
Management committee member - COST action entitled: "The Core Outcome Measures for Food Allergy".
Programme committee member - the Graduate School Graubünden.
Editotial activities
Reviewer board member - Journal of Allergy and Clinical Immunology (JACI), Frontiers in Allergy.
Editorial board member - Allergy
Scientific referee for peer-reviewed journals: Journal of Allergy and Clinical Immunology (JACI), Allergy, PLOS ONE, Nature Scientific Reports, Journal of Investigational Allergology and Clinical Immunology (JIACI), European journal of immunology (EJI), International Archives of Allergy and Immunology, Immunotherapy Advances, Frontiers in Immunology, Frontiers in Allergy, npj vaccines.

NATIONAL AND INTERNATIONAL COLLABORATIONS

Department of Food Science, Aarhus University (DK), Prof. L. Bach Larsen, Prof. N. Aagaard Poulsen

Amsterdam UMC, Department of Pulmonary Medicine, (NL), Dr. E Weersink, Prof S Vijverberg

Allergopharma GmbH & Co. KG., Reinbek (DE), Dr. A. Nandy, Dr. C. Willers, Dr. H. Kahlert, Dr. N. Berek

Allgem. Krankenhaus (AKH) Wien (AT), Institut für Allgemeine und Experimentelle Pathologie, Prof. H. Breiteneder, Dr. P. Ebersteiner, Prof. E.-J. Jarolim, Dr. S. Natter, Prof. O. Scheiner, Prof. R. Valenta, Dr. S. Vrtala

AO Research Institute Davos, (CH), Dr. S. Grad, Prof. M. Alini, Dr. F. Moriarty, Prof. R.G. Richards, Dr. K. Thompson, Prof. M. Stoddart, Prof. B. Gueorguiev, Dr. J. Barcik, Dr. T. Serra, Prof. M. D'Este, Dr. E. Della Bella

Beckman Research Institute, Department of Molecular and Cellular Biology, City of Hope (US), Dr. M. Boldin

Benaroya Research Institute at Virginia Mason; Department of Medicine, University of Washington (US), Dr. W. Kwok, IT Chow

Bilkent University, Ankara (TR), Prof. I. Gürsel

Biognosys AG, Schlieren, Dr. Nigel Beaton, Dr. M. Tognetti

Charité - Universitätsmedizin Berlin, Institut für Biochemie, Prof. M. Ralser

Center for Inflammation Research, University of Edinburgh (UK), Prof. J. Schwartze

Cantonal Office for Nature and Environment of the Grisons, Chur (CH); Cantonal Office for Food

Security and Animal Health of GR, Cantonal Office for Anture and Environment, Cantonal for Military and Civil Protection, Cantonal office for Health

Centre Suisse d'Electronique et Microtechnique SA (CSEM) Landquart (CH), Dr. S. Generelli, Dr. D. Ulrich

Complutense University Madrid (ES), Dr. O. Palomares, Dr. M. Martin-Fonseca, Dr. A. Querencias

Consejo Superior de Investigaciones Cienti cas (CSIC), Madrid (ES), Dr. C. Bernabéu

CURE partners: Prof. N. Papadopoulous, Assistant Prof. P. Xepapadaki, Dr. S. Taka, Assistant Prof. N. Rovina, Prof. D. Robertson, Dr. T. Gilman, Dr. S. Megremis, Dr. E. Andreakos, Prof. KB. Marcu, Dr. I. Galani, Prof. ML. Kowalski, Prof. X. Thibert-Plante, Dr. N. Cahnishivili, Dr. M. Goderdzishvili, G. De Carlo

Endophyte Service Laboratory in Corvallis (US), Dr. Jenni Duringer

Erasmus MC, Rotterdam (NL), Dr. R. de Swart, Prof. S. Pasmans, Dr. M. Schreurs

ETH Zürich (CH), Computational Systems Biology Group, Prof. J. Stelling; Institute of Pharmaceutical Sciences, Prof. G. Folkers; Department of Biosystems Science and Engineering, DS. Roqueiro; ETH Studio Davos
Forschungszentrum Borstel (DE), Prof. U. Jappe, Prof. H. Fehrenbach, Prof. Dr. O. Holst

Franciscus Gasthuis & Vlietland, Dept of Paediatric Medicine, Rotterdam (NL), Dr. G. A. Tramper-Stranders

Functional Genomics Center Zurich (CH), Prof. Dr. R. Schlapbach, Dr. H. Rehrauer, Dr. C. Aquino, Dr. F. Castro Giner, Dr. W. Wolski, Dr. P. Nanni, Dr. C. Fortes

GlaxoSmithKline (GSK), Stevenage (UK), Dr. E. Hessel, Dr. D. Michalovich

Genoskin SAS, Toulouse (FR), Prof. N. Gaudenzio

Hacettepe University, Ankara (TR), Prof. O. Kalayci, Prof. E. Birben, Prof. C. Karaaslan, Prof. Dr. B. Seker, Dr. P. Gür

Harvard University (US), T.H. Chan School of Public Health, Prof. K. Nadeau

Hochgebirgsklinik Davos Wolfgang (CH), Prof. H.W. Duchna, Dr. M. Möhrenschlager, Dr. A. Kalweit, Dr. C. Steiner, Dr. A. Kirsch, Dr. G. Menz, Dr. J. Vontobel, Dr. F. Yong-Zing

Immunologie et Neurogénétique Expérimentales et Moléculaires (INEM), Department of Molecular Immunology, Orleans (FR), Prof. B. Ry el, Dr. D. Togbe

Imperial College, London (UK), Prof. S. Durham, Dr. K. Nouri-Aria, Dr. MH Shamji, Prof. S. Johnston, Dr. M.R. Edwards, Dr. D.J. Jackson, Dr. T. Kebadze

Institute for Research in Biomedicine, Bellinzona (CH), Prof. G. Guarda

Izmir Biomedicine and Genomic Center, Dokuz Eylul University, Izmir (TR), Prof. I. Gürsel

Jagiellonian University, Krakow (PL), Prof. M. Sanak, Dr. B. Jakiela

Kantonsspital Graubünden, Chur (CH), Dr. M. Kuhn, Prof. T. Fehr, Dr. E. Riedi, Dr. HB. Fahrner, Dr. C. Bretschneider, Dr. D. Batusic

Kantonsspital St. Gallen, Institute of Immunobiology (CH), Prof. L. Flatz, Prof. R. Lauener

Karolinska Hospital, Stockholm (SE), Prof. Dr. G. Gavfelin, Dr. H. Grönlund, Prof. O. Rasool, Prof. A. Scheynius, Prof. M. van Hage, Dr. S. Thunberg, Prof. N. Bostanci, Dr. K. Bao

LEO Pharmaceutical Products Sarath Ltd (CH), Dr. M. Fähndrich

King's College London, Asthma UK Centre in Allergic Mechanisms of Asthma, School of Immunology and Microbial Sciences (UK), Dr. G. Woszczek

Leiden University Medical Center, Department of Biomedical Data Sciences (NL), Dr. J Sont

National and international collaborations

Marmara University, Istanbul (TR), Prof. T. Akkoç

Medical Center Leeuwarden, Department of Pulmonary Diseases, (NL), Dr. A ten Brinke

Medical University of Bialystok, Department of Regenerative Medicine and Immune Regulation (PL), Prof. M. Moniuszko, Dr. A. Eljaszewicz

Medical University of Brasov (RO), Prof. I. Agache, Dr. C. Agache

Medical University of Lodz (PL), Prof. J. Makowska, Prof. M. Chalubinski, Dr. F. Styrzynsk

Medical University of Vienna (AT), Department of Pediatrics, Vienna, Prof. Z. Scephaluzi; Department of Dermatology, PM. Brunner; Institute of Pathophysiology and Allergy Research, Prof. E. Untersmayr

Medical University of Warsaw (PL), Prof. W. Feleszko

National Research Institute for Child Health and Development, Department of Allergy and Clinical Immunology (JP), Dr. H. Morita, Prof. K. Matsumoto, Prof. H. Saito

Nederlands Astmacentrum Davos (CH), Dr. D. Prins, Dr. M. Drijver, Dr. R. Wolters, Dr. K. Fieten

Noble Research Institute LLC (US), Prof. C. Young

Ostschweizer Kinderspital, St. Gallen (CH), Prof. R. Lauener, Dr. C. Roduit

Padua University Hospital, Italy (IT), Prof. A. Muraro

Paul-Ehrlich-Institut, Langen (DE), Dr. E. Flory, Prof. S. Vieths

Paul Scherrer Institute (CH), Prof. R. Schibli, Dr. R. Waibel

Philipps University of Marburg, Medical Faculty Marburg (DE), Prof. H. Garn and Prof. H. Renz, Dr. D. Potaczek

Red Cross Finland, Blood Service, Stem Cell, Transplantation Services, Research Laboratory, Helsinki (FI), Dr. N. Woolley

Saga University (JP), Division of Dermatology, Department of Internal Medicine, Faculty of Medicine, Prof. K. Sugita

Scibase AG, Stockholm (SE), S. Grant, P. Svedenag, N. L. Askary, A. Karsfeld, D. Melin

Sean N. Parker Center for Allergy Research at Stanford University (US), Prof. K. Nadeau, Prof. S. Chinthrajah

Semmelweis University, Department of Genetics, Cell- and Immunobiology, Prof. Z. I. Komlósi

Seoul National University, Seoul National University Bundang Hospital, Department of Internal Medicine, Prof. YS Chang, Dr. P Losol

Spital Davos, Dr. W. Kistler, Dr. M. Villiger, Dr. T. Rothe, Dr. A. Speiser

Stanford University, Department of Pathology (US), Dr. S. Boyd, Prof. S.J. Galli

Swiss Research Institute for Sports Medicine, Davos (CH), Dr. M. Villiger, Dr. W. Kistler

Technische Universität München (DE) - Klinik und Poliklinik für Dermatologie und Allergologie am Biederstein, Prof. J. Ring - Forschungszentrum für Umwelt und Gesundheit, Prof. C. Schmidt-Weber, Prof. Dr. C. Traidl-Hofmann

The Hospital for Sick Children, Cancer and Blood Research Program, Toronto (CN), Dr. M. Letarte

The Netherlands Cancer Institute, Divison of Cellular Biochemistry, Amsterdam (NL), Prof. P. ten Dijke, Dr. S. Itoh

Toulouse Institute for Infectious and Inflammatory Diseases (Infinity) INSERM, University Toulouse III, Toulouse (FR), Prof. N. Gaudenzio

The Seventh Affiliated Hospital, Sun Yat-sen University, Prof. Z. Zhiyu

Uludag University of Bursa, Bursa (TR), Prof. H.B. Oral, Prof. F. Budak

Universidad CEU San Pablo, Madrid (SP), Prof. Coral Barbas, Dr. D. Barber, Prof. M.M. Escribese, Dr. A. Villaseñor

Universität Bern (CH), Dept. Clinical Vet. Medicine, PD Dr. E. Marti, Prof. A. Zurbriggen; Vetsuisse Faculty, Institute of Virology and Immunology, Prof. V. Thiel, Prof. Dr. C. Favrot, Dr. A. Rostaher, Dr. S. Steiner

University of Edinburgh, Wellcome Centre for Cell Biology, Dr. G. Kustatscher

Universität Freiburg (D), Institut für Molekulare Medizin und Zellforschung, Prof. O. Schilling

Universität Graz (AT), Deptartement of Pediatrics, Dr. E.M. Varga; Inst. Pharm. Chem., Prof. A. Kungl

Universität Zürich (CH), Biochemical Institute, Prof. M. Grütter, Dr. P Mittl; Clinical Trial Center (CH), PD Dr. G. Senti

Universitätsklinikum Freiburg (DE), COPD & Asthma Research-group (CARG), Abtl. für Pneumologie, PD Dr. M. Idzko

Universität Salzburg (AT), Prof. Emeritus M. Breitenbach Universität Zürich, Clinical Trials Center (CH), PD Dr. G. Senti Universität Tübingen (DE), Prof. L. Flatz

Universitätsspital Bern (CH), Eggel Lab, Prof. A. Eggel; Kinderklinik, Inselspital, Prof. R. Kraemer, Dr. C. Aebischer-Casaulta, Prof. M.H. Schöni; Universitätsklinik für Rheumatologie, Immunologie und Allergologie, Inselspital, Prof. A. Helbling, Dr. A. Gschwend; Universitätsklinik für Hals-, Nasen- und Ohrenkrankheiten, Kopf- und Halschirurgie, Dr. U. Borner, Dr. S. Negoias, Dr. S.L. Hool

Universitätsspital Zürich (CH); Allergiestation, Dr. C. Cardoso; Abteilung für Klinische Immunologie, Prof. Dr. O. Boyman; Abteilung ENT, PD Dr. D. Holzmann, PD Dr. M. Soyka; Abfteilung Pneumologie, Prof. Dr. M. Kohler, PD Dr. C. Clarenbach; Abteilung Gastroenterologie, Prof. R. Gerhard, Dr. M. Wawrzyniak; Abteilung Kardiologie, Prof. F. Duru, Dr. D. Akdis; Dermatologische Klinik, Prof. R. Dummer, PD Dr. T. Kündig, Prof. Dr. P. Schmid-Grendelmeier, Prof. Dr.

M.C. Brüggen, PD Dr. E. Guenova, PD Dr. G. Hofbauer; Swiss EoE Clinics and Research Network, Prof. Dr. A. Straumann, Dr. L. Biedermann, Dr. P. Schreiner; Klinik für Medizinische Onkologie und Hämatologie, Prof. T. Zenz

Universitäts-Kinderspital Zürich (CH), Prof. J. Reichenbach, Prof. R. Lauener, Dr. C. Roduit, Dr. A. Jung

Universitäts-Kinderspital Zürich (CH), Forschungszentrum für das Kind, Klinische Chemie und Biochemie, Dr. P. Wawrzyniak

University of Applied Sciences of the Grisons / Fachhochschule Graubünden (FHGR), DAViS Center (CH), Dr. Heiko Rölke, Marco Schmid, PD Dr. Ralf-Peter Mundani, Keller Thomas, Dr. Yves Staudt

University of Cambridge (UK), Prof. G. Griffith, Dr. C. Ma

University of Cape Town, Department of Dematology (ZA), Assoc Prof. M. Levin, Dr. C. Hlela

University College Cork, Alimentary Pharmabiotic Centre (IE), Prof. Dr. L. O'Mahony, Dr. N. Lunjani, Dr. D. Groeger, Dr. T. Tan

University of Istanbul, Institute of Experimental and Medical Research (TR), Prof. G. Deniz, Prof. Dr. G. Erten, Prof. Dr. U. Kücüksezer, Prof. C. Ozdemir

University of Lausanne, Department of Biochemistry, Lausanne (CH), Prof. M. Thome

University of Manchester (UK), Prof. N.G. Papadopoulos

University of Natural Resources and Life Sciences, BOKU Wien (AT), Dr. F. Altmann

University of Nottingham (UK), Department of Chemical and Environmental Engineering, Prof. A. Mata

University of Szeged, Department of Dermatology and Allergology, Szeged (HU), Dr. N. Nagy, Prof. L. Kemeny

University of Tartu (EE), Dr. A. Rebane, Prof. P. Peterson, Prof. K. Kingo

Universitätsklinikum St. Pölten, Universitätsklinik für Kinder- und Jugendheilkunde, Prof. T. Eiwegger

University of Turku, Paediatrics and Adolescent Medicine (FI), Prof. T. Jartti

University of Wisconsin-Madison (US), Prof. J. E. Gern

Wroclaw Medical University, Wroclaw (PL), Prof. M. Jutel, Dr. S. Smolinska, Dr. P. Gajdanowicz

Zhongnan Hospital of Wuhan University, Department of Allergology, Dr. Y-D Gao, Dr. M. Ding


ILC2s selectively co-localize with NMU^pos cholinergic neurons in the intestinal submucosa
confocal
light sheet
1. Intrinsic enteric neurons
2. Extrinsic (para)sympathetic neurons
3. Extrinsic sensory neurons
NMU KLRG1^pos ILC2s
Co-localization of Lin^neg KLRG1^pos ILC2s with NMU+ cholinergic neurons
NMU^Cre:tdT
ILC2s selectively co-localize
cholinergic neurons in the intesti
confocal
1. Intrinsic enteric neurons
2. Extrinsic (para)sympathetic neurons
3. Extrinsic sensory neurons
NMU KLRG1^pos ILC2s
Co-localization of Lin^neg KLRG
ILC2s with NMU+ cholinerg
neurons


with NMU^pos
nal submucosa
light sheet
NMU^Cre::AI14

Bilanz per 31. Dezember 2023

(inklusive Drittmittel)

	31.12.2023	31.12.2022
	CHF	CHF
AKTIVEN		
Flüssige Mittel	1'410'084.55	1'817'392.46
Forderungen	426'128.88	187'894.99
Übrige kurzfristige Forderungen	73'238.29	40'708.24
Kontokorrent SFI Stiftung	2'302.35	0
Aktive Rechnungsabgrenzungen	336'209.53	217'552.34
	2'247'963.60	2'263'548.03
PASSIVEN		
Verbindlichkeiten	489'724.78	134'202.58
Kontokorrent SFI Stiftung	0	18'360.20
Übrige kurzfristige Verbindlichkeiten	9'051.95	16'628.95
Passive Rechnungsabgrenzungen	1'457'580.72	1'718'121.80
Rückstellungen	195'700.27	195'700.27
Eigenkapital	95'905.88	180'534.23
	2'247'963.60	2'263'548.03

Schweizerisches Institut für Allergie- und Asthmaforschung

Betriebsrechnung 2023

(inklusive Drittmittel)

	Rechnung 2023	Budget 2023	Rechnung 2022
	CHF	CHF	CHF
ERTRAG			
Beitrag Bund Forschungsgesetz Art. 15	1'311'700.00	1'311'200.00	1'299'600.00
Beitrag Kanton Graubünden	520'000.00	520'000.00	520'000.00
Beitrag Gemeinde Davos	524'560.00	524'560.00	524'560.00
Beitrag Universität Zürich	419'148.90	369'688.00	371'517.10
Beitrag Stiftung SFI	120'000.00	180'000.00	120'000.00
Beitrag Stiftung vormals Bündner Heilstätte Arosa	54'383.50	54'096.00	56'971.00
Beitrag Stiftungen/Drittmittel	10'000.00	0	154'108.25
Overheadbeiträge	0	0	132'558.00
Übriger Ertrag	14'334.75	3'000.00	14'958.95
Finanzertrag	1'725.95	0	0
Ausserordentlicher Ertrag	46'984.93	20'000.00	35'341.93
Auflösung von Rückstellungen	0	0	82'737.46
WIRM-Kongress	225'651.41	0	236'138.98
Drittmittel	3'921'453.59	3'856'782.00	2'591'731.69
	7'169'943.03	6'839'326.00	6'140'223.36
AUFWAND			
Personalaufwand	3'434'687.61	3'747'688.00	3'404'220.40
Verbrauchsmaterial	2'077'083.18	1'356'603.00	1'339'332.18
Raumaufwand	371'486.79	325'000.00	357'423.88
Unterhalt/Reparaturen/Ersatz	449'709.73	362'335.00	326'148.28
Investitionen	100'963.16	425'000.00	66'561.80
Sachversicherungen/Abgaben	18'465.60	10'000.00	9'735.00
Energie- und Entsorgungsaufwand	209'187.87	145'000.00	161'240.34
Verwaltungsaufwand	105'294.38	99'500.00	95'282.94
Werbeaufwand	20'970.03	0	10'938.61
Reisespesen	115'615.01	50'000.00	80'890.67
WIRM-Kongress	235'986.73	300'000.00	195'395.23
Übriger Betriebsaufwand	7'503.87	11'000.00	8'545.46
Abschreibungen	105'200.00	105'200.00	105'200.00
Finanzaufwand	2'514.75	1'000.00	18'561.58
Bildung von Rückstellungen	0	0	0
Ausserordentlicher Aufwand	- 97.33	1'000.00	368.57
Zuweisung/Hertrag Drittmittel	0	0	0
	7'254'571.38	6'939'326.00	6'179'844.94
Ergebnis	- 84'628.35	-100'000.00	-39'621.58
	7'169'943.03	6'839'326.00	6'140'223.36

Swiss Institute of Allergy and Asthma Research (SIAF)
Associated Institute of the University of Zurich
Herman-Burchard-Strasse 9
CH-7265 Davos Wolfgang
T: +41 (0)81 410 08 48
siaf@siaf.uzh.ch
www.siaf.uzh.ch