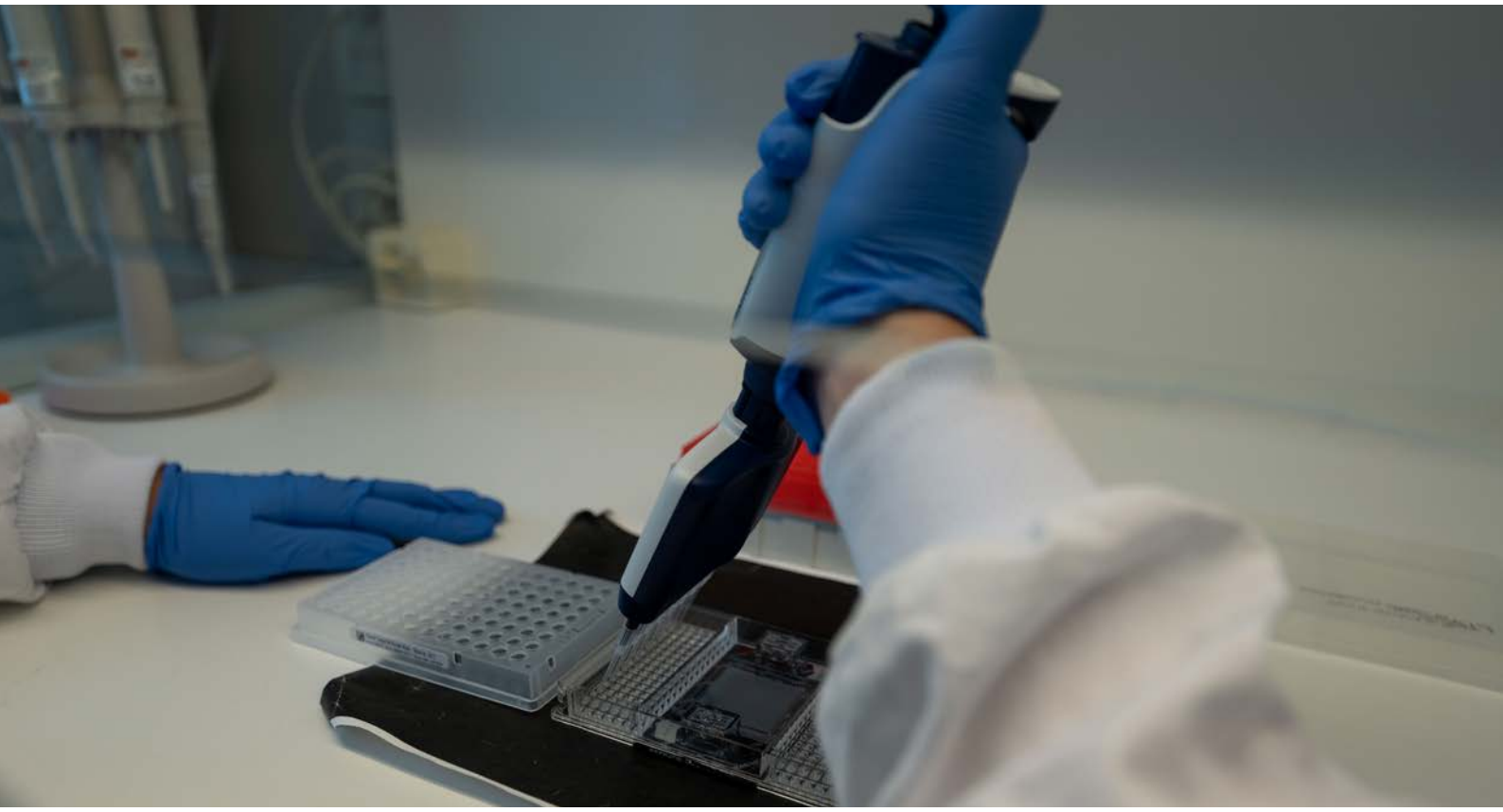
SIAF

Swiss Institute of Allergy and Asthma Research

ANNUAL REPORT 2022



Universität Zürich[UZH]

Index

About us

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

Als Folge von Veränderungen in der Umwelt und im Lebensstil nehmen Allergien sowie virale und bakterielle Atemwegsinfektionen immer mehr zu. Die vergangenen Jahre der COVID-19-Pandemie und die bevorstehenden Jahre mit den anhaltenden post-pandemischen Folgen stellen das bemerkenswerteste Beispiel für diesen Trend dar. Es ist immer noch unklar, warum manche Menschen empfindlicher und anfällig für Allergien und Atemwegserkrankungen sind als andere.

Das Schweizerische Institut für Allergie- und Asthmaforschung (SIAF), das 1988 von der Medizinischen Abteilung der Stiftung Schweizerisches Forschungsinstitut für Hochgebirgsklima und Medizin Davos (SFI) gegründet wurde, versucht mit seiner Forschung das Verständnis über Allerigen und Asthma zu verbessern, damit in Zukunft Behandlungen entwicklet werden können, welche die Zukunft der Betroffenen verbessern sollen. Das SIAF ist seit 1996 der Universität Zürich angegliedert und seit 2008 Mitglied der Life Science Zurich Graduate School, einem gemeinsamen Ausbildungs-Projekt der Universität Zürich und der ETH Zürich. Diese Angliederung ermöglicht dem SIAF eine vollumfängliche PhD-Ausbidlung anzubieten. Darüber hinaus ist das SIAF aktives Mitglied der Academia Raetica und der Graduiertenschule des Kantons Graubünden.

Die Forschung am SIAF ist auf eine direkte Kooperation mit den Kliniken in Davos, der Universität Zürich und weiteren spezialisierten Instituten ausgelegt. Die Forschung im Institut konzentriert sich auf die patientenrelevante translationale Forschung und Untersuchung der immunologischen Grundlagen allergischer und asthmatischer Erkrankungen, die Ansatzpunkte für neue präventive und kurative Behandlungen zugunsten der Betroffenen schafft. Ausserdem ist das SIAF in das europäische Netzwerk nationaler Kompetenzzentren (Projekt GA2LEN: Global Allergy and Asthma European Network of Excellence), in die Europäische Akademie für Allergologie und Klinische Immunologie (EAACI), in die Amerikanische Akademie für Allergie, Asthma und Immunologie (AAAAI) sowie in die World Allergy Organization (WAO) eingebunden. Mit der Universität Stanford (Sean Parker Asthma and Allergy Center) besteht eine intensive Zusammenarbeit.

2022 wurden 70 wissenschaftliche Arbeiten in begutachteten internationalen Fachzeitschriften mit “Impact Factor” veröffentlicht oder sind noch in Druck. 2022 erreichte das SIAF einen Gesamtwert des “Impact Factors” von 935.062 und einen Durchschnitt von 13.358 Punkten pro Publikation. Die neusten Ergebnisse wurden zudem in 59 Abstracts an verschiedenen Fachtagungen mitgeteilt. Unsere Mitarbeitenden wurden zu 100 verschiedenen Seminaren und Vorträgen an nationalen und internationalen Kongressen eingeladen. Solche Einladungen sind wichtig für die Verbreitung der erzielten Ergebnisse und für die internationale Akzeptanz der Forschung des Instituts. Bei 41 verschiedenen Sessionen hatten SIAF-Mitarbeitende den Vorsitz. Zusätzlich übernehmen SIAF-Mitarbeitende 81 wissenschaftliche Ämter in internationalen Gesellschaften und internationalen Zeitschriften. Zudem hält Prof. CA. Akdis seit 2018 das Amt des Chefredaktors der Fachzeitschrift Allergy inne. Unter seiner Leitung stieg der Impact Factor von Allergy von 6,02 auf 14,71 und wurde damit zur führenden Zeitschrift des Fachgebiets Allergie und klinische Immunologie. Als Folge seiner international höchst angesehenen wissenschaftlichen Publikationen wurde Prof. Dr. CA. Akdis 2022 zum siebten Mal von Thomson Reuters Clarivate in die Gruppe der meistzitierten Forscher aus allen wissenschaftlichen Fachbereichen weltweit aufgenommen. Das SIAF hat rund 1'630 Fachbeiträge veröffentlicht und gehört zu den meistzitierten Instituten weltweit. Die vom SIAF publizierten Artikel wurden 88'000 Mal zitiert.

Eines der Schlüsselprojekte des Instituts ist die Etablierung des Präzisionsproteomik-Zentrums im SIAF in Zusammenarbeit mit dem Kanton Graubünden und der Universität Zürich. Das Zentrum konnte erfolgreich etabliert werden und befindet sich nun im personellen sowie infrastrukturellem Ausbau unter der Leitung von Prof. C. Messner. Im Zentrum werden modernste Massenspektrometrie-basierte Technologien für die Proteomanalyse von klinischen Proben entwickelt und angewendet. Das Ziel des Zentrums ist die Identifikation neuer Biomarker und Krankheitsmechanismen, welche zur Entwicklung der nächsten Generation von personalisierten Behandlungen beitragen werden.

Das SIAF realisiert in enger Zusammenarbeit mit den eigenständigen Partnern CK-CARE, HGK, Cardio-CARE und die Stiftungsprofessur MC Brüggen auf dem Medizincampus Davos Medizin Forschung auf höchstem Niveau. Diagnostik, Forschung und Therapie ergänzen sich auf dem Medizincampus in idealer Weise. Diese Synergien kommen den Patienten direkt zugute: Forschungsergebnisse werden in Therapieoptionen und Behandlungen umgesetzt und direkt angewendet, was ein umfassendes Diagnose- und Therapiekonzept ermöglicht. Darüber hinaus sind Aus-, Weiter- und Fortbildung von Akademikern (MSc, PhD sowie Postdocs) und medizinischen Fachpersonen zentrale Bausteine des Leistungsangebots. Das strategische Ziel des Medizincampus ist es, ein international anerkanntes Exzellenzzentrum im Bereich der Diagnostik der personalisierten Prävention und Behandlung von allergischen und kardiovaskulären Erkrankungen zu schaffen.

Ein umfassendes Verständnis der Ursachen von allergischen und anderen chronischen, nicht übertragbaren Krankheiten: Die Theorie der epithelialen Barriere

Die Theorie der epithelialen Barriere ist eine umfassende Erklärung für den weltweiten, epidemischen Anstieg chronischer Erkrankungen in den letzten 65 Jahren. Die von CA. Akdis postulierte Theorie besagt, dass die Exposition gegenüber toxischen Stoffe, die durch die Industrialisierung und die Veränderungen des modernen Lebensstils eingeführt wurden, die Epithelbarriere der Haut, der oberen und unteren Atemwege und der Darmschleimhaut stört und eine entzündliche Immunreaktion auslöst, die viele chronische Entzündungskrankheiten auslösen oder verschlimmern kann.
Die Oberflächen unserer Haut, der Atemwege und des Darms sind mit schützenden Zellschichten ausgekleidet, den so genannten Epithelbarrieren. Intakte Epithelbarrieren sind für die Homöostase von entscheidender Bedeutung, da sie das Wirtsgewebe vor Infektionen, Umweltgiften, Schadstoffen und Allergenen schützen.
Es ist bekannt, dass viele der chemischen Stoffe, die in gängigen Konsumgütern (wie Zahnpasta, Shampoo, Reinigungsmitteln und

verarbeiteten Lebensmitteln) enthalten sind, diese kritischen Barrieren schädigen und die Durchlässigkeit für Bakterien, Toxine, Schadstoffe und Allergene erhöhen. Wenn die Epithelbarrieren gestört (oder „undicht") sind, können Substanzen und Mikroben in tiefergelegenes Gewebe eindringen, wo sie nicht hingehören, und eine Immun-/Entzündungsreaktion auslösen, die viele chronische Entzündungskrankheiten auslösen oder verschlimmern kann.

Störende Auswirkungen von Lebensmittelemulgatoren und Detergenzien auf Darmepithelzellen

Untersuchung der Auswirkungen häufig verwendeter Lebensmittelemulgatoren und Detergenzien auf Zytotoxizität, Barrierefunktion, Transkriptom und Proteinexpression in gastrointestinalen Epithelzellen. Eine gestörte Integrität der Epithelbarriere im Magen-Darm-Trakt ist für die Pathogenese vieler entzündlicher Erkrankungen von Bedeutung. Dementsprechend bewerten wir das Potenzial von Biomarkern für die Dysfunktion der Epithelbarriere zur Vorhersage von Krankheiten wie COVID-19 und Asthma. Um die Auswirkungen von Disruptoren und Rettungsmitteln auf Darmepithelzellen zu untersuchen, konnten wir aus induzierten pluripotenten Stammzellen abgeleitete menschliche Darmorganoide und organoide Organ-on-a-Chip-Modelle entwickeln.

Maschinelles Lernen erkennt erfolgreich COVID-19-Patienten vor den PCR-Ergebnissen und sagt ihr Überleben anhand von Standard-Laborparametern voraus

Im klinischen Umfeld ist es wichtig, SARS-CoV-2-positive Patienten schnell zu identifizieren und Patienten mit COVID-19 durch die Überwachung von Parametern, die mit einem schlechten Krankheitsverlauf verbunden sind, angemessen medizinisch zu versorgen. In unserem Kooperationsprojekt zwischen SIAF, DAViS und dem medizinischen Personal des COVID-19-Krankenhauses in Zgierz, Polen, haben wir uns daher die Frage gestellt, ob Teilmengen klinischer Parameter identifiziert werden können, um SARS-CoV-2-positive Patienten zu diagnostizieren, um COVID-19-Patienten mit einem hohen Risiko für einen tödlichen Ausgang bei der Aufnahme ins Krankenhaus zu identifizieren und um longitudinale Parametermuster als Warnzeichen für einen möglichen tödlichen Ausgang von COVID-19 während des Krankenhausaufenthalts zu erkennen. Mit Hilfe des maschinellen Lernens konnten wir starke Prädiktoren für einen tödlichen Ausgang von COVID-19 bei der Aufnahme ins Krankenhaus ermitteln. Die identifizierten Untergruppen von Parametern können bei der Annahme und Anpassung einer wirksamen Behandlung für Patienten mit COVID-19 mit Warnzeichen für einen tödlichen Krankheitsausgang in der klinischen Umgebung helfen.

Profilfeld 5 – Life Science

Im Profilfeld 5 wurde 2022 das Zentrum für Präzisions-Proteomics unter der Interim-Projektleitung von Prof. Dr. C. Akdis und PD Dr. K. Bärenfaller weitergeführt. Parallel führte die Medizinische Fakultät der Universität Zürich Berufungsverhandlungen. Dr. Christoph Messner wurde zum 1. August 2022 als Assistenzprofessor für die Sonderprofessur Life Science eingesetzt. Das Forschungsteam des Zentrums für Präzisions-Proteomics konzentrierte sich im Jahr 2022 auf die Etablierung des Zentrums durch nationale und internationale Kollaborationen sowie Massenspektrometrie-Studien in SIAF-relevanten Themenfeldern. Ab August 2022 wurden neue Kollaborationen und Investitionen angestrebt, um das Proteomics-Zentrum entsprechend dem neuen Forschungsprogramm von Prof. Dr. Christoph Messner auszurichten. Es laufen Bewerbungsverfahren zur Erweiterung der Forschungsgruppe. Nach dem Antritt der Sonderprofessur von Prof. Dr. C. Messner wird das Zentrum für Präzisions-Proteomics in Publikationen nun als Teil der Affiliation aufgeführt. Im Jahr 2022 konnte eine weitere Publikation in Zusammenarbeit mit der Gruppe von Prof. Dr. O. Schilling von der Universität Freiburg in Deutschland veröffentlicht werden. Die Finanzierung erfolgte durch den Kanton Graubünden. Zudem wurde ein Beitrag zu einem Positions-Papier veröffentlicht, das die Finanzierung durch den Kanton Graubünden erwähnt. In Zusammenarbeit mit dem DAViS-Zentrum wurden Anfang 2022 eine gemeinsam geplante Datenspeicher- und Backup-Infrastruktur für das Proteomics-Zentrum installiert, um eine solide und ausreichende IT-Infrastruktur für die umfangreichen Massenspektrometer-Daten für mindestens 6 Jahre bereitzustellen.

Profilfeld 6 - Computational Science

Profilfeld 6 Computational Science: Neben der IT-Infrastruktur-Installation gab es weitere Projekte in Zusammenarbeit zwischen dem DAViS-Zentrum und dem Zentrum für Präzisions-Proteomics. Dazu gehörten ein Projekt zur verbesserten statistischen Auswertung von Massenspektrometer-Daten von angereicherten Proteinen sowie ein Projekt mit dem Swiss Institute for Sports Medicine (SRISM) zur statistischen Analyse von Proteomics-Daten, die nicht massenspektrometerbasiert sind. Eine Veröffentlichung erfolgte in Zusammenarbeit mit der Fachhochschule Graubünden (FHGR), dem SIAF und der Medizinischen Universität Lodz, Polen, im Rahmen der kollaborativen COVID-19-Studie. Die Studie identifizierte diagnostische Laborparameter und Prädiktoren für einen schweren Verlauf von COVID-19. Im ML-SOS-ALL-Projekt wurden Daten zu südafrikanischen Kindern mit und ohne atopische Dermatitis analysiert, um relevante Transkriptenlisten zu erstellen. Die Analyse von Abwasserproben und die Sequenzierung von SARS-CoV-2-RNA-Fragmenten wurden fortgesetzt und werden zum WEF23 abgeschlossen.

Klinische Dienstleistung

Das SIAF bietet den Davoser und allen weiteren interessierten Kliniken und praktizierenden Ärzten spezielle zelluläre immunologische Untersuchungen an. Mit Hilfe der durchfluss-zytometrischen Analyse (FACS Analyse) von Blut, bronchoalveolären Lavagen (BAL), aber auch weiteren Gewebsflüssigkeiten, werden die verschiedenen Immunzellen und Subpopulationen in ihrer Entwicklung, ihren Mengenverhältnissen und ihrem Aktivierungszustand gemessen. Zudem ist das SIAF seit 2019 ein Dienstanbieter der OLINK-Technologie und bietet seinen akademischen sowie industriellen Kunden spezielle Messungen zur Bestimmung von Biomarkern an, welche als Parameter dienen, um die Entwicklung einer Krankheit zu bestimmen und das Monitoring zu überwachen. Zudem können mit diesen Messungen verschiedene Krankheitsausprägungen und -verläufe besser verstanden werden. Zum jetzigen Zeitpunkt ist das SIAF, das einzige Labor in der gesamten Schweiz, welches

diese speziellen Messungen für In- und Ausland anbietet.

Ausbildung, Lehrverpflichtungen, Kongress
Eine wichtige Aufgabe erfüllt das SIAF in der Ausbildung von Studierenden sowie im Nachdiplomstudium. Gleichzeitig werden durch das SIAF Lehrverpflichtungen an der Universität Zürich erfüllt. Diese bestehen aus verschiedenen Vorlesungsstunden im Rahmen der Biochemie am Biochemischen Institut. Prof. C. A. Akdis ist Fakultätsmitglied der Medizinischen Fakultät der Universität Zürich mit Promotionsrecht in der Mathematischen und Naturwissenschaftlichen Fakultät und Honorarprofessor an der Bezmialem Universität Istanbul. Prof. C. A. Akdis und Prof. M. Akdis haben zudem eine Honorarprofessur am Tungren Spital der Peking-Universität, der Universität Bursa-Uludag und der Universität Wuhan. Prof. Dr. C. Messner, PD Dr. K. Bärenfaller, PD Dr. M. Sokolowska und Dr. W. van de Veen sind Mitglieder des Lehrkörpers der UZH.

Nach zweijähriger Pandemie konnte die sechszehnte Durchführung des World Immune Regulation Meetings (WIRM) endlich wieder als Face-to-Face Meeting im Kongresszentrum Davos durchgeführt werden. Rund 600 Wissenschaftler aus über 40 Länder dieser Welt trafen sich vom 6. - 9. Juli 2022 zu dem viertägigen Kongress, um sich über die neuesten Erkenntnisse in der Immunologie auszutauschen. Dort traffen talentierte Nachwuchsforscher auf erfahrene Experten. Die Wissenschaftler hielten 121 Vorträge und trugen 188 Abstracts vor und tauschten sich über die neuesten Erkenntnisse in der Immunologie aus. Dieser globale Austausch von aktuellen Erkenntnissen hilft, neue Behandlungstherapien und neue Lösungsansätze für Patienten und Patientinnen zu entwickeln.

Vom 7. bis 24. Juni 2022 fand die dritte Auflage des Blockkurses Biomedical Data Mining statt, endlich wie vor der Pandemie geplant, für eine Woche vor Ort im SIAF, gefolgt von zwei Wochen online. Die verantwortlichen Dozenten waren PD Dr. K. Bärenfaller und PD Dr. M. Sokolowska, mit Unterstützung der Doktoranden J. Koch, D. Zhakparov, E. Barletta, M. Huang und Y. Xiao. Hintergrundinformationen zu verschiedenen Technologien und Analysewerkzeugen der funktionellen Genomik wurden in Vorlesungen über Transkriptomik, Einzelzellsequenzierung, Translatomik, Multiplex-Immunoassays, Proteomik, Mikrobiom, Durchflusszytometrie, funktionelle Kategorisierung, Statistik und Versuchsplanung, die STRING-Datenbank, Cytoscape und Genevestigator vermittelt. Zu Beginn des Kurses bekamen die Studierenden Ergebnislisten der RNA-Sequenzierung ausgehändigt und wurden in verschiedenen Aufgaben aufgefordert, diese Listen zunächst mit R zu analysieren und dann die Ergebnisse in einen Kontext zu setzen. Am Ende des Kurses mussten die Studierenden einen schriftlichen Bericht über ihre Data-Mining-Aufgabe abgeben.

Finanzielle Grundlage
Die Ausgaben und der finanzielle Ertrag des SIAF haben sich im Vergleich zu den vergangenen Jahren nur unwesentlich verändert. Eine Grundfinanzierung des Instituts ist durch die Hauptsponsoren gegenwärtig sichergestellt. Sie besteht vor allem aus einem Beitrag des Bundes (Forschungsförderungsgesetz Art. 15), Beiträge des Kantons Graubünden und der Gemeinde Davos, Beiträge der Universität Zürich, Beitrage des Schweizerischen Nationalfonds sowie Beiträge von Stiftungen, wie der Novartis FreeNovation, die PROMEDICA Stiftung und die Stiftung vormals Bündner Heilstätte Arosa, die Doktorandenprogramme fördern. Die zusätzlichen Ausgaben wurden aus Erträge von zusätzlichen kompetitiv erworbenen Drittmitteln und des WIRM-Kongresses gedeckt.

Dank
Für die grossartige Arbeit und die gute Arbeitsatmosphäre im SIAF danke ich allen Mitarbeitenden herzlich. Gleichzeitig danke ich den Davoser Kliniken, ihren Chefärzten und deren Mitarbeitenden sowie der Universität Zürich für die stetige und wirkungsvolle Unterstützung unseres Institutes.

Insbesondere möchte ich hier unsere fruchtbare Zusammenarbeit mit den Partnern auf dem Medizincampus Davos betonen. Dank dieser wird eine Forschung zur Findung von nachhaltigen Lösungen für bessere Diagnosen und Behandlungen von Betroffenen ermöglicht.

Mein Dank geht vor allem auch an die Stiftung Schweizerisches Forschungsinstitut für Hochgebirgsklima und Medizin (SFI), dessen Stiftungsrat und Stiftungsratsausschuss für die stets gewährte Unterstützung. Ebenso bin ich und das gesamte SIAF Dr. Walter Ammann, der Ende 2022 von seinem Amt als SFI-Präsident zurückgetreten ist, für seine stete und unermüdliche Unterstützung sehr dankbar. Nicht zuletzt gilt mein spezieller Dank dem Kanton Graubünden, dem Staatssekretariat für Bildung, Forschung und Innovation und allen Behörden, die sich unermüdlich für die Forschung des SIAF interessieren und das Institut in jeder Hinsicht fördern.

Davos, Mai 2023

Prof. Dr. Cezmi A. Akdis

Due to changes in the environment and lifestyle, allergies, as well as viral and bacterial respiratory infections, are increasing. The past years of the COVID-19 pandemic and the upcoming years with its ongoing post-pandemic effects are the most notable example of this trend. It is still unclear why some people are more sensitive and prone to allergies and respiratory diseases than others.
There was a quick adaptation to COVID-19 and SARS-CoV-2 research in the institute and we published more than 40 articles. These early papers received a huge attention including the first paper showing the spered of the infection by human to human contact which was published on the 19th of February before the start of the European cases. This was because Prof. Yadong Gao a fellow in SIAF returned to his university in Wuhan and started to take care of patients in the intensive care and then the collaboration continued with daily teleconferences.

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 training 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 network of national competence centers (GA2LEN: Global Allergy and Asthma European Network of Excellence), 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).

In 2022, 70 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 935.062 and an average of 13.358 points per publication in 2022. The latest findings were also presented in 59 abstracts at various professional conferences. Our employees were invited to participate in 100 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 41 different sessions. Additionally, SIAF employees hold 81 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 his 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 seventh time in 2022. The SIAF has published around 1,630 scientific contributions and is among the most cited institutes worldwide. The articles published by the SIAF have been cited 88,000 times.

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. C. 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.

The SIAF, in close collaboration with its independent partners CK-CARE, HGK, Cardio-CARE and the and the endowed professorship MC Brüggen on the Davos 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.

A comprehensive understanding of the causes of allergic and other chronic non-communicable diseases: The theory of epithelial barrier

The theory of epithelial barrier provides a comprehensive explanation for the worldwide epidemic rise of chronic diseases in the last 65 years. The theory postulated by C.A. Akdis 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 toothpaste, shampoo, 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"), substances and microbes can penetrate deeper tissues where they do not belong, triggering an immune/inflammatory reaction that can initiate or exa-

cerbate 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 evaluate 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.

Machine learning successfully identifies COVID-19 patients before PCR results and predicts their survival based on standard laboratory parameters
In the clinical setting, it is important to quickly identify SARS-CoV-2 positive patients and provide appropriate medical care to patients with COVID-19 by monitoring parameters associated with a poor disease course. In our collaborative project between SIAF, DAViS, and the medical staff of the COVID-19 hospital in Zgierz, Poland, we therefore investigated whether subsets of clinical parameters could be identified to diagnose SARS-CoV-2 positive patients, identify COVID-19 patients at high risk of fatal outcome upon admission to the hospital, and recognize longitudinal parameter patterns as warning signs of a potential fatal outcome of COVID-19 during hospitalization. Using machine learning, we were able to identify strong predictors of a fatal outcome of COVID-19 upon hospital admission. The identified subsets of parameters can help guide the adoption and adaptation of effective treatment for patients with COVID-19 showing warning signs of a fatal disease course in the clinical setting.

Profile Field 5 - Life Science
In profile field 5, in 2022, the Center for Precision Proteomics was continued under the interim project leadership of Prof. Dr. C. Akdis and PD Dr. K. Bärenfaller. Parallelly, the Medical Faculty of the University of Zurich conducted appointment negotiations. Dr. Christoph Messner was appointed as Assistant Professor for the special chair of Life Science, effective from August 1, 2022. The research team of the Center for Precision Proteomics focused on establishing the center through national and international collaborations, as well as mass spectrometry studies in SIAF-relevant fields in 2022. Starting from August 2022, new collaborations and investments were sought to align the Proteomics Center with the new research program of Prof. Dr. Christoph Messner. Application procedures for expanding the research group are currently ongoing. After the assumption of the special professorship by Prof. Dr. C. Messner, the Center for Precision Proteomics is now listed as part of the affiliation in publications. In 2022, another publication could be released in collaboration with the group of Prof. Dr. O. Schilling from the University of Freiburg in Germany. The funding was provided by the Canton of Graubünden. Furthermore, a contribution to a position paper mentioning the funding by the Canton of Graubünden was published. In collaboration with the DAViS Center, a jointly planned data storage and backup infrastructure for the Proteomics Center was installed in early 2022 to provide a solid and sufficient IT infrastructure for the extensive mass spectrometry data for at least 6 years.

Profile Field 6 - Computational Science
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.

Clinical service
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. Furthermore, 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.

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.

From June 7 to 24 June 2022, the third edition of the Biomedical Data Mining block course took place. Finally, as planned before the pandemics, it was held on-site at SIAF for one week, followed by two weeks online. The responsible lecturers were PD Dr. K. Bären-

faller and PD Dr. M. Sokolowska, with the support of the doctoral students J. Koch, D. Zhakparov, E. Barletta, M. Huang, and Y. Xiao. Background information on various technologies and analysis tools in functional genomics was provided through lectures on transcriptomics, single-cell sequencing, translatomics, multiplex immunoassays, proteomics, microbiome, flow cytometry, functional categorization, statistics and experimental design, the STRING database, Cytoscape, and Genevestigator. At the beginning of the course, the students were given result lists from RNA sequencing and were asked to analyze these lists using R in various tasks and then contextualize the results. At the end of the course, the students had to submit a written report on their data mining task.

After two years of the pandemic, the sixteenth edition of the World Immune Regulation Meetings (WIRM) could finally be held as a face-to-face meeting at the Davos Congress Centre. Around 600 scientists from over 40 countries around the world gathered from July 6th to 9th 2022, for the four-day congress to exchange the latest findings in immunology. Talented young researchers met experienced experts, as scientists delivered 121 presentations and presented 188 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, 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.

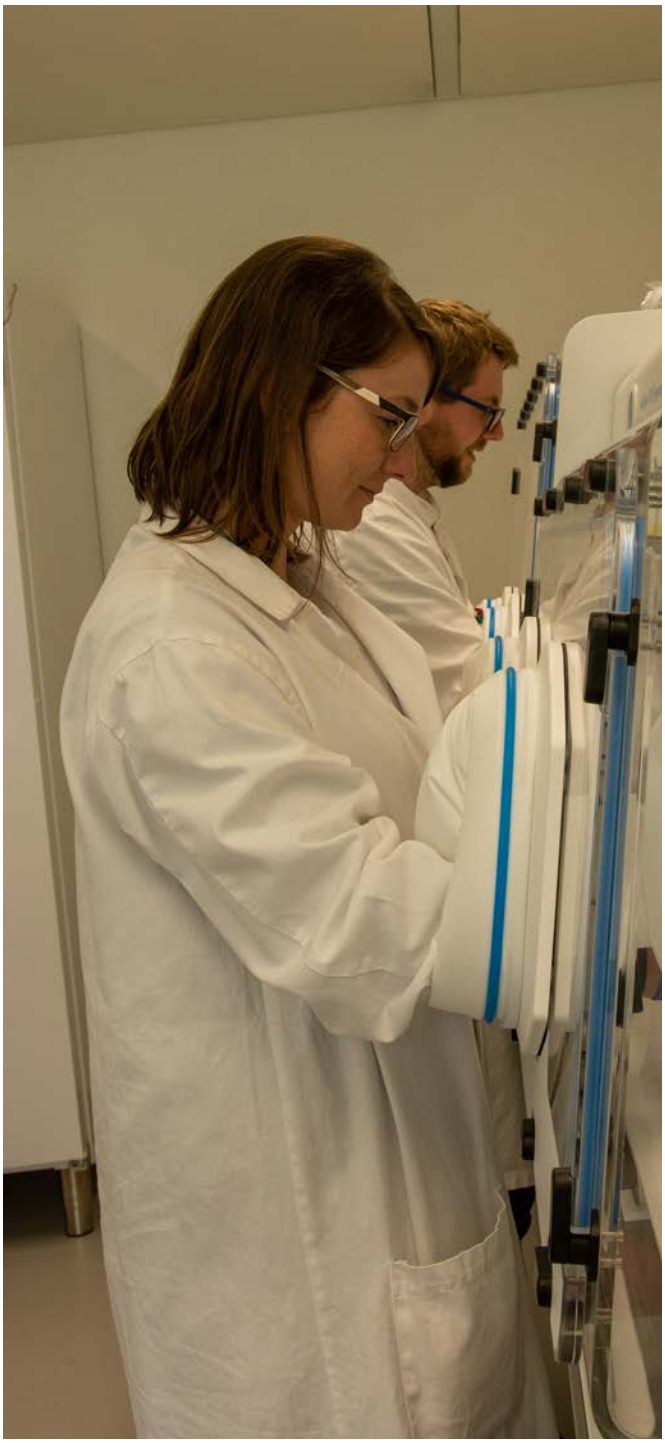
Acknowledgements

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.

Above all, my thanks also go to the Swiss Research Institute for High Altitude Climate and Medicine (SFI) Foundation, its Board of Trustees and Board Committee 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. 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 tireless interest in SIAF's research and who support the Institute in every way.

Davos, May 2023



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
Ammann W., Dr., President SFI 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
Akdis C.A., Prof. Dr., Director SIAF, Davos
Ammann W., Dr., President GRForum, Davos
Binder P., Dr., MeteoSchweiz, Zurich
Maissen C., Dr., Mayor, Ilanz/Glion
Harra L. Prof. Dr., Director PMOD/WRC, Davos
Waelti H., Wälti Treuhand AG, Bad Ragaz
Wenger R.H., Prof. Dr., University Zurich, Zurich
Wilhelm P., City Mayor, Davos

SFI Foundation Council
Bezzola D., MSc, Academia Raetica, Davos
Buol Chr., Dr. med., Medical Association Davos, Davos
Christoffel JH., Schmid-Christoffel, Davos
Fehr T., Prof. Dr. med., Graubünden Cantonal Hospital, Chur
Günther D., Prof. Dr., Vice President for Research ETH Zurich
Menz G., PD Dr. med., HGK, Davos
Müller C., Dr. med., Swiss Red Cross, Sarnen
Ottmer B., MSc ETH Environmental Sc., WSL, SLF Davos
Pfister J., Dr., SCNAT, Bern
Ring J., Prof. Dr. Dr., Klinik am Biederstein, Munich

Scientific Staff

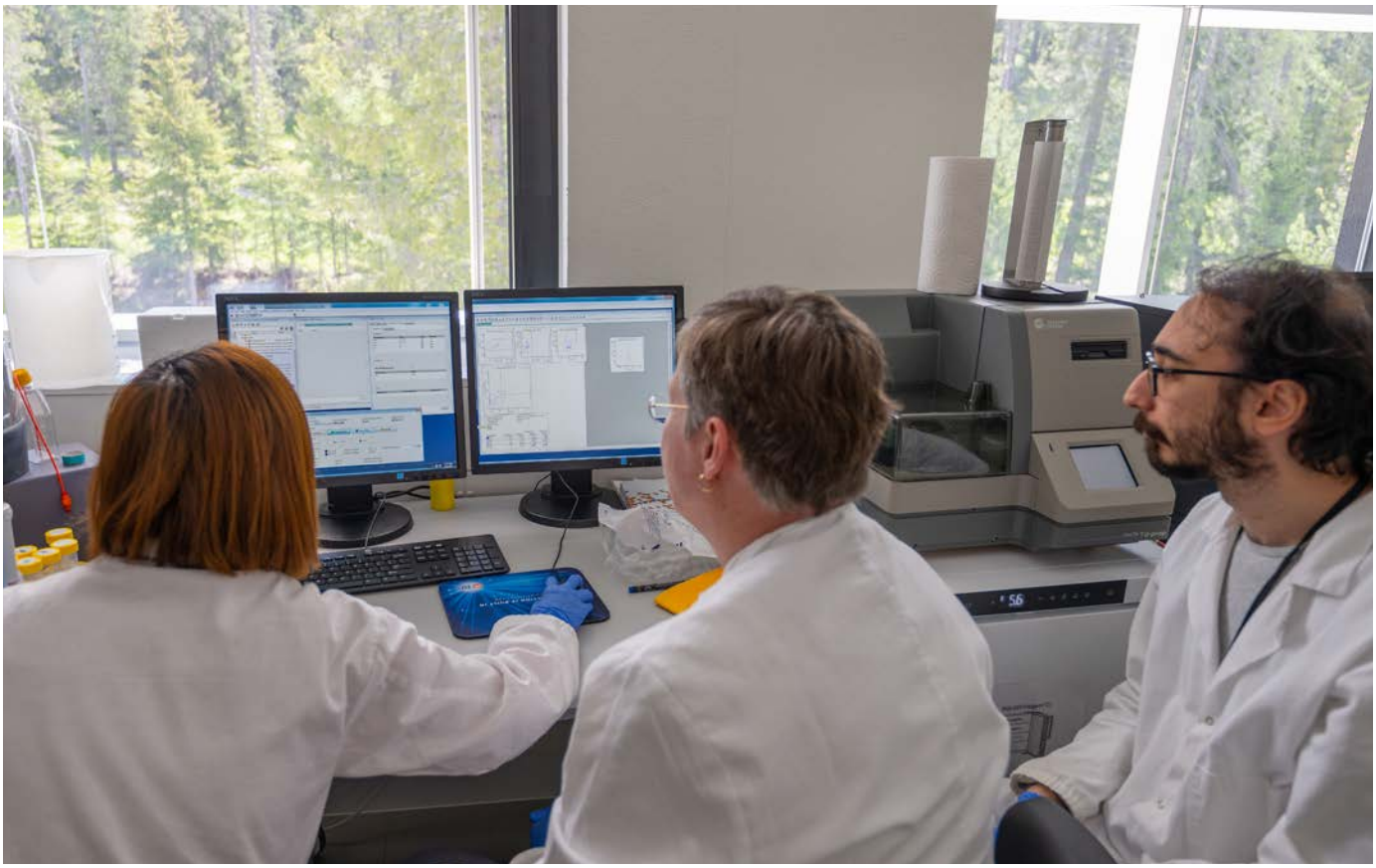
Ameri Milad	Bioinformatician Endowed Professorship Brüggen (- Oct. 22) ***
Barletta Elena	PhD student ***
Bel imam Manal	PhD student ***
Bu Xiangting	Acad. guest, MSc ***
Bürgi Laura	Technician *
Chang Iris	PhD studen t***
D'Avino Paolo	PhD student ***
Ferstl Ruth	Post-doc, PhD (- Sept. 22) ***
Fieten Karin	Post-doc, PhD ***
Heider Anja	Technician *
Huang Mengting	PhD student (- July 22) **
Koch Jana	PhD student ***
Küçükkase Ozan Can	PhD student (bis September 2022) **
Kulkarni Abhijeet	PhD student **
Li Manru	PhD student ***
Lopez Crespo Juan Felipe	PhD studen t**
Maurer Debbie	PhD student ***
Meisser Sanne	Post-doc, PhD (-Oct.22)***
Mitamura Yasutaka	Post-doc, MD *
Ögülür Ismail	Post-doc, MD ***
Pat Yağız	Post-doc, MD ***
Radzikowska Urszula	PhD student **
Rückert Beate	Head Technicians *
Satitsuksanoa Pattraporn	Post-doc, PhD **
Stocker Nino	Technician *
Schneider Stephan	PhD student **
Sun Na	Acad. guest,, MD ***
Wallimann Alexandra	PhD student (- July 22) ***
Wawrocki Sebastian	Post-doc, PhD ***
Westermann Patrick	Technician ***
Xiao Yi	PhD student (- June 22) ***
Yang Minling	PhD student ***
Yazici Duygu	Post-doc, PhD ***
Zhakparov Damir	PhD student ***
Zhu Xueyi	Acad. guest, MSc ***

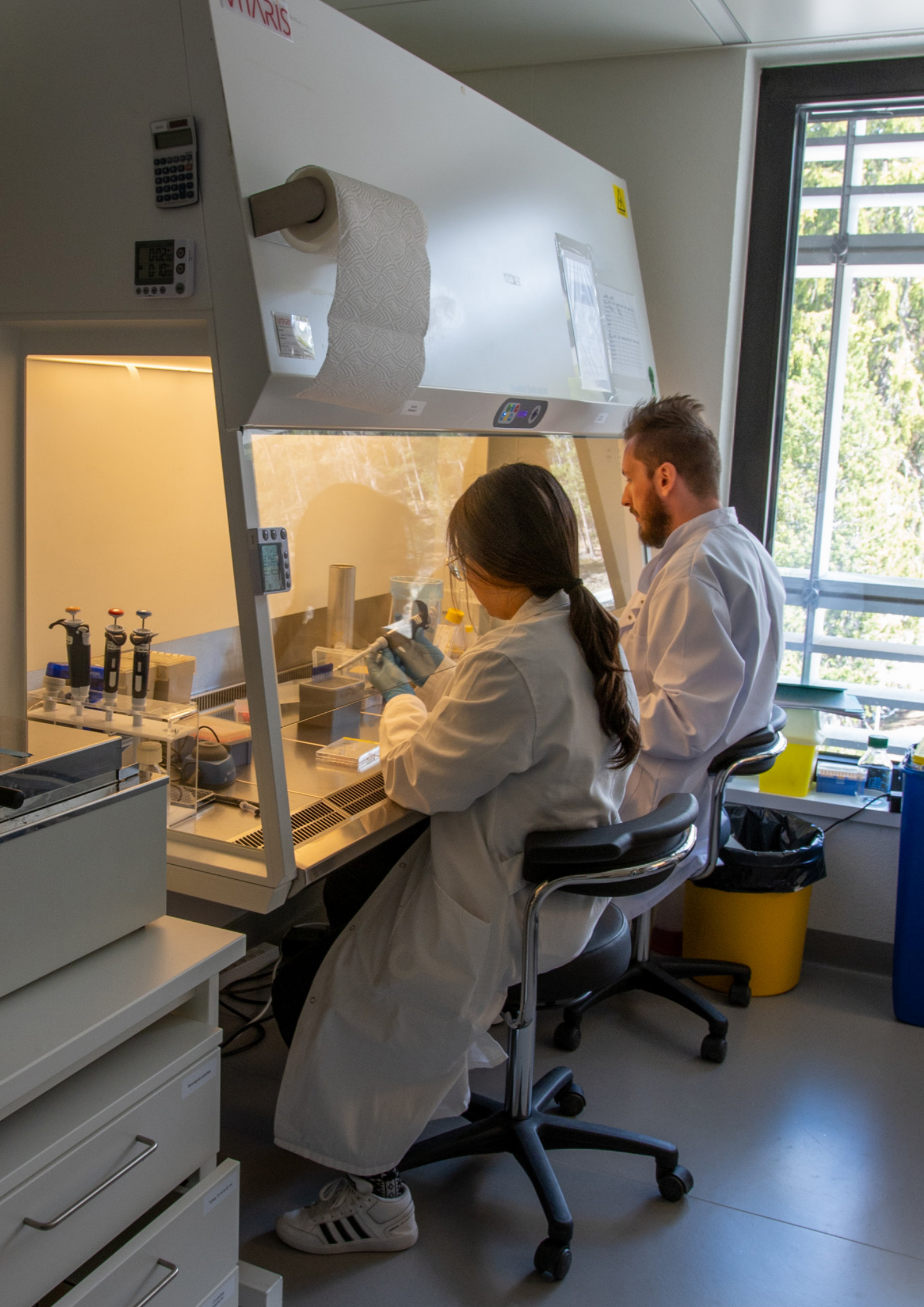
Allergy Office

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

A comprehensive understanding of the origins of allergic and other chronic non-communicable diseases: The epithelial barrier theory

Definition

The Epithelial Barrier Theory is a comprehensive explanation for the global, epidemic-level rise in chronic health conditions over the past 65 years. The theory, postulated by Akdis, proposes that exposure to toxic substances introduced by industrialization and modern lifestyle changes disrupts the epithelial barrier of the skin, upper and lower airways, and gut mucosa, triggering an inflammatory immune response that can initiate or aggravate many chronic inflammatory diseases.

Background

The surfaces of our skin, respiratory tract, and gut are all lined with protective cellular layers known as epithelial barriers. Intact epithelial barriers are crucial for homeostasis, as they protect host tissues from infections, environmental toxins, pollutants and allergens.

Many of the chemical agents found in common consumer products (including toothpaste, shampoo, detergents, and processed foods), are known to damage these critical barriers, increasing permeability to bacteria, toxins, pollutants and allergens (Figure 1). When epithelial barriers are disrupted (or “leaky”), substances and microbes can pass into deeper tissues, where they don’t belong and trigger an immune/inflammatory response that can initiate or aggravate many chronic inflammatory diseases.

These diseases –– like asthma, rhinitis, atopic dermatitis, food allergy, inflammatory bowel disease, diabetes, rheumatoid arthritis, and chronic depression –– are more common in industrialized countries, and their prevalence continues to rise in developing countries in parallel with urbanization and industrialization. This steep increase in chronic, non-communicable diseases has been linked to changes in hygiene, decreased bacterial and worm infections, less microbial and food diversity, increased allergen exposure, changes in indoor environment, and nutrition.

The Epithelial Barrier Theory posits that the increase in barrier-damaging agents linked to industrialization, urbanization and modern life underlies the global rise in allergic, autoimmune, neuropsychiatric chronic conditions that now affect more than two billion people worldwide.

Characteristics of the Epithelial Barrier Theory

1.Increased prevalence over the last 60 years: The sharp rise in the prevalence of allergic and autoimmune diseases suggests that environmental factors are impacting our immune system. Early reports from the 1960s indicated an increased prevalence of asthma in children and higher hospitalization rates. After the 2000s, a new wave of epidemics emerged, including food allergy and anaphylaxis, eosinophilic esophagitis, and drug-induced anaphylaxis. Interestingly, the increase in autoimmune diseases, such as diabetes, rheumatoid arthritis, multiple sclerosis, and celiac disease, began in the 1960s, and this trend continues in developing countries.

2.Disturbed epithelial barriers: Evidence of epithelial barrier disruption in these conditions suggests that our body's first line of defense against harmful pathogens is not functioning correctly. Epithelial barrier damage has been demonstrated in most cases through direct biopsies of affected tissues. three reasons have been identified for this disruption:

a.Genetical defects and mutations in barrier proteins: In the skin, the stratum corneum forms a relatively stronger barrier with its filaggrin repeats and other molecules such as loricrin, involucrin and hornerin. Mutations in filaggrins, polymorphisms in tight junction (TJ) claudin and occludin genes have been reported to play a role on epithelial barrier integrity (Figure 2).

b.Direct exposure to pollutants, chemicals, and other environmental factors that are in the exposome can disrupt the epithelial barriers and affect the microbiome and immune system.

c.Inflammation in the affected epithelial barriers takes place in asthma, atopic dermatitis, rhinitis, sinusitis and colitis activates the epithelial cells, and these epithelial cells open their barriers.

3.Microbial dysbiosis: A healthy microbiota on the surface of the mucosal barrier regulates numerous aspects of barrier homeostasis. However, reduced biodiversity and alterations in the composition of gut and skin microbiota are associated with various inflammatory conditions, including asthma, allergic diseases, inflammatory bowel disease, type 1 diabetes, and obesity. Dysbiosis refers to an imbalance in the microorganisms residing in our tissues, with microbial dysbiosis and bacterial translocation being linked to the development and exacerbation of allergic and autoimmune diseases.

4.Immune response to commensal bacteria and opportunistic pathogens: In areas with leaky epithelial barriers, the immune system struggles to distinguish between harmful and harmless microorganisms. This inability triggers a chronic inflammatory response to harmless microorganisms, decreasing biodiversity and contributing to the development of allergic and autoimmune diseases (Figure 2). In addition, immune response to S. aureus, an opportunistic pathogen is taking place in most of the atopic dermatitis, chronic rhinosinusitis and asthma patients and a high prevalence of IgE antibodies correlates with the disease severity.

5.Peri-epithelial inflammation, epithelitis, and expulsion response:

Individuals with leaky epithelial barriers exhibit local inflammation in their epithelial cells, referred to as "epithelitis". Epithelitis is the initial event that attracts proinflammatory cells to the damaged epithelial barrier area, prompting the immune system to expel tissue-invading commensals and opportunistic pathogens through a process called the "expulsion response", similar to an essential defense mechanism against helminth parasites.

6.Migration of inflammatory cells to distant organs: Immune cells activated at leaky barrier sites can migrate to distant organs, causing inflammation in those areas. Moreover, increased inflammatory mediators in the circulation, namely, “circulating microinflammation”, consisting of acute phase reactants, chemokines, and cytokines, can be detected. There are clear examples of inflammatory cell migration from barrier leaky areas to diseased tissues. Cutaneous lymphocyte antigen-expressing T cells can get activated in the gut with food allergen exposure and then migrate to skin and exacerbate atopic dermatitis. In polyallergic patients, activated and circulating T cells express chemokine receptors and have the capacity to migrate towards various allergic tissues. This mechanism could be responsible for the atopic march of allergic diseases, sequentially manifesting as atopic dermatitis, food allergy, asthma, and allergic rhinitis during childhood.

Harmful environmental substances that disturb epithelial barriers

Exposure to harmful environmental substances can disturb epithelial barriers, leading to leaky epithelial barriers, microbial dysbiosis, bacterial translocation to inter- and sub-epithelial areas, and tissue microinflammation in and around the barriers. The term "exposome" refers to all environmental factors individuals encounter throughout their lifetime. These factors are categorized into three groups: the general external environment, the specific external environment, and the host-dependent internal environment. The general external environment includes factors such as climate, urban-rural settings, and education level, while the specific external environment comprises individual factors like lifestyle choices, exposure to pollutants, and infectious diseases. The host-dependent internal environment encompasses both the biological effects of external exposure and biological responses, such as metabolic factors, inflammation, and oxidative stress.

Over the last 60 years, industrialization, urbanization, and technological advancements have significantly changed the exposome, raising concerns about their health effects on humans and animals. A recent meta-analysis of 22 chemical inventories from 19 countries revealed that more than 350,000 new substances have been introduced to human lives since the 1960s, with little control over their health effects. Many of these substances may have become pollutants or entered the daily exposome. Unfortunately, 50,000 of them are publicly unknown due to confidential submissions, and nearly 70,000 have been ambiguously described.

Since the 1950s, plastic production has increased nearly 200-fold, with an estimated 8.3 billion metric tons produced worldwide by 2017. Consequently, the human body is continuously exposed to a variety of potentially harmful substances, including particulate matter, diesel exhaust particles, cigarette smoke, nano and microplastic, nanoparticles, ozone, NO, NO2, CO, SO2, household cleaners, laundry and dishwasher detergents, toothpaste, surfactants, emulsifiers, preservatives in processed food, and pesticides.

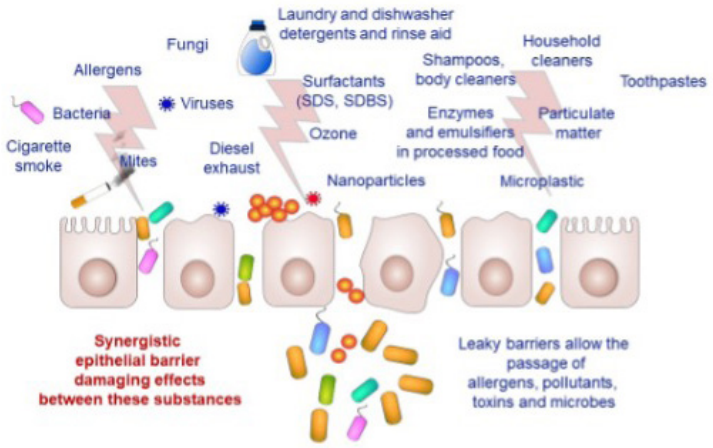


Figure 1. The increase in the prevalence and exacerbations of many allergic, autoimmune, metabolic and neurodegenerative diseases was associated with damage to the epithelial layer induced by exposure to infections agents, allergens, particulate matter, diesel exhaust, cigarette smoke, laudry and dishwasher detergents and rinse aids, household cleaners, toothpastes, microplastics, nanoparticles, ozone, processed food additives and emulsifiers and other unidentified chemical substances. Some of these substances may have synergistic effects in the damage of epithelial barriers. Leaky barriers allow the passage of allergens, pollutants, toxins and microbes.

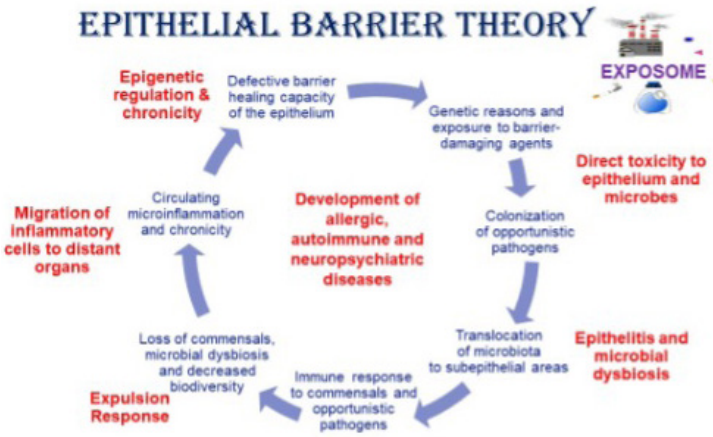


Figure 2. Pathogenetic events as mechanisms of the epithelial barrier theory: A cascade of events play a role in the pathogenesis of diseases associated with the epithelial barrier theory and development of many chronic noncommunicable diseases. Direct toxicity to epithelium and microbes: Genetic defects in barrier-related molecules or exposure to epithelial barrier-damaging agents cause a disruption of the skin and mucosal tight junction barriers and may also show a direct toxicity to health-promoting commensal microbes. Epithelitis and microbial dysbiosis: It is followed by translocation of microbiota to inter and subepithelial areas and colonization of opportunistic pathogens, such as Staphylococcus aureus (S. aureus), Moraxella catarrhalis, Haemophilus influenzae and pneumococcus bacteria. It is associated with microbial dysbiosis and decreased biodiversity of commensal bacteria. Epithelitis starts with the release of multiple alarmins. Expulsion response: An immune response develops towards commensals and opportunistic pathogens in the gut and respiratory system, and systemic inflammation takes place. Decreased biodiversity takes place because of loss of commensals and colonizing opportunistic pathogens. Migration of inflammatory cells to distant organs: Chronic inflammation in the subepithelial area prevails as one of the main reasons for the development of chronic diseases in the affected tissues. Distant organs are affected because

of circulating microinflammation and migration of activated immune system cells to distant organs. 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.

A compilation answering 50 questions on monkeypox virus and the current monkeypox outbreak.

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. Allergy. 2022 Dec.

The current monkeypox disease (MPX) outbreak constitutes a new threat and challenge for our society. With more than 55,000 confirmed cases in 103 countries, World Health Organization declared the ongoing MPX outbreak a Public Health Emergency of International Concern (PHEIC) on July 23, 2022. The current MPX outbreak is the largest, most widespread, and most serious since the diagnosis of the first case of MPX in 1970 in the Democratic Republic of the Congo (DRC), a country where MPX is an endemic disease. Throughout history, there have only been sporadic and self-limiting outbreaks of MPX outside Africa, with a total of 58 cases described from 2003 to 2021. This figure contrasts with the current outbreak of 2022, in which more than 55,000 cases have been confirmed in just 4 months. MPX is, in most cases, self-limiting; however, severe clinical manifestations and complications have been reported. Complications are usually related to the extent of virus exposure and patient health status, generally affecting children, pregnant women, and immunocompromised patients. The expansive nature of the current outbreak leaves many questions that the scientific community should investigate and answer in order to understand this phenomenon better and prevent new threats in the future. In this review, 50 questions regarding monkeypox virus (MPXV) and the current MPX outbreak were answered in order to provide the most updated scientific information and to explore the potential causes and consequences of this new health threat.

Characterization and regulation of microplastic pollution for protecting planetary and human health.

Jung YS, Sampath V, Prunicki M, Aguilera J, Allen H, LaBeaud D, Veidis E, Barry M, Erny B, Patel L, Akdis C, Akdis M, Nadeau K.Environ Pollut. 2022 Dec 15;315:120442.

Microplastics are plastic particles <5 mm in diameter. Since the 1950s, there has been an exponential increase in the production of plastics. As of 2015, it is estimated that approximately 6300 million metric tons of plastic waste had been generated of which 79% has accumulated in landfills or the natural environment. Further, it is estimated that if current trends continue, roughly 12,000 million metric tons of plastic waste will accumulate by 2050. Plastics and microplastics are now found ubiquitously-in the air, water, and soil. Microplastics are small enough to enter the tissues of plants and animals and have been detected in human lungs, stools, placentas, and blood. Their presence in human tissues and the food chain is a cause for concern. While direct clinical evidence or epidemiological studies on the adverse effects of microplastic on human health are lacking, in vitro cellular and tissue studies and in vivo animal studies suggest potential adverse effects. With the ever-increasing presence of plastic waste in our environment, it is critical to understand their effects on our environment and on human health. The use of plastic additives, many of which have known toxic effects are also of concern. This review provides a brief overview of microplastics and the extent of the microplastic problem. There have been a few inroads in regulating plastics but currently these are insufficient to adequately mitigate plastic pollution. We also review recent advances in microplastic testing methodologies, which should support management and regulation of plastic wastes. Significant efforts to reduce, reuse, and recycle plastics are needed at the individual, community, national, and international levels to meet the challenge. In particular, significant reductions in plastic production must occur to curb the impacts of plastic on human and worldwide health, given the fact that plastic is not truly recyclable.

Effect of altered human exposome on the skin and mucosal epithelial barrier integrity.

Pat Y, Ogulur I, Yazici D, Mitamura Y, Cevhertas L, Küçükkase OC, Mesisser SS, Akdis M, Nadeau K, Akdis CA.Tissue Barriers. 2022 Oct 19:2133877.

Pollution in the world and exposure of humans and nature to toxic substances is continuously worsening at a rapid pace. In the last 60 years, human and domestic animal health has been challenged by continuous exposure to toxic substances and pollutants because of uncontrolled growth, modernization, and industrialization. More than 350,000 new chemicals have been introduced to our lives, mostly without any reasonable control of their health effects and toxicity. A plethora of studies show exposure to these harmful substances during this period with their implications on the skin and mucosal epithelial barrier and increasing prevalence of allergic and autoimmune diseases in the context of the "epithelial barrier hypothesis". Exposure to these substances causes an epithelial injury with peri-epithelial inflammation, microbial dysbiosis and bacterial translocation to sub-epithelial areas, and immune response to dysbiotic bacteria. Here, we provide scientific evidence on the altered human exposome and its impact on epithelial barriers.

Differentiation of bronchial epithelial spheroids in the presence of IL-13 recapitulates characteristic features of asthmatic airway epithelia.

Pat Y, Rückert B, Ogulur I, Yazici D, Pérez-Diego M, Küçükkase OC, Li M, Akdis CA. Allergy. 2022 Jul;77(7):2229-2233.

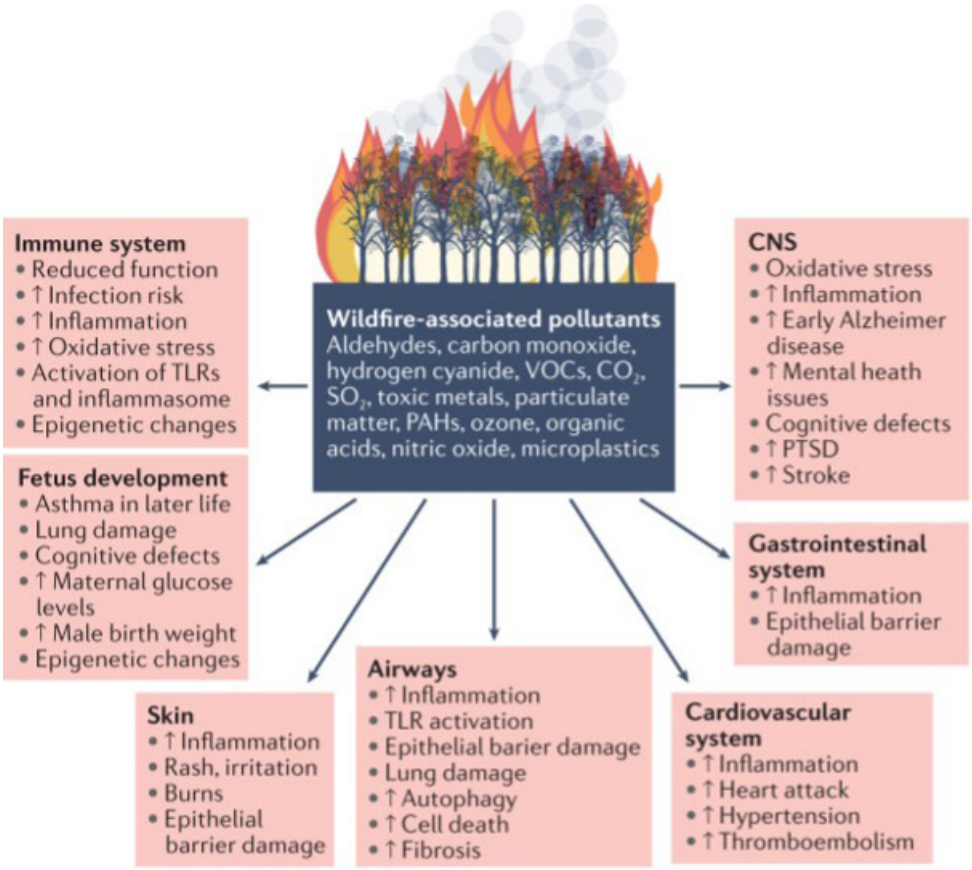
There is a substantial need to better understand the pathophysiology of asthma to develop preventive approaches and better treatments. Preclinical models as close as possible to human in vivo situations are essential to fulfil these aims. 3D airway culture models, particularly airway organoids, have several advantages over traditional 2D cultures, such as mimicking organ structure, ability to generate in vivo relevant cell–cell interaction models, suitability for high-throughput experiments, and applications in epithelial self-assembly, morphogenesis, differentiation and repair studies. A dominant endotype of asthma is characterized with an impaired airway epithelial barrier, remodelling and the involvement of type 2

inflammation with cytokines such as interleukin (IL)-4, IL-5 and IL-13. Here, we demonstrate the establishment a 3D airway organoid model from primary bronchial epithelial basal cells to investigate the characteristic features of asthma, such as epithelial cell differentiation, epithelial remodelling and mucosal tight junction barrier impairment in the presence of a main pathogenetic type 2 cytokine, IL-13.

Alpine altitude climate treatment for severe and uncontrolled asthma: An EAACI position paper.
Fieten KB, Drijver-Messelink MT, Cogo A, Charpin D, Sokolowska M, Agache I, Taborda-Barata LM, Eguiluz-Gracia I, Braunstahl GJ, Seys SF, van den Berge M, Bloch KE, Ulrich S, Cardoso-Vigueros C, Kappen JH, Brinke AT, Koch M, Traidl-Hoffmann C, da Mata P, Prins DJ, Pasmans SGMA, Bendien S, Rukhadze M, Shamji MH, Couto M, Oude Elberink H, Peroni DG, Piacentini G, Weersink EJM, Bonini M, Rijssenbeek-Nouwens LHM, Akdis CA. Allergy. 2022 Jul;77(7):1991-2024.
Currently available European Alpine Altitude Climate Treatment (AACT) programs combine the physical characteristics of altitude with the avoidance of environmental triggers in the alpine climate and a personalized multidisciplinary pulmonary rehabilitation approach. The reduced barometric pressure, oxygen pressure, and air density, the relatively low temperature and humidity, and the increased UV radiation at moderate altitude induce several physiological and immunological adaptation responses. The environmental characteristics of the alpine climate include reduced aeroallergens such as house dust mites (HDM), pollen, fungi, and less air pollution. These combined factors seem to have immunomodulatory effects controlling pathogenic inflammatory responses and favoring less neuro-immune stress in patients with different asthma phenotypes. The extensive multidisciplinary treatment program may further contribute to the observed clinical improvement by AACT in asthma control and quality of life, fewer exacerbations and hospitalizations, reduced need for oral corticosteroids (OCS), improved lung function, decreased airway hyperresponsiveness (AHR), improved exercise tolerance, and improved sinonasal outcomes. Based on observational studies and expert opinion, AACT represents a valuable therapy for those patients irrespective of their asthma phenotype, who cannot achieve optimal control of their complex condition despite all the advances in medical science and treatment according to guidelines, and therefore run the risk of falling into a downward spiral of loss of physical and mental health. In the light of the observed rapid decrease in inflammation and immunomodulatory effects, AACT can be considered as a natural treatment that targets biological pathways.

Human and planetary health on fire.
Akdis CA, Nadeau KC. Nat Rev Immunol. 2022 Nov;22(11):651-652.
Wildfires are increasing globally, with several recent catastrophic wildfires linked to climate change. Here, we consider the negative impact of the toxic contaminants arising from these fires on the immune system, with a focus on how wildfire pollution can exacerbate inflammatory diseases.

Davos, May 2023



Prof. Dr. Mübeccel Akdis, MD, PhD

Characterization of antigen-specific B cells; expression of G-protein coupled receptors

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 accumulation1. In the presence of histamine in the environment, high affinity HR1is triggered causing cellular activation, followed by expression of 10 times lower affinity HR2 to regulate the over-inflammatory events. These HRs trigger different intracellular events upon activation, with HR1 as a Ca2+ flux-inducing activating receptor and HR2 as an adenyl cyclase-stimulating suppressive receptor1,2. Therefore, to explore the response of B-cells in allergic diseases, we analyzed the expression profile of HRs and other GPCRs in B cell clones. 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.

A total of 27 IgG1 and IgG4 expressing B cell clones were isolated for gene expression analysis under BCR stimulated and unstimulated conditions. Interestingly, we observed B-cell clones with mutually exclusive expression profile of HRH1 and HRH2 genes, with more HRH1+ B-cell clones in BCR-stimulated samples than unstimulated samples. The subsequent HRH1+ vs HRH2+ differential gene expression analysis, reveal 27 differentially expressed (DE) GPCRs in unstimulated samples, with up-regulated P2RY13 and C5AR1 genes in HRH2+ B-cell clones (Figure 1), which are associated with the cAMP signaling and suppressive pathway. To further prioritize the DE GPCRs specifically associated with Ca2+ and cAMP signaling pathways, we reconstructed the co-expression networks and performed the weighted degree analysis across HRH1+ vs HRH2+ clones. The analysis reveals that the purinergic receptor family of GPCRs (i.e. P2RY1, P2RY13) and complement component 5a receptor family of genes (i.e. C5AR1 and C5AR2) share highest degree of interactions. These genes are up-regulated in HRH2+ samples and are well-known to either increase intracellular Ca2+ or dampen cAMP signaling pathway (Figure 1A). Intriguingly, we also observed upregulation of GPR35 in HRH2+ B cells, which is associated in maintaining a low baseline Ca2+ level. Similarly, we also observed up-regulation of GPR68 and GPR171 in HRH1+ B cells; both are known to stimulate Ca2+ flux (Figure 1). Similarly, 28 GPCRs were differentially expressed in BCR-stimulated samples (Figure 1B), including higher expression of serotonin receptor type 1A (HTR1A) and HCAR1 (or GPR81) in HRH2+ samples, with a cAMP-linked suppressive function. In addition, we also observed upregulation of complement component 5a receptor family of genes (i.e., C5AR1 and C5AR2) and GPR35, in agreement with the trend observed in unstimulated HRH2+ B-cell clones. Surprisingly, we observed a higher expression of prostaglandin E2 receptor subtype EP4 (PTGER4) and adenosine A2A receptor (ADORA2A) in HRH2+ samples6, which are known to be associated with activation of cAMP production and share the highest strength of interactions with the cAMP signaling sub-network. Among the up-regula-

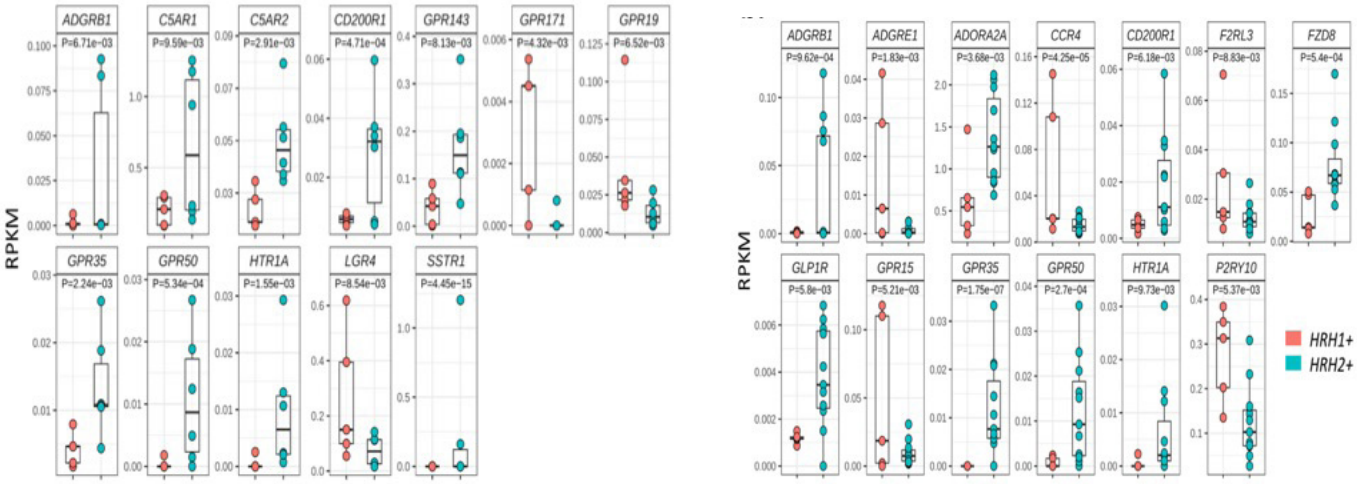


Figure 1: Differentially expressed GPCRs in HRH1+ vs HRH2+ samples. (A) The boxplot showing topmost significantly differentially expressed GPCR genes in (p < 0.001) unstimulated samples. (B) The boxplot showing topmost significantly differentially expressed GPCR genes in (p < 0.001) BCR-stimulated samples.

ted genes in HRH1+ samples, we found three Ca2+ mobilizing genes, i.e., GPR34, P2RY10 and PTAFR. The results reported in this study provides data for a novel hypothesis suggesting investigation of co-expressed GPCRs genes that may play important synergistic or antagonistic regulatory roles in B-cell function.

Allergen-specific B cell tolerance

Although cow's milk is one of the most important and basic nutrients introduced early in life in the diet, it can induce IgE-associated food allergy that causes severe allergic manifestations in the gut, skin, and even in the respiratory tract and may lead to life-threatening anaphylactic shock. The major cow's milk allergens belong to the casein group of proteins (αS1, αS2-, β-, and κ-casein) and whey proteins (α-lactalbumin and β-lactoglobulin). We focused our investigation on a direct analysis of freshly isolated αS1-casein allergen-specific B cells, which are not manipulated by cell culture or other procedures. There was a clear difference between remission and desensitized B cells suggesting that desensitization is an intermediate step on the way to remission and tolerance development. In both the remission and desensitized groups, antigen binding, cytokines and receptors, B cell activation, chemotaxis, BCR signaling, B cell differentiation, and B cell Ig heavy chain genes were altered. There was an increase of Breg cell-related genes, BCR signaling and differentiation. Within these most significantly expressed genes, IL10RA, a receptor for the binding of suppressor cytokine IL-10 and TGFB3, a regulatory cytokine for antigen/allergen tolerance were highly expressed in desensitized OIT patients. In addition, the expression of the gut homing chemokine CCR6 was upregulated in desensitized individuals, suggesting the OIT-induced-remission state might occur in the gut. Changes in the expression of B cell IGH genes showed interesting findings. While in desensitized patients, only an increase in IGHG2 was observed, in remission subjects, we observed a significant increase in genes encoding the heavy chains for IgG4, IgG1, IgA1, IgA2, and IgD. Elevated levels of all these specific antibody isotypes have been linked to remission in serum in OITs with different allergens. Among all immunoglobulin isotypes, IgG4 always appeared at the forefront as an immune tolerance/remission-linked antibody isotype particularly induced by IL-10 (Figure 2).

The present study demonstrates how specific memory B cells are characterized in NT. The mechanisms of NT development were unraveled by comparing the gene expression prior to OIT (Figure 3 A-B) and by comparing it with remission induced after OIT (Figure 4). Our main finding was a similar downregulation of many B cell genes in NT compared to remission after OIT. A type 2 immune response (IL4R and IL13RA1) is the hallmark of food allergy. The ameliorated allergic response observed in NT could be attributed to the significantly lower expression of the IL4R and IL13RA1 and the B cell costimulatory receptor (CD40) that are all required for B cell activation. Similarly, TAP1 was lower in NT, suggesting a downregulation of the antigen-presentation capacity of specific B cells. Other downregulated genes associated with allergic diseases, such as BATF, HRH2, TLR2, and ADA, were all downregulated in NT. ADA is also associated with elevated IgE in atopic and food allergic patients.

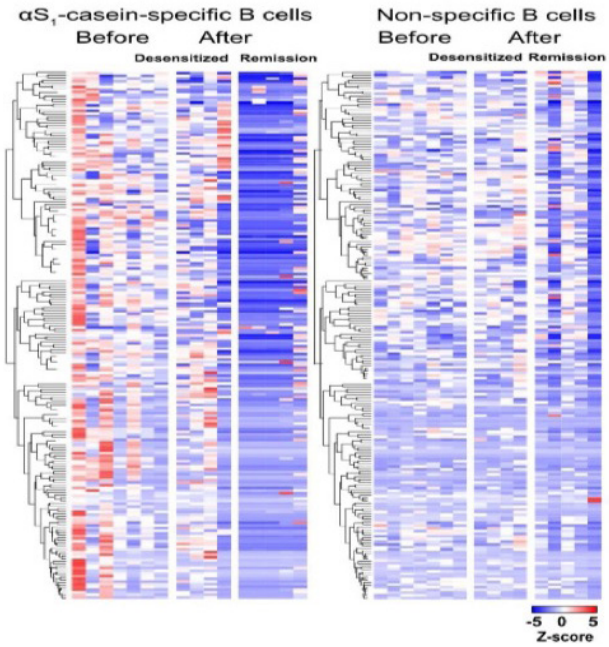


Figure 2: DGEs signatures in αS1-casein-specific and non-specific B cells before and after OIT (desensitized & remission). Heatmap of the top 200 most DGEs in αS1-casein-specific and non-specific B cells from before and after OIT, nbefore OIT=7, nafter OIT (desensitized)=4, nafter OIT (remission)=5

NT decreases the levels of B cell cytokines or their receptors that control homeostasis of allergen-specific memory CD4+T cells in the lung and airways (e.g., IL7R), contribute to allergen-induced airway inflammation in asthma (IL12RB1and IL12RB2), involved in the stimulation of Th1 cells to produce Th2 cytokines and lead to pathophysiology of allergic diseases (IL18R1), and enhance Th2 polarization and regulate allergic airway inflammation (IL23A). As part of specific B cell suppression in NT, there is a downregulation of PLAU (Treg suppressor) involved in chemotaxis, CXCR3 encoding a receptor that binds to chemokine CXCL-10 and enhances antigen-specific Th1 responses in healthy humans, XCL1 and XCL2 that play a crucial role in intestinal immune homeostasis, and chemokine genes CCL3L3, CCL4L2, CCRL2 that control airway inflammatory responses. In addition, GZMB and GZMH that act as mediators of allergic inflammation in human asthma, TGFB3 and its family gene ACVR1B that act in the initiation and effector phases of allergic disease, as well as in consequent tissue dysfunction, and PIK3R3 that is involved in B cell co-stimulation signaling were also downregulated. In addition, some genes that contribute to B cell activation were upregulated, such as NOTCH2 that suppresses food antigen-induced mucosal mast cell hyperplasia and mediates the development and plasticity in marginal zone B cells and regulate innate immunity. FOXP1 that plays a critical role in human plasma cell differentiation was also upregulated. Two cytokine receptors IL21R and IL2RG via STAT3-dependent induction of transcription factors required for B cell expansion and plasma cell generation were increased in specific cells in NT. TNFRSF1B, a member of the TNFRSF family, which acts as a co-signaling chemokine in the BAFFR system for B cell activation was higher in NT. Toll-like receptor genes expression (TLR1, TLR6, TLR9) on B cells in NT, displayed the potential to induce secretion of cytokines, chemokines, and regula-

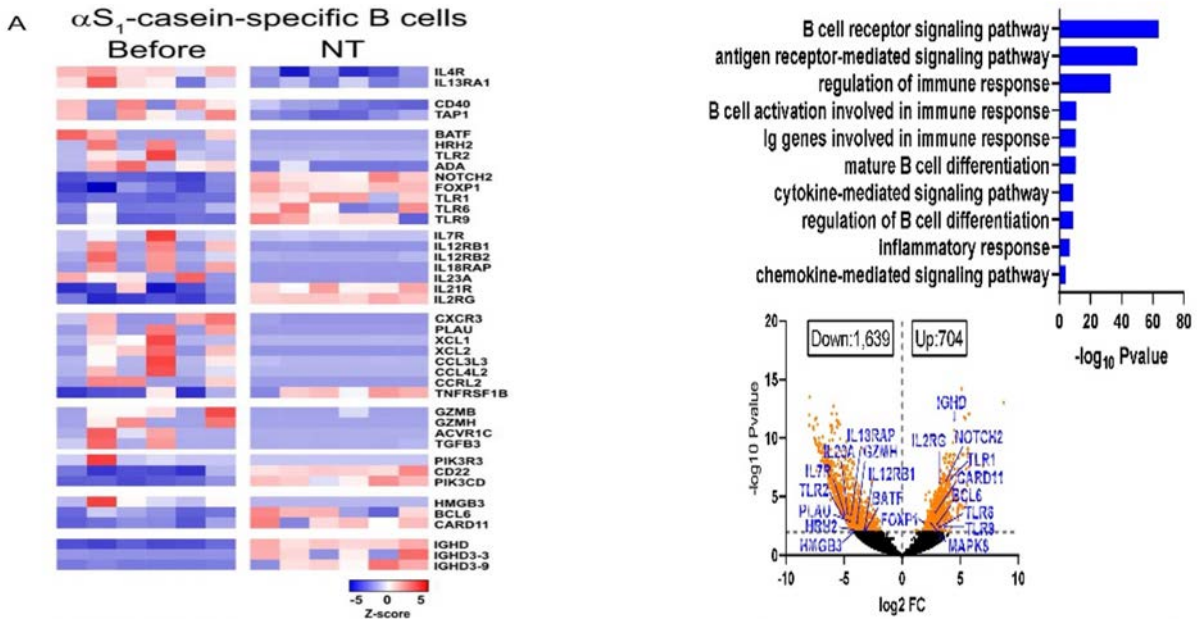


Figure 3: DGEs signatures in αS1-casein-specific B cells from before OIT vs NT. (A) Heatmap showing top significant DEGs of αS1-casein-specific B cells from before OIT and NT, nbefore OIT=6 and nNT= 6. (B) Top B cell-related pathways analysis. Volcano plot shows differentially expressed genes with top 20 significant genes (p-value <0.05).

te immune homeostasis. In addition, TLR9 is an important stimulus for Breg cell development. CD22 is an essential B cell suppressor molecule, which plays a role in allergen remission and was found to be highly expressed in NT. PIK3CD also increased in NT, suggesting a role in the control of B cell development and function. The significantly increased gene in specific B cells, BCL6, suppresses IL-4 production in memory phenotype Th2 cells and suppresses Th2 immune responses in allergies. CARD11 mutations affect B cell development and cause cellular defects in congenital lymphoproliferative patients and atopic dermatitis individuals. In CMA and house dust mite allergic patients, allergen-specific IgD was secreted after the course of OIT in serum samples. In the present study, we compared two types of immune tolerance to allergens, namely the natural and OIT-remission in specific B cells (Figure 4 A-D). One of the main differences between OIT-remission and NT is that NT is a long-lasting tolerance, whereas OIT-remission is newly established and there is no guarantee that it will persist for long time. It has been shown that viral infections can revert remission even in the course of OIT. It should be noted that our analysis of the DEGs indicated similar changes in expression for a large number of genes in both OIT and NT samples compared to pre-OIT samples. In conclusion, we present a detailed characterization of the transcriptome, secreted proteins and specific antibodies by allergen-specific B cells in cow's milk in OIT-remission and NT individuals. Allergen-specific B cells showed distinctive changes in induction of desensitization and in remission. The transcriptomic changes in specific B cells in OIT-remission correspond to further silencing of B cell activation genes after desensitization. A significant downregulation of gene expression mechanisms related to B cell suppression are evident in OIT-remission when compared to desensitized individuals. In contrast, a proinflammatory environment is observed in allergen-specific B cells in allergic individuals arising from type 2 cytokine-related genes. This proinflammatory environment is altered in specific B cells that gain a suppressor capacity after OIT. There are similarities and differences in the immune profile of children outgrowing food allergy compared to OIT-remission.

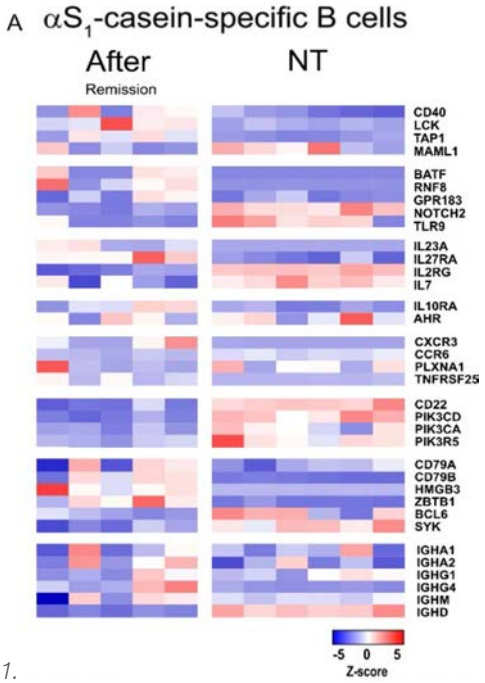


Figure 4.1.

In NT, B cells were identified to differentiate to pre-plasma and marginal zone B cell stage with the expression of more innate immune receptors in NT. Breg cell-related genes are still active in OIT-remission with a higher expression of previously reported immune tolerance-related IGHG4, IL10 and TGF-β genes. The limitations of the study are the low frequencies of allergen-specific B cells in some of the subjects, especially in healthy controls and the lack of base-

line in natural tolerance individuals. Due to this limitation, the RNA sequencing results were not measurable in all subjects as, well as, the change of natural tolerance individuals from their baseline. Altogether, our data demonstrated that allergen-specific B cells are induced during OIT and natural tolerance and that the altered gene expression is important in induction and maintenance of immune tolerance to food antigens.

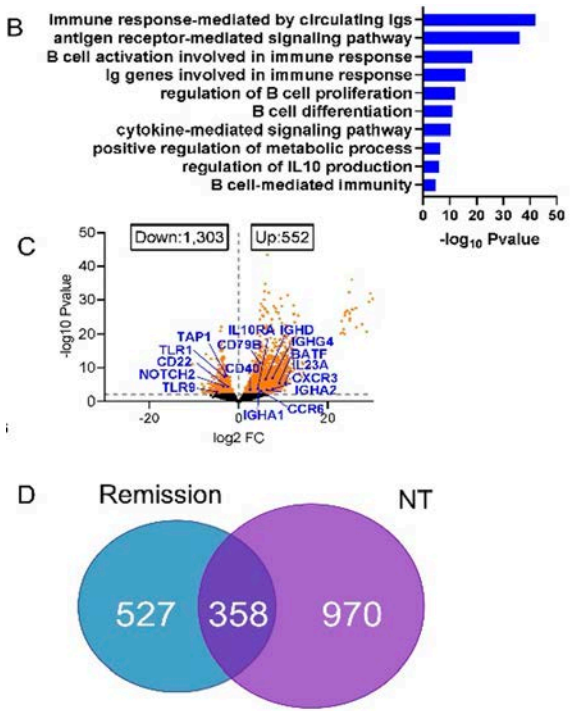


Figure 4.1 & 4: DGEs signatures in αS1-casein-specific B cells from after OIT (remission) vs NT. (A) Heatmap of the top significant DEGs of αS1-casein-specific B cells from after OIT (remission) vs NT, nafter OIT (remission)=5, nNT OIT=6, (B) Top B cell-related pathways analysis (C) Volcano plot shows 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).

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. Submitted)

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.

Experimental rhinovirus infection induces an antiviral response in circulating B cells which is dysregulated in patients with asthma

(Oliver F. Wirz et al. Allergy 2022 Jan;77(1):130-142.)

Rhinoviruses are the predominant cause of respiratory viral infections and are strongly associated with asthma exacerbations. While humoral immunity plays an important role during virus infections, cellular aspects of this response are not well understood. Here, we investigated the antiviral response of circulating B cells upon experimental rhinovirus infection in healthy individuals and asthmatic patients. We demonstrated that B cells from healthy subjects exhibited an anti-viral gene profile linked to IFN-alpha, carried viral RNA in vivo, and were transiently infected by rhinovirus in vitro. Importantly, B cells themselves lacked expression of interferons in response to rhinovirus exposure. Furthermore, IFN-alpha stimulated B cells upregulated pro-inflammatory cytokines in response to rhinovirus infection. Asthmatic individuals showed extensive upregulation and dysregulation of antiviral gene expression. This study contributes to the understanding of systemic effects of local rhinovirus infections on lymphocytes in the periphery and findings might also have implications during infection with other respiratory viruses.

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. I

Innate lymphoid cell subsets in obese asthma patients: Difference in activated cells in peripheral blood and their relationship to disease severity.

(Zeynep Celebi Sozener et al. Allergy. 2022 Sep;77(9):2835-2839)

The parallel increase in the prevalence of obesity and asthma has suggested a relationship between these two diseases in recent years. The identification of common or distinct pathophysiological mechanisms associated with these two chronic diseases has not yet been clarified. Although Type 2 asthma has classical characteristics of Th2 cells, group 2 innate lymphoid cells (ILC), their cytokines, IL-4, IL-5 and IL-13 and eosinophilia, the classical Type 2 immune response is more complex in obese patients, mainly due to the involvement of fat tissue in immune responses. In obese asthmatics, asthma is generally nonatopic, and ILC3s play a critical role in obesity-induced airway hyperreactivity. However, it has recently been shown that eosinophils are also predominant in the lung tissue of obese asthma patients. In addition, increased T2 response and ILC2s are observed in obese asthmatic patients.

Davos, May 2023

Prof. Dr. Christoph Messner, PhD

Implementation of the cantonal University and Research Strategy
Profile Area 5 - Life Science
I have started my position in SIAF as head of the Precision Proteomics Center in August 2022, where I am currently establishing my research group and program.

Key activities in 2022 involved establishing and further developing mass spectrometry-based proteomics workflows at the Precision Proteomics Center, with a specific focus on enhancing their robustness and efficiency for clinical applications. These established technologies have been applied in various collaborations with national and international partners. Extensive analyses of large cohorts have been conducted to identify protein biomarkers across diverse disease areas. Notably, comprehensive cohorts of plasma/serum samples have been studied, including individuals with autoimmune diseases, allergic diseases, and cancer. Additionally, advanced bioinformatics pipelines incorporating machine learning techniques have been developed to facilitate patient stratification and predict treatment response. For instance, in collaboration with the Swiss company Biognosys, patient samples from a pancreatic cancer clinical trial underwent an in-depth proteomics plasma workflow, leading to the discovery of protein markers capable of predicting the response to immunotherapy/chemotherapy combinations. This breakthrough finding has significant implications for identifying patient subgroups that would derive the greatest benefit from such a combination therapy.

In addition to protein abundance measurements, we also focused on developing workflows for utilizing peptide-level information and analyzing post-translational modifications. Currently I am leading an international collaboration to develop an innovative high-throughput workflow for analyzing glycosylation. This new technology represents a significant advancement in the field of glycoproteomics, providing insights into disease-related glycosylation changes. The successful development of this novel technique has the potential to revolutionize disease diagnostics by enabling the identification of disease-specific biomarkers beyond traditional protein abundance measurements.

Currently I am spearheading a large-scale international study in collaboration with Charité University Hospital, the University of Edinburgh, and the Francis Crick Institute in London. This study aims to comprehensively understand the functions of proteins and their roles in disease by systematically studying the proteome response to knockouts. For the first time, the research team has successfully mapped protein changes on a genome-wide scale. This groundbreaking study provides invaluable insights into the expression and regulation of proteins, serving as a valuable resource for understanding the functions of proteins and genes in cell biology and various diseases.

Davos, May 2023

Molecular Allergology

PD Dr. Katja Bärenfaller, PhD

Molecular Allergology
PD Dr. Katja Baerenfaller

The molecular profile of Th cell differentiation and activation

In the PhD project of Jana Koch that was funded by "Stiftung vormals Bündner Heilstätte Arosa" and by the Center for Precision Proteomics, the main aim is to better understand the molecular regulatory processes in T helper (Th) cell differentiation and activation. To this end, Jana Koch has established experimental workflows to characterize the molecular profile of these processes in Th1 and Th2 cells using cell cytometry, metabolic profiling, transcriptomics, translatomics and mass spectrometry-based proteomics. Our current research efforts are focused on the detailed investigation of some of the exciting findings.

When we looked at translationally regulated genes between Th1 cells and unstimulated CD4+ T cells we found that some important enzymes in the prenylation pathway showed changes only in translation or changes in translation that buffered changes in transcription (Figure 1). As prenylation itself is known to play an important role in T cells, we followed this up experimentally.

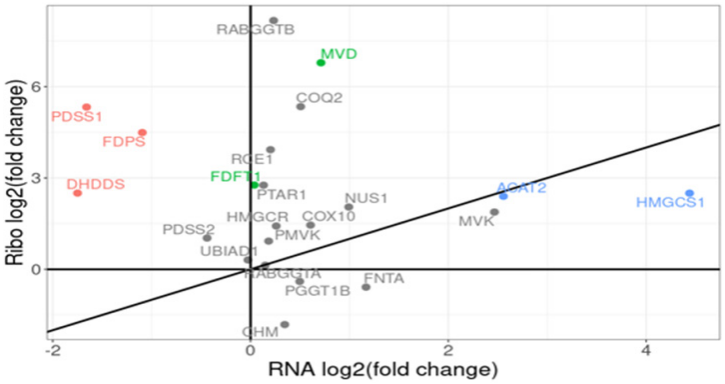


Figure 1: Plot of the fold changes between stimulated Th1 cells and unstimulated CD4+ T cells at day 2 in transcription (x axis) and in translation (y axis). In blue, genes for which translation follows transcriptional change; in green, genes with changes only in translation; in red, genes for which translation buffers transcriptional change.

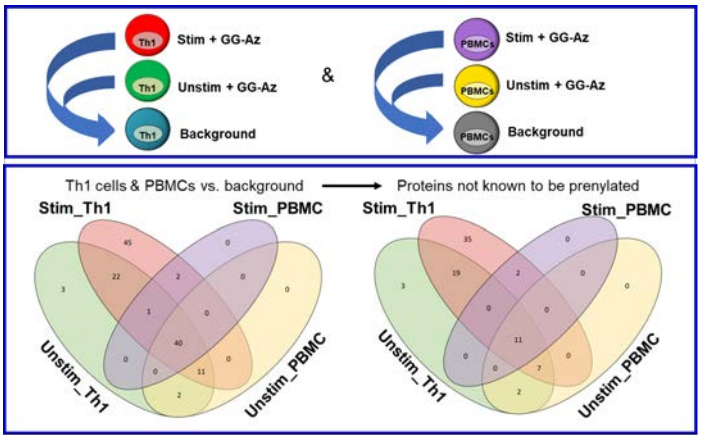


Figure 2: Identification of prenylated proteins. PBMCs or Th1 cells were either stimulated wit CD-Mix or nor, and geranylgeranyl-azide (GG-Az) was either added or not. In the Venn diagrams the number of identified prenylated proteins are given comparing samples with GG-Az against

To investigate differential prenylation events in Th cell activation, azide-coupled geranylgeranyl (GG-Az) was added first to peripheral blood mononuclear cells (PBMCs), and later to ex vivo differentiated Th1 cells to metabolically label newly prenylated proteins. The GG-Az-labelled proteins were then covalently bound to alkyne labelled resin by using click chemistry. After washing and proteolytic cleavage, the tryptic peptides from these bound proteins were identified with mass spectrometry, which resulted in the identification of known prenylated proteins, and in the detection of proteins not yet annotated as prenylated (Figure 2). These findings are currently further investigated and validated using both bioinformatics and experimental approaches.

Additional experiments that keep the Orbitrap ECLIPSE running hot

Additional major projects running at the Center for Precision Proteomics were the identification and quantification of the post-translational modifications phosphorylation and glycosylation, the isolation of characterization of extracellular vesicles, the molecular characterization of skin biopsy samples, and the detection of allergen proteins in food samples. In the latter experiment, soy has now also been included as a potential source for the presence of food allergen proteins. This work is mainly carried out by PhD student Elena Barletta, and Patrick Westermann is actively involved in all the proteomics experiments and is responsible for ensuring that the mass spectrometer works.

In a new collaborative project with the group of Oliver Schilling, the capacities of the Orbitrap ECLIPSE were used to acquire a large-scale dataset from clinical samples comprising real-world patient heterogeneity. Using this dataset, analysis strategies for data-independent acquisition proteomics could be benchmarked, and it was found that the reliability and reproducibility of proteomics data analyses heavily depend on appropriate data processing options at each proteomics workflow step. With this, the proteomics community could be supported with a benchmark that mimics the complexity that is encountered in realistic biomedical settings (Fröhlich et al., Nat Commun, 2022).

The DAViS Center went even more viral

The Center for Data Analytics, Visualization and Simulation (DAViS) was established in 2019 at Fachhochschule Graubünden (FHGR) in Chur with SIAF as primary partner. Since then, several collaborative projects have been carried out. This also included interactions with the Center for Proteomics Center for which, for example, a data storage and backup infrastructure was designed and implemented in 2022. In different research projects in DAViS we investigated various aspects of the COVID-19 pandemic. The topics ranged from the analysis of molecular and clinical data from COVID-19 patients that were either hospitalized in a COVID-19 hospital in Zgierz, Poland, or were diseased local ice hockey players (Styrzynski, Zhakparov et al., Infectious Diseases and Therapy, 2022; Maurer, Barletta et al., Allergy, 2022) to the continued analysis of waste water samples to determine the relative frequency of the circulating SARS-CoV-2 variants. In another project we continued our efforts to use machine learning to select specific features in molecular data and in patient information on the health and living conditions of children with and without atopic dermatitis that had been established in the SOS-ALL consortium (Zhakparov et al., Conference proceedings ECML PKDD Workshop on Machine Learning for Pharma and Healthcare Applications 2022).

- Machine learning successfully detects COVID-19 patients prior to PCR results and predicts their survival based on standard laboratory parameters

Filip Styrzynski, Damir Zhakparov, Marco Schmid, Damian Roqueiro, Zuzanna Lukasik, Julia Solek, Jakub Nowicki, Milosz Dobrogowski, Joanna Makowska, Milena Sokolowska and Katja Baerenfaller, Infectious Diseases and Therapy 2022 1:19, doi: 10.1007/s40121-022-00707-8

In the clinical setting it is important to rapidly identify SARS-CoV-2 positive patients, and to provide patients with COVID-19 with appropriate medical support by monitoring parameters that are associated with poor disease outcomes. In our collaborative project between the DAViS team, SIAF group leader Milena Sokolowska, and medical staff at the COVID-19 hospital in Zgierz, Poland, we have therefore asked whether subsets of clinical parameters can be identified to diagnose SARS-CoV-2 positive patients, to identify patients with COVID-19 with a high risk of a fatal outcome on admission to hospital, and to recognize longitudinal parameter patterns as warning signs of a possible fatal COVID-19 outcome during hospitalization.

To determine the best set of features to predict the risk of dying from COVID-19 already on admission to hospital, we used a machine learning survival analysis with a feature space including the on-admission laboratory results, patients' demographics, reported comorbidities, and medications. After a test–training split and a further division of the training data into a training and validation set for the tenfold cross-validation, three different machine learning algorithms were run with specified hyperparameter ranges to evaluate the model with the highest median score, which was then run on the so far unseen test data. This was repeated for ten different test–training splits. Analysis of the machine learning results revealed that procalcitonin (PCT), troponin I (TnI), age, hemoglobin (HGBI), the ratio platelets/lymphocytes (PLT/NEU), and C-reactive protein (CRP) were amongst the most important prognostic features. This was further confirmed by calculating the importance of all features across the top ten models using permutation (Figure 3). With the use of machine learning we could therefore determine strong predictors of a fatal outcome of COVID-19 on admission to hospital. In addition, we found that the strongest predictors in the longitudinal parameter patterns measured during hospitalization were CRP, white blood cells, and D dimers. The identified subsets of parameters can assist in the adoption and adjustment of effective treatment for patients with COVID-19 with warning signs of a fatal disease outcome in the clinical setting.

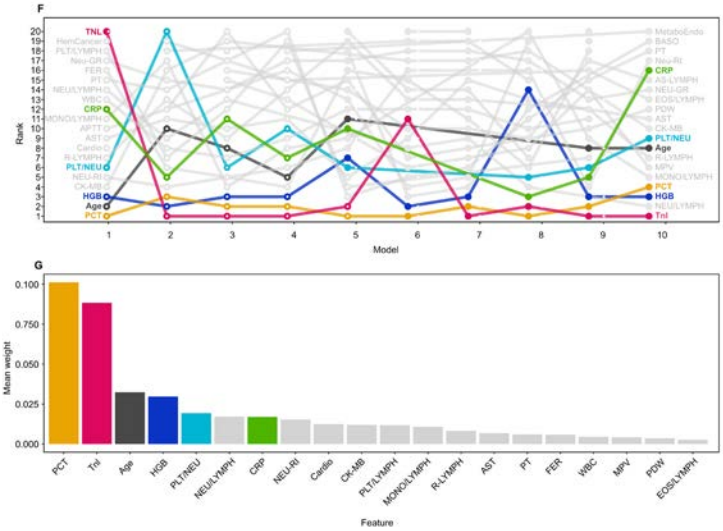


Figure 3: Figure 2 FG from Styrzynski, Zhakparov et al., (2022); Survival analysis of patients with COVID-19 based on features that were measured at hospital admission. F) Bump chart of feature ranks in the machine learning survival analysis with cross-validation on 10 different training–test splits, where a low rank indicates high feature importance. G) The mean weights of the different features as assessed in a permutation feature importance analysis confirm the importance of those features in distinguishing deceased and surviving SARS-CoV-2 positive patients.

- Waste water analysis during the World Economic Forum 2022 in Davos and St. Moritz

Following up on the sequencing of waste water during the international sports events in December 2021, we monitored the spread of different SARS-CoV-2 variants during the World Economic Forum (WEF) in May 2022 in Davos, and during the same time in St. Moritz. In the sequencing workflow, the waste water is collected in the waste water plants in different locations and sent to the cantonal laboratory in Chur, where the RNA is extracted. This RNA is then sent to the Functional Genomics Center Zurich for amplicon sequencing. Upon completion of the sequencing, PhD student Damir Zhakparov downloads the data and uses the V-Pipe pipeline to map the sequencing reads to the variant sequences, and to estimate the relative prevalence of the different variants in the population. We found that in contrast to the sports events in December 2021 no spread of a new variant occurred during WEF 2022, but only an increase to 26% in the relative prevalence of variant B.1.1.7 in Davos (Figure 4, left), compared to 18% in St. Moritz.

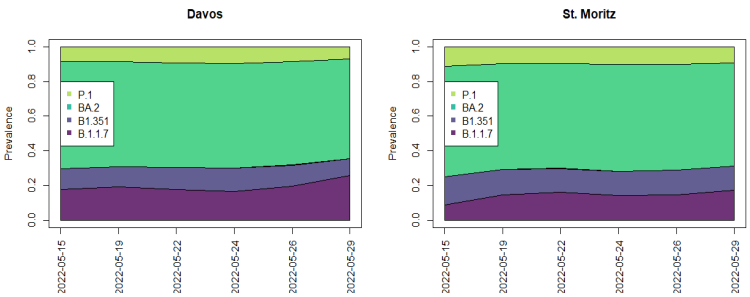


Figure 4: The relative prevalence of the different variants of SARS-CoV-2 in the waste water plant of Davos (left) and St. Moritz (right) during WEF 2022; B.1.1.7 (alpha), B.1.351 (beta), BA.2 (omicron.2), P.1 (gamma).

- 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. ECML PKDD Workshop on Machine Learning for Pharma and Healthcare Applications 2022, doi: 10.3929/ethz-b-000565782

The aim of the MLM-SOS-ALL project is to use machine learning to identify significant features that separate healthy children from children that have atopic dermatitis depending on whether they live in an urban or rural environment. The data that go into these analyses were established in the SOS-ALL consortium from Xhosa children in South Africa, and comprise both information on health status and living conditions, and on transcript expression levels in peripheral blood mononuclear cells (PBMCs). Combining these two types of data requires that the data on the levels of 20'099 transcripts first get reduced to a set of significant features that carry important information. The use of statistical differential gene expression analysis or of different machine learning algorithms allowed to generate subsets of selected, specific features, yet the size and composition of these feature lists varied considerably depending on the applied method and algorithm. The statistical p-values and the confidence measures given by the machine learning algorithms, respectively, did not allow a clear decision on the best list. We therefore decided to assess the lists for their biomedical relevance. To this end, the selected genetic features were subjected to a Gene Ontology (GO) functional enrichment analysis, and the significantly enriched GO terms were evaluated applying a semantic similarity analysis combined with binary cut clustering (Figure 5). In addition, comparisons with consensus gene lists associated with AD were performed, and the previous identification of the selected features in related studies was assessed. Based on the results we argue that machine learning-based methods are capable of selecting features with high biomedical relevance, and that feature selection followed by a careful evaluation of the selected feature sets allows to select lists that are appropriate for downstream analyses.

This work is published as a part of European Conference on Machine Learning and Principles and Practice of Knowledge Discovery in Databases (ECML-PKDD) 2022 conference proceedings.

Davos, May 2023

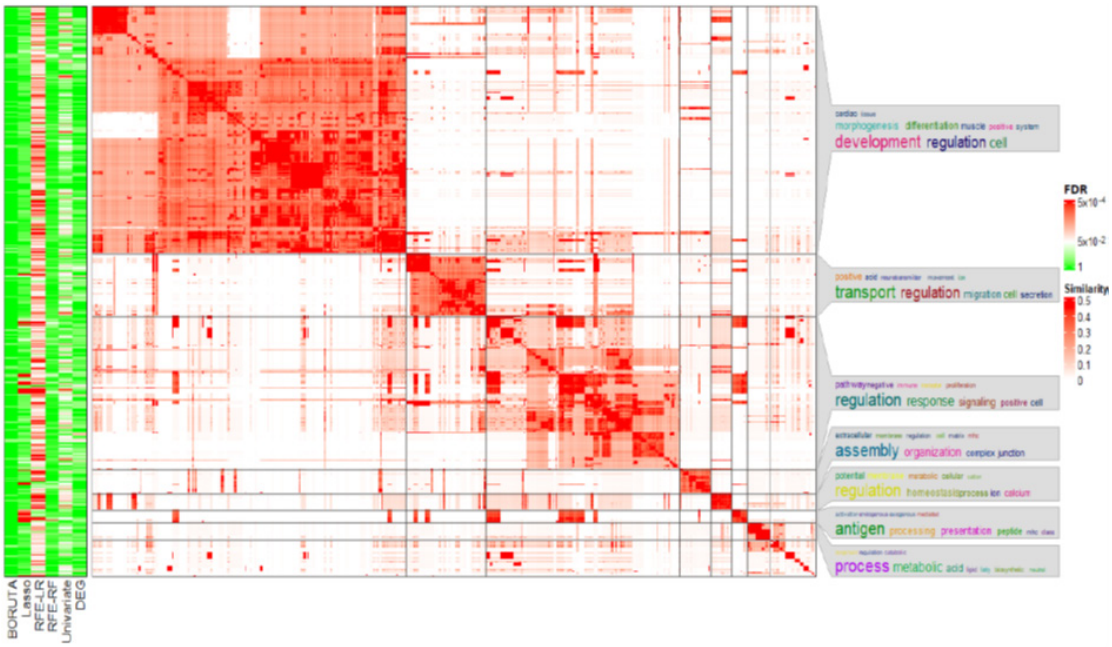


Figure 5: Figure 4 from Zhakparov et al., (2022); heatmap of semantic similarity scores of most significant Gene Ontology (GO) Biological Process (BP) terms in all of the lists clustered with the binary cut method. At the left, the methods and the respective adjusted p-values for the over-representation of a given GO BP term are indicated. The color encoding shows the semantic similarity scores. On the right side, the word clouds demonstrate the most common keywords for every cluster.

Component-resolved microarray analysis of IgE sensitization profiles to Culicoides recombinant allergens in horses with insect bite hypersensitivity.

Allergy to bites of blood-sucking insects, including biting midges, can affect both human and veterinary patients. Horses are often suffering from an IgE-mediated allergic dermatitis caused by bites of midges (Culicoides spp). With the aim to improve allergen immunotherapy (AIT), numerous Culicoides allergens have been produced as recombinant (r-) proteins. This study aimed to test a comprehensive panel of differently expressed Culicoides r-allergens on a cohort of IBH-affected and control horses using an allergen microarray. IgE levels to 27 Culicoides r-allergens, including 8 previously unpublished allergens, of which 11 were expressed in more than one expression system, were determined in sera from 347 horses. ROC analyses were carried out, cut-offs selected using a specificity of 95% and seropositivity rates compared between horses affected with insect bite hypersensitivity (IBH) and control horses. The combination of r-allergens giving the best performing test was determined using logistic regression analysis. Seropositivity was significantly higher in IBH horses compared with controls for 25 r-allergens. Nine Culicoides r-allergens were major allergens for IBH with seven of them binding IgE in sera from > 70% of the IBH-affected horses. Combination of these top seven r-allergens could diagnose > 90% of IBH-affected horses with a specificity of > 95%. Correlation between differently expressed r-allergens was usually high (mean = 0.69, range: 0.28-0.91). This microarray will be a powerful tool for the development of component-resolved, patient-tailored AIT for IBH and could be useful for the study of allergy to biting midges in humans and other species.

An allergen-fused dendritic cell-binding peptide enhances in vitro proliferation of equine T-cells and cytokine production.

Allergen-specific immunotherapy (AIT) constitutes the only curative approach for allergy treatment. There is need for improvement of AIT in veterinary medicine, such as in horses suffering from insect bite hypersensitivity, an IgE-mediated dermatitis to Culicoides. Dendritic cell (DC)-targeting represents an efficient method to increase antigen immunogenicity. It is studied primarily for its use in improvement of cancer therapy and vaccines, but may also be useful for improving AIT efficacy. Immunomodulators, like the Toll-like receptor 4 (TLR-4) agonist monophosphoryl lipid-A (MPLA) has been shown to enhance the IL-10 response in horses, while CpG-rich oligonucleotides (CpG-ODN), acting as TLR-9 agonists, have been shown to induce Th1 or regulatory responses in horses with equine asthma. Our aim was to evaluate in vitro effects of antigen-targeting to equine DC with an antigen-fused peptide known to target human and mouse DC and investigate whether addition of MPLA or CpG-ODN would further improve the induced immune response with regard to finding optimal conditions for equine AIT. For this purpose, DC-binding peptides were fused to the model antigen ovalbumin (OVA) and to the recombinant Culicoides allergen Cul o3. Effects of DC-binding peptides on cellular antigen uptake and induction of T cell proliferation were assessed. Polarity of the immune response was analysed by quantifying IFN-γ, IL-4, IL-10, IL-17 and IFN-α in supernatants of antigen-stimulated peripheral blood mononuclear cells (PBMC) in presence or absence of adjuvants. Fusion of DC-binding peptides to OVA significantly enhanced antigen-uptake by equine DC. DC primed with DC-binding peptides coupled to OVA or Cul o3 induced a significantly higher T-cell proliferation compared to the corresponding control antigens. PBMC stimulation with DC-binding peptides coupled to Cul o3 elicited a significant increase in the pro-inflammatory cytokines IFN-γ, IL-4, IL-17, as well as the anti-inflammatory IL-10, but not of IFN-α. Adjuvant addition further enhanced the effect of the DC-binding peptides by significantly increasing the production of IFN-γ, IL-4, IL-10 and IFN-α (CpG-ODN) and IL-10 (MPLA), while simultaneously suppressing IFN-γ, IL-4 and IL-17 production (MPLA). Targeting equine DC with allergens fused to DC-binding peptides enhances antigen-uptake and T-cell activation and may be useful in increasing the equine immune response against recombinant antigens. Combination of DC-binding peptide protein fusions with adjuvants is necessary to appropriately skew the resulting immune response, depending on intended use. Combination with MPLA is a promising option for improvement of AIT efficacy in horses, while combination with CpG-ODN increases the effector immune response to recombinant antigens.

Davos, May 2023

Immune Metabolism

PD Dr. Milena Sokolowska, MD, PhD

As a result of changes in the environment and people's lifestyles, allergies and respiratory viral and bacterial infections are becoming more and more frequent. The past years of COVID-19 pandemics and the forthcoming years of enduring post-pandemic consequences have constituted and will continue to exemplify the most remarkable illustration of this trend. It is still not well understood why the same substances are leading to the development of allergic inflammation in some people, while being well tolerated by others. Similarly, it is unclear why some people are more susceptible to viral infections or for the development of more severe forms of respiratory diseases, leading sometimes to the respiratory failure and death. Several reasons are postulated, such as lack of proper microbiome stimulation early in life, recurrent viral infections and exposure to environmental pollutants. In addition, central metabolic disorders such as obesity or even an unbalanced diet itself also influence the proper function of immune responses. We have been working intensively in recent years to understand the susceptibility to viral infections in patients with asthma and allergies and the role of allergens in these phenomena. We discovered that many the above-mentioned factors are able to impact the proper cross-talk between several elements of innate and the adaptive immunity, as well as they alter cellular responses on the metabolic level. Immune cell needs to engage in a wide array of energetically demanding intracellular processes in order to respond to external stimuli, such as allergen, virus or bacteria. These processes encompass changing the expression of a large number of genes, translating proteins, synthesis of lipids, activation of intracellular signaling cascades, altering cytoskeleton, and as a result production of cytokines, lipid mediators and proliferation or migration. To be competent to perform all those duties, the cell needs active metabolic processes, shifting nutrients into different pathways - a process called metabolic reprogramming. Our group applies high throughput transcriptomic, proteomic, metabolomic methods coupled with gene editing, multi-color flow cytometry, confocal microscopy and live cell metabolic assays to understand immune and metabolic reprogramming. Our aim is to understand immune and metabolic crosstalk, provide new biomarkers, and prevention and treatment targets in (1) respiratory viral diseases and microbial dysbiosis; (2) allergy and immune tolerance (3) severe asthma and other phenotypes of asthma.

1. Understanding SARS-CoV-2 and other viral infections in allergy and in chronic respiratory diseases:
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 (Fig. 1). 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.

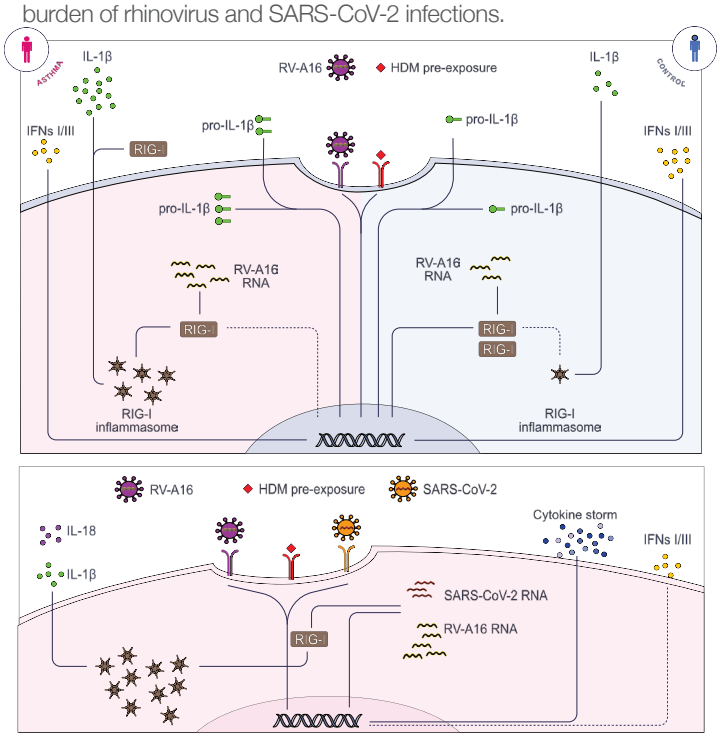


Figure 1. The role of epithelial RIG-I signaling in viral-induced asthma exacerbations and in COVID-19. (Upper panel) Rhinovirus infection in humans is sensed in bronchial airway epithelium via retinoic acid-inducible gene I (RIG-I) helicase. This leads to the recruitment of apoptosis-associated speck like protein containing a caspase recruitment domain (ASC), oligomerization and RIG-I inflammasome activation. Virus-induced RIG-I inflammasome activation- and IL-1-mediated immune responses are highly augmented in patients with asthma, which is responsible for the functional impairment of the RIG-I-dependent antiviral response, prolonged viral clearance, and unresolved inflammation in asthma. Pre-exposure to house dust mite (HDM) amplifies rhinovirus-induced epithelial injury in patients with asthma. (Lower panel) Pre-existing rhinovirus infection followed by SARS-CoV-2 infection augments RIG-I inflammasome activation and epithelial inflammation in patients with asthma, especially in the presence of HDM.

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. 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. This comparative study was performed in 515 patients in the Maria Skłodowska-Curie Specialty Voivodeship Hospital in Zgierz, Poland. The study groups comprised 314 patients with COVID-like symptoms who tested negative and 201 patients who tested positive for SARS-CoV-2 infection; of the latter, 72 patients with COVID-19 died and 129 were released from hospital. Data on which we trained several machine learning (ML) models included clinical findings on admission and during hospitalization, symptoms, epidemiological risk, and reported comorbidities and medications. 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.

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 (Fig. 2).

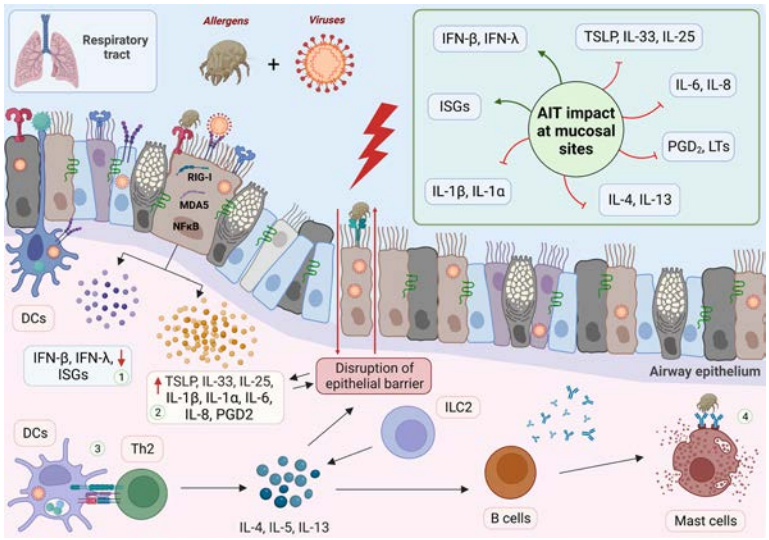


Figure 2. Interactions between allergens and viruses in the airways represent potential targets of allergen immunotherapy (AIT). Allergen exposure can lead to decreases of type I and III IFNs and ISGs (1), which, in combination with enhanced viral infection, can aggravate damage of airway epithelium and subsequently trigger the release of alarmins and other proinflammatory and proremodeling mediators (2). This interaction can also affect the processing of allergens by DCs and macrophages, as well as the subsequent immune response (3). In addition, it can influence allergen-induced IgE-dependent mast cell degranulation (4). Figure created using BioRender.com.

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.

Effects of non-steroidal anti-inflammatory drugs and other eicosanoid pathway modifiers on antiviral and allergic responses: EAACI task force on eicosanoids consensus report in times of COVID-19.

Sokolowska M, Rovati GE, Diamant Z, Untersmayr E, Schwarze J, Lukasik Z, Sava F, Angelina A, Palomares O, Akdis C, O'Mahony L, Jesenak M, Pfaar O, Torres MJ, Sanak M, Dahlén SE, Woszczek G. Allergy. 2022 Aug;77(8):2337-2354. doi: 10.1111/all.15258. Epub 2022 Feb 25.

Here, we summarize currently available knowledge, novel discoveries, and controversies regarding the use of non-steroidal anti-inflammatory drugs (NSAIDs) and other eicosanoid pathway modifiers in COVID-19, and the role of NSAIDs in asthma and viral asthma exacerbations. We also describe novel mechanisms of action of leukotriene receptor antagonists (LTRAs), outline how to predict responses to LTRA therapy and discuss a potential role of LTRA therapy in COVID-19 treatment. Moreover, we discuss interactions of novel T2 biologicals and other eicosanoid pathway modifiers on the horizon, such as prostaglandin D2 antagonists and cannabinoids, with eicosanoid pathways, in context of viral infections and exacerbations of asthma and allergic diseases.

2. Understanding immunometabolism in immune tolerance, allergy and asthma:

Metabolomics of circulating human memory CD4+T effector and T regulatory cells reveals that phenylalanine is a metabolic checkpoint of pathogenic Th2 cells development.

Rodriguez-Coira J, Kulkarni A, Stocker N, Garcia-Civico A, Radzikowska U, Jardon-Parages I, 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*. * Last co-authors. Under revision.

Metabolism has a profound impact on T cell fate and function. Uncovering the metabolome of circulating human CD4+ T effector memory (Teff) and T regulatory (Treg) cells would enable better understanding of Th2-driven diseases, such as allergy or asthma. Here, we demonstrated that in healthy humans, energy metabolism and functions of memory CD4+ Teff cells mainly relied on amino acids, whereas Treg cells predominantly used fatty acids. Arginine and phenylalanine increased T cell receptor-induced glycolysis and oxidative phosphorylation in total and memory CD4+ T cells, but high levels of phenylalanine limited CD4+ T cell proliferation via disrupting mitochondrial respiration and activation of L-phenylalanine oxidase, IL4I1.

Accordingly, lowest levels of phenylalanine were linked with the pathogenic Th2a cells, and impaired Treg cells in patients with the most severe forms of allergies. It all suggests that phenylalanine is a metabolic checkpoint of pathogenic Th2 cells development (Figure 3).

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 me-

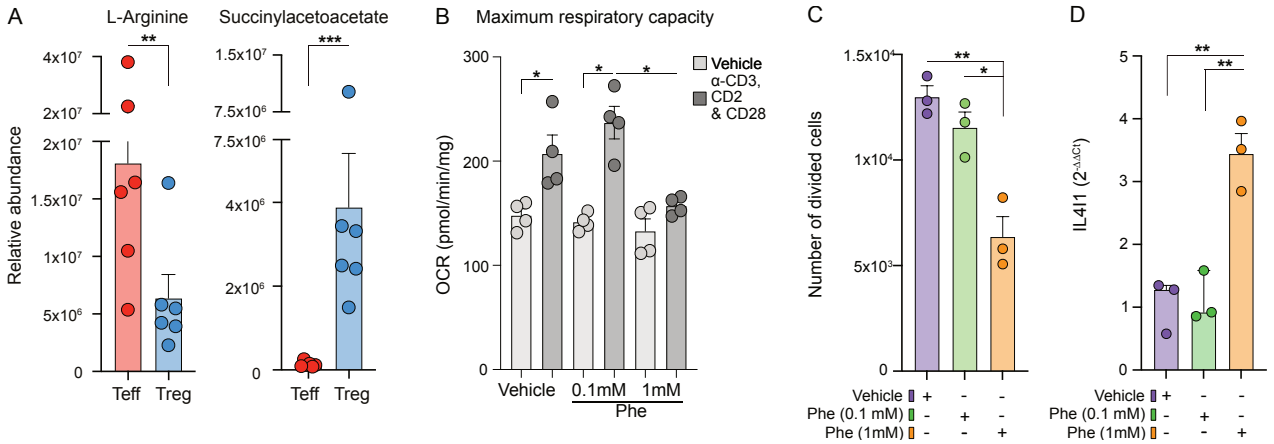


*Figure 3. Metabolomics of circulating human memory CD4+ T cells reveals that phenylalanine is a metabolic checkpoint of pathogenic Th2 cells development. A) Bar plots of relative abundance of L-arginine and Succinylacetoacetate that present a significant increase in T effector (Teff) and T regulatory (Treg) cells, respectively (n=6 per group). Student t-test corrected by FDR was used to compare abundance between groups. B) High levels (1mM) of Phenylalanine (Phe) impaired TCR-induced oxidative phosphorylation (OXPHOS) activation in memory CD4+ T cells. Representative plot of 3 independent Seahorse experiments with 4 replicates in each condition. C) High intracellular levels of Phe decreased T cell proliferation in freshly isolated CD4+ T cells in the presence or absence of anti-CD3, CD2, and CD28 stimulation for 72h assessed by flow cytometry by promoting D) the gene expression of IL4I1 in CD4+ memory T cells after Phe supplementation (n=3). Data was analyzed by one-way ANOVA with Tukey multiple testing correction. All column graphs present the mean +/- SEM. * p<0.05, ** p<0.01, *** p<0.001.*

mory 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.

Immunometabolic reprogramming of bronchial epithelium in asthma and during viral infection.

Radzikowska U*, Jardón Parages I *et al. * equally contributed. In preparation.

Human rhinovirus (RV-A16) plays a major role in exacerbation of asthma in children and in adults. However, limited studies focused on immunometabolic changes in airway epithelium in response to RV-A16. We aim to determine if there are any abnormalities in mitochondrial respiration, oxidative phosphorylation (OXPHOS), beta-oxidation and glycolysis in airway epithelium of patients with asthma at baseline and in response to RV-A16 infection. We use in vitro cultures of human primary bronchial epithelial cells grown in air-liquid interphase (ALI), RNA-seq, qPCR, targeted-proteomics, immunoassays and Seahorse real time cell metabolic analysis, as well as we analyze bronchial samples from patients with asthma and healthy controls at the steady state and after experimental in vivo infection with RV-A16. We determined that bronchial epithelium of patients with asthma, both in vitro and in vivo, has a defect in generation of energy from OXPHOS, both at baseline and post-HRV16 infection, which is substituted by enhanced utilisation of glycolysis. This phenomenon is functionally connected to the abnormal phenotype and function of mitochondria, enhanced early RIG-I inflammasome activation, and is followed by inefficient antiviral response and resolution of airway inflammation. Our data suggest that metabolic rewiring of the epithelium could be a potential target in prevention and treatment of viral exacerbations of asthma.

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

Mitamura Y*, Duphey S* et al. * 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.

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

Leukocyte redistribution as immunological biomarker of corticosteroid resistance in severe asthma.

Cardoso-Vigueros C, von Blumenthal T, Rückert B, Rinaldi AO, Tan G, Dreher A, Radzikowska U, Menz G, Schmid-Grendelmeier P, Akdis CA, Sokolowska M. Clin Exp Allergy. 2022 Mar 19. doi: 10.1111/cea.14128

Earlier studies have suggested that the leukocyte redistribution can be considered as an immunological marker of the clinical response to corticosteroids (CS), representing an easy measurable potential biomarker in severe asthma. The aim of this study was to determinate the utility of the leukocyte redistribution as a biomarker of disease heterogeneity in patients with severe asthma and as a bioindicator of potential CS resistance. We developed an unbiased clustering approach based on the clinical data and the flow cytometry results of peripheral blood leukocyte phenotypes of 142 patients with severe asthma before and after systemic CS administration. Based on the differences in the blood count eosinophils, neutrophils and lymphocytes, together with the flow cytometry measurements of basic T cell, B cell and NK cell subpopulations before and after systemic CS administration, we identified two severe asthma clusters, which differed in the cell frequencies, response to CS and atopy status. Patients in cluster 1 had higher frequency of blood eosinophils at baseline, were sensitized to less allergens and had better steroid responsiveness, measured as the pronounced leukocyte redistribution after the administration of systemic CS. Patients in cluster 2 were determined by the higher frequency of B-cells and stronger IgE sensitization status to the multiple allergens. They also displayed higher steroid resistance, as the clinical correlate for the lower leukocyte redistribution after administration of systemic CS. The flow cytometry-based profiling of the basic populations of immune cells in the blood and its analysis before and after systemic corticosteroid administration could improve personalized treatment approaches in patients with severe asthma.

Novel candidate biomarkers of the efficacy of allergen immunotherapy.

Van Elst D*, Agache I*, Ram I, Jardón Parages I et al. * 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. Interestingly, 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.

Role of dietary fiber in promoting immune health-An EAACI position paper.

Venter C, Meyer RW, Greenhawt M, Pali-Schöll I, Nwaru B, Roduit C, Untersmayr E, Adel-Patient K, Agache I, Agostoni C, Akdis CA, Feeney M, Hoffmann-Sommergruber K, Lunjani N, Grimshaw K, Reese I, Smith PK, Sokolowska M, Vassilopoulou E, Vlieg-Boerstra B, Amara S, Walter J, O'Mahony L. Allergy. 2022 Nov;77(11):3185-3198. doi: 10.1111/all.15430.

In this review, we highlight the importance of fiber as a dietary ingredient, its effects on the microbiome, its effects on immune regulation, the importance of appropriate timing of intervention to target any potential window of opportunity, and potential mechanisms for dietary fibers in the prevention and management of allergic diseases. In addition, we review the human studies examining fiber or prebiotic interventions on asthma and respiratory outcomes, allergic rhinitis, atopic dermatitis, and overall risk of atopic disorders.

Davos, May 2023

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. Characterization of allergen-specific B cell and antibody responses in allergy and allergen tolerance:

B cells can bind to conformational epitopes through their B cell receptor. Therefore, allergen-specific B cells can be detected by labeling them with fluorescently-conjugated native allergens. Biotinylated allergens and fluorescently labeled streptavidin can be coupled to generate fluorescent allergen-multimers that can be used to identify B cells specific for a certain allergen. In addition to allergen-streptavidin-PE multimers, we also use allergen-streptavidin-AF635 multimers (Figure 1). By only gating the double positive B cells, we ameliorate the potential problem of detecting B cells that specifically bind to PE, which has been described in the literature and was also observed by us. To characterize B cells with different allergen-specificity simultaneously, we couple the allergen-streptavidin-PE multimers with a unique oligonucleotide 'barcode' sequence that can be read using single-cell sequencing. PE and AF647 double-positive B cells can then be sorted using flow cytometry and subjected to single-cell transcriptomics. This enables the detection and purification of a mixture of B cells that are specific for different allergens and the analysis of gene expression profiles of B cells with different specificities. This method can provide us with two key datasets I) overview of the V(D)J heavy and light chain sequences encoding for allergen-specific BCRs, which can be used to identify allergen-specific V(D)J sequences, produce and characterize the antibodies they encode, II) The transcriptomes of individual allergen-specific B 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 how tolerance to allergens develops is crucial for targeted therapies in allergic disease. Beekeepers provide a unique model for studying this, as they are exposed to high levels of bee venom allergens. This study aimed to track the development of allergen-specific B cells in 12 beekeepers over 20 years. Blood samples were taken before and during beekeeping season, and PLA-specific B cells were identified, purified, and subjected to BCR repertoire analysis using deep sequencing of the B cell repertoire.

The frequency of PLA-specific B cells was higher during beekeeping season compared to before. PLA-specific clones were more prominent in IgE and IgG4 isotypes than others. Additionally, the clones had higher V-gene mutations at the end of the season. Some individuals had PLA-specific clones that were present at different time points, spanning over 20 years. Clonal lineages had various immunoglobulin heavy chain isotypes, including IgE, IgG1, IgG2, IgG3, and IgG4. In clonal lineages that had an IgE member, the most frequently seen clones with high sequence similarity to the IgE member were IgG2 or IgG4 clones, indicating a possible sequential class switch recombination. Public antibody clonotypes against PLA were discovered in different beekeepers, showing clusters of PLA-specific clones with >90% CDR3 AA similarity and identical V and J gene usage.

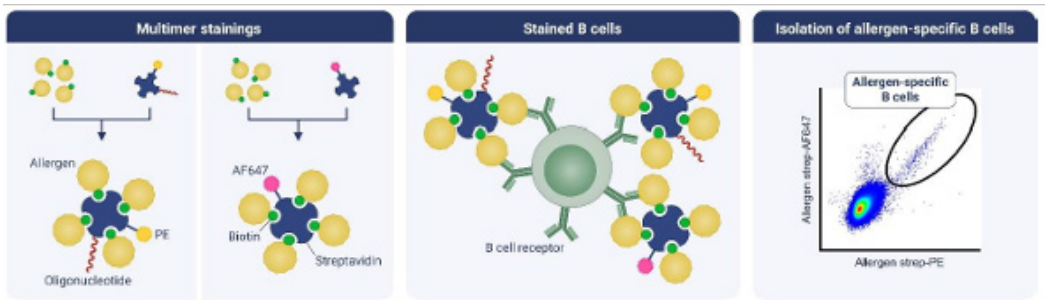


Figure 1. Schematic overview of the isolation of allergen-specific B cells using allergen-streptavidin multimers. The multimer stainings were prepared by mixing biotinylated food allergens with streptavidin PE conjugates and streptavidin Alexa Fluor 647 conjugates in a 4:1 molar ratio resulting in two different multimers: PE-multimers and AF647-multimers. The multimer stainings were used to stain B cells, as B cells specific for the allergen will bind the PE- and AF647-multimers. With flow cytometry, allergen-specific B cells were isolated as double positive PE+ AF647+ cells. The oligonucleotide conjugated to the streptavidin PE conjugate allows identification of allergen-specific B cells during single-cell omics.

Our research indicates that non-allergic individuals who are highly exposed to allergens have allergen-specific clonal lineages that persist for many years, and these lineages exhibit clonal expansion and a significant level of diversity. Furthermore, in response to seasonal allergen exposure, allergen-specific clones expand and accumulate V-gene mutations. PLA-specific IgE clones may be created via an IgG2 or 4 intermediate, and public PLA-specific antibody clonotypes exist. We have yet to determine which aspects of the B cell repertoire demonstrate allergen tolerance. A comparative examination of the allergen-specific B cell repertoire of allergic individuals before and after allergen-specific immunotherapy is currently in progress and may identify key

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 beta-lactams (BLs), especially those triggered by amoxicillin (AX), are increasing over recent years. During the sensitization phase, B cells produce a high amount of specific immunoglobulin E (sIgE), which couples to the high-affinity receptors of basophils and mast cells. After the re-exposure to the drug, these cells degranulate, releasing proinflammatory mediators and cytokines. Little is known about how different immunoglobulins, B cell subsets, and B regulatory (Bregs) cells change over time after the reaction. In this study, we aimed to analyze both humoral and cellular B cell responses in patients with IDHRs to AX at different time points after the acute reaction.

Blood and serum samples were obtained from 20 selective allergic patients to AX and from 10 healthy controls. Samples from AX-allergic patients were obtained at different time points from the acute reaction (<6, 6-12, 12-24, >24 months). Serum AX-sIgE was measured by radioallergosorbent test (RAST) and ImmunoCAP; serum AX-sIgG and -sIgG4 by immunoCAP; and other different AX-sIgG subclasses by ELISA. Peripheral blood mononuclear cells (PBMCs) were isolated and the frequencies of B cells expressing BCRs of different immunoglobulin heavy chain isotypes as well as Breg cells were analyzed by flow cytometry.

Higher serum-sIgE levels were observed in samples from allergic patients <6 months after the reaction, which showed a significant decrease after 6 months. In contrast, AX-sIgG was reduced during the first 12 months compared to after 12 months from the reaction. This increase was also observed in AX-IgG2, while AX-IgG3 showed a tendency to decrease over time. The frequencies of IgA1+ and IgA2+ B cells were increased between 6 and 24 months from the reaction. Interestingly, the frequency of IgG2+ B cells increased between 12 and 24 months, while IgG4+ B cells increased significantly between 6 and 12 months, decreasing again after 12 months. The frequencies of plasmablasts, B10, and Br1 cells producing IL-10 and/or IL1Ra were significantly reduced in samples of <6 months after the reaction, although slowly increased over time since the reaction (Figure 2).

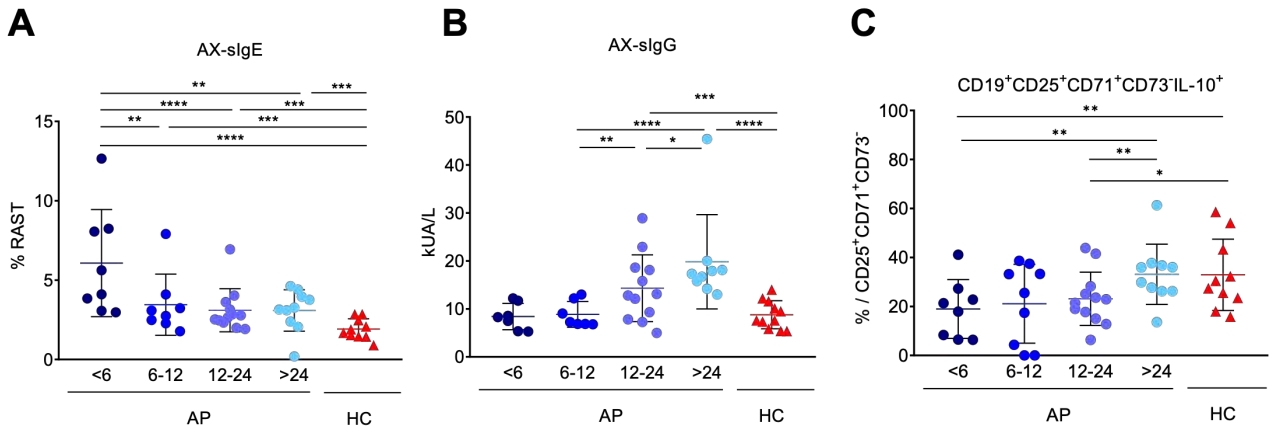


Figure 2. Amoxicillin-specific IgE (A) and IgG (B) antibodies and CD19+CD25+CD71+CD73-IL-10+ Breg cells (C) at different timepoints (<6, 6-12, 12-24 and >24 months) after allergic reaction to amoxicillin. AP: Amoxicillin allergic patients, HC: Healthy control

Serum AX-sIgE was closely related to the acute phase of the IDHR, whereas AX-sIgG, and concretely IgG2 and IgG4 seem to have a protective role, as it has been shown at humoral and cellular levels. The reduced frequency of IL10+ and IL1Ra+ plasmablasts, B10, and Br1 cells in the first months after the reaction seems to be relevant during the first steps of IDHRs to AX.

Mechanisms and biomarkers of successful allergen-specific immunotherapy.

López JF, Bel Imam M, Satitsuksanoa P, Lems S, Yang M, Hwang YK, Losol P, Choi JP, Kim SH, Chang YS, Akdis M, Akdis CA, van de Veen W. Asia Pac Allergy. 2022 Oct 31;12(4):e45.

Allergen-specific immunotherapy (AIT) is considered the only curative treatment for allergic diseases mediated by immunoglobulin E (IgE). Currently, the route of administration depends both on the different types of causal allergens and on their effectiveness and safety profile. Several studies have reported the mechanisms and changes in humoral and cellular response underlying AIT; however, the full picture remains unknown. Knowledge of who can benefit from this type of treatment is urgently needed due to the patient safety risks and costs of AIT. In vivo or in vitro biomarkers have become a strategy to predict clinical outcomes in precision medicine. There are currently no standardized biomarkers that allow determining successful responses to AIT, however, some studies have found differences between responders and non-responders. In addition, different candidates have been postulated that may have the potential to become biomarkers. In this review, we summarized the findings to date related to biomarkers in different IgE-mediated allergic diseases (respiratory, food, and venom allergy) with the potential to define who will benefit from AIT.

2. Immunopathogenesis of 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. Clinical and Experimental Allergy – in press

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.

Identification of immunological markers for monitoring disease activity in eosinophilic esophagitis

Manal Bel imam, Sayuri Iwasaki, Eleni Meuffels, Sophieke Lems Pattraporn Satitsuksanoa, Stephan R. Schneider, Mübeccel Akdis, Luc Biedermann, Alex Straumann, Willem van de Veen. In preparation.

Eosinophilic esophagitis (EoE) is a chronic inflammatory condition, which has shown an increased prevalence over the last two to three decades. Despite numerous studies, the mechanisms underlying EoE are not yet fully elucidated. However, some studies suggest the involvement of Th2 cytokines and antibody production in its pathogenesis. While food intake may trigger EoE, several observations indicate that it is not an IgE-mediated food allergy. Rather, research has shown that EoE patients exhibit elevated levels of IgG4 in their esophageal biopsies and circulating food antigen-specific IgG4. It is not known whether IgG4 plays a role in the pathogenesis of EoE or is rather a bystander effect of chronic antigen exposure in the inflamed esophagus.

The objective of this study is to uncover the fundamental mechanisms of EoE regarding antigen-specific B cell responses and to identify non-invasive biomarkers to aid in the diagnosis and monitoring of EoE. Blood samples were obtained from EoE patients who visited the Swiss EoE Clinics at the University Hospital Zurich. A total of 120 samples were collected from patients with varying levels of disease activity, including inactive, moderate-active, and highly-active disease (determined by endoscopic and histological assessments). These samples were analyzed to detect food antigen-specific antibodies of all isotypes. We focused on cow's milk antigens as cow's milk is one of the strongest food-associated triggers of EoE. IgG1, IgG2, IgG3, IgG4, IgA1, and IgA2 antibodies specific for different cow's milk allergens were quantified using ELISA. Cow's milk allergen-specific antibodies were significantly increased in EoE patients compared to healthy controls, while no significant differences were found between active and inactive EoE patients. Interestingly, a striking difference in the antibody response to casein- and whey-derived allergens was observed. IgG antibodies specific for casein-derived proteins (αS1 casein and β-casein) of all subclasses (IgG1-4) were increased in EoE patients, whereas, the response to whey fraction derived proteins (α lactalbumin and β-lactoglobulin), consistently lacked IgG3.

We also completed a biomarker screening in active and inactive EoE patients using proximity extension assays, identifying several candidate biomarkers that were associated with disease activity. These will be validated using independent methods and assessed for their potential applicability in the clinics. In addition, we optimized a method for the simultaneous isolation of proteins, RNA, and DNA from esophageal biopsies of EoE patients. Proteomics analyses are underway to characterize the tissue expression of EoE-associated proteins.

3. B cell responses and viral 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. Manuscript submitted.
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.

Exposure to avian coronavirus vaccines is associated with increased levels of SARS-CoV-2-cross-reactive antibodies
Ozge Ardicli, Tayfun Carli, Pattraporn Satitsuksanoa, Anita Dreher, Alexia Cusini, Sandra Hutter, David Mirer, Beate Rückert, Hulda R. Jonsdottir, Benjamin Weber, Carlo Cervia, Mubeccel Akdis, Onur Boyman, Alexander Eggel, Marie-Charlotte Brüggen, Cezmi Akdis, Willem van de Veen. Allergy. 2022 Dec;77(12):3648-3662.
Although avian coronavirus infectious bronchitis virus (IBV) and SARS-CoV-2 belong to distinct genera within the Coronaviridae family, exposure to IBV may lead to the production of cross-reactive antibodies to SARS-CoV-2 as a result of homologous epitopes. The objective of this study was to examine whether the antibody responses to IBV can cross-react with SARS-CoV-2 in poultry farm personnel, who are occupationally exposed to aerosolized IBV vaccines.
We employed in-house ELISAs to investigate IgG levels against the SARS-CoV-2 antigens S1, RBD, S2, and N, as well as peptides corresponding to the SARS-CoV-2 ORF3a, N, and S proteins, and whole virus antigens of the four main S1-genotypes 4/91, IS/1494/06, M41, and D274 of IBV. We also analyzed antibodies specific for distinct SARS-CoV-2 peptides as well as peptides derived from unrelated pathogens. Additionally, we conducted a live virus neutralization test (VNT).
A subset of poultry farm workers had higher levels of specific IgG antibodies for all tested SARS-CoV-2 antigens than pre-pandemic controls. Poultry farm workers, COVID-19 patients, and pre-pandemic controls all had IgG antibodies against IBV strains, with higher titers in long-term vaccine users. We found a strong correlation between IBV-specific IgG and SARS-CoV-2 S1, RBD, S2, and N-specific IgG in poultry farm workers compared to pre-pandemic controls and COVID-19 patients. However, no neutralization was observed for these cross-reactive antibodies in poultry farm workers using the VNT.
Interestingly, we found that hospitalized patients showed high levels of SARS-CoV-2-specific IgG but low IBV-specific IgG. It cannot be excluded that some of the comorbidities in hospitalized COVID-19 patients influence the levels and cross-reactivity of antibodies against SARS-CoV-2. IgG against IBV could not be measured in the same COVID-19 patients before infection because samples of this time point were not available. Therefore, it remains unclear whether SARS-CoV-2 infection resulted in a reduction of IBV-reactive IgG levels in COVID-19 patients or whether these levels were already reduced before infection. Similarly, we observed reduced IgG levels against rhinovirus A and human herpesvirus 4 in COVID-19 patients (Figure 3). This reduction was most pronounced in hospitalized COVID-19 patients.
Recent findings indicate that SARS-CoV-2 can directly infect T cells in an ACE2-independent manner that is consistent with the previously reported mechanism of SARS-CoV-2-induced lymphopenia. Hence, reduced IgG levels against IBV, rhinovirus A, and human herpesvirus 4 observed in hospitalized COVID-19 patients may be caused by a mechanism similar to measles-induced immune amnesia affecting systemic immune memory.
We report here for the first time the detection of cross-reactive IgG antibodies against SARS-CoV-2 antigens in humans exposed to IBV vaccines. These findings have implications for future vaccination strategies and possibly cross-reactive T-cell immunity.

4. Using biologics to study human in vivo immune responses with a focus on B cells:
In-depth analysis of the immunological changes in response to dupilumab and conventional treatments in children with atopic dermatitis.
T. Nguyen, M. Starrenburg, L. Bürgi, R. Schappin, P. Caspers, S. Pasmans, W. van de Veen. In preparation:
Atopic dermatitis (AD) is an inflammatory skin disease that results in erythema, severe itch, and sleep deprivation, especially in children. In industrialized countries, up to 20% of children are affected, and this number is increasing. AD is driven by immune dysregulation, with a preference for type 2 immunity. Topical corticosteroids or systemic treatment with cyclosporine A (CsA) or dupilumab, a biological targeting the IL-4a receptor, are used to treat AD. However, the variable treatment response of AD patients necessitates personalized medicine with confirmed biomarkers. Known biomarkers associated with AD severity include TARC, PARC, periostin, and

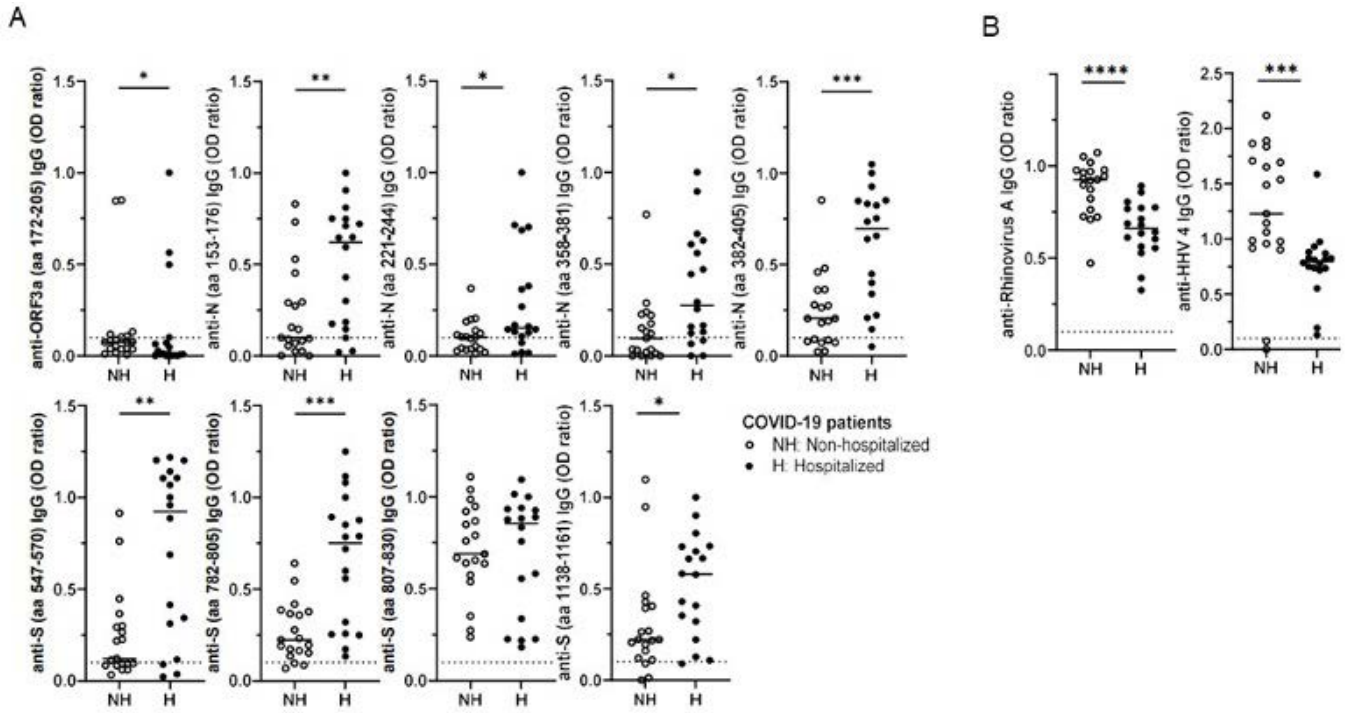


*Figure 3. Hospitalized COVID-19 patients show elevated levels of IgG specific for SARS-CoV-2 peptides and reduced levels of specific IgG for Rhinovirus and Herpes virus peptides compared to non-hospitalized patients. (A) anti-ORF3a (aa 172-205) IgG, anti-N (aa 239 153-176) IgG, anti-N (aa 221-244) IgG, anti-N (aa 358-381) IgG, anti-N (aa 382-405) IgG, anti-S (aa 547-570) IgG, anti-S (aa 782-805) IgG, anti-S (aa 807-830) IgG, anti-S 241 (aa 1138-1161) IgG, (B) anti-Rhinovirus A (aa 567-591) IgG, anti-HHV 4 (aa 398-422) IgG, IgG OD levels in sera from non-hospitalized COVID-19 patients (n=19, black circles open) and hospitalized COVID-19 patients (n=18, black 244 circles closed). Dashed lines indicate the threshold level at 0.1. Statistical analyses 245 were performed using the Mann-Whitney U test. *P< 0.05, **P< 0.01, ***P< 0.001, 246 ****P< 0.0001. Horizontal lines represent median values.*

soluble IL-2R. A reduction in TARC levels is associated with clinical improvement during dupilumab treatment. We aim to identify biomarkers in pediatric AD patients that will facilitate the distinction of patient subsets correlating with therapy response and reveal novel insights into therapeutic mechanisms of action and disease pathophysiology. To achieve this, children with moderate to severe AD are randomized into three groups: dupilumab, CsA, and a control group. The immune response of participants will be analyzed longitudinally in blood samples taken at baseline and 6 months for all groups, plus samples collected at 1 and 3 months for the dupilumab and CsA groups. Cryopreserved PBMCs from blood samples will be immunophenotyped using mass cytometry. To this end, we developed a comprehensive immunophenotyping panel for use in CyTOF that allows in-depth analysis of all major immune cell types and includes a set of B-cell-specific markers to allow even more detailed analysis of the B cell compartment. Moreover, soluble biomarkers in plasma samples will be analyzed using a proximity extension assay.

Changes in immunophenotype during treatment will be compared between treatment arms and correlated to known biomarkers such as TARC and PARC, as well as to possible new biomarkers. New biomarkers associated with each type of treatment and the immunological effects of these treatments may be useful for physicians in choosing an effective treatment and monitoring immunological changes during treatment, thereby reducing over- and under-treatment of pediatric AD patients.

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. n preparation.

Immune checkpoint inhibitor (ICI) therapies have been approved for treating malignant melanoma; however, not all patients respond to these treatments, highlighting the need for identifying novel biomarkers to predict patient response and eligibility for ICI treatment. The characterization of B cell phenotypes through surface markers can enhance understanding of B cell immunity in melanoma and ICI's effect on B cells. Thus, we analyzed circulating B cells in healthy controls and a cohort of 25 metastatic melanoma patients before and after receiving anti-PD1 and/or anti-CTLA4 mAbs at early and late response visits. Non-responding patients (n=12) showed significant changes in naïve B cell, switched B cell, and IgA+ B cell frequencies during therapy. We observed higher BAFF receptor expression on all B cell subsets in responders compared to non-responders at baseline and early response. Additionally, non-responders had significantly higher serum BAFF levels than responders at baseline. Therefore, our findings suggest that ICI treatment alters B cell characteristics through BAFF receptor expression, and soluble protein BAFF could be a predictive biomarker for metastatic melanoma patient response to ICI therapy

Davos, May 2023

Articles in peer reviewed journals 2022

PUBLICATIONS

Akkoc T, O'Mahony L, Ferstl R, Akdis C, Akkoc T. Mouse Models of Asthma: Characteristics, Limitations and Future Perspectives on Clinical Translation. Adv Exp Med Biol. 2022;1376:119-133. doi: 10.1007/5584_2021_654. IPF: 2.622

Yazici D, Ogulur I, Kucukkase O, Li M, Rinaldi AO, Pat Y, Wallimann A, Wawrocki S, Celebi Sozener Z, Buyuktiryaki B, Sackecen C, Akdis M, Mitamura Y, Akdis CA. Epithelial barrier hypothesis and the development of allergic and autoimmune diseases. Allergo J Int. 2022 May;31, 91–102. DOI: https://doi.org/10.1007/s40629-022-00211-y. IPF: 1.946

Yazici, D., Ogulur, I., Kucukkase, O. et al. Epithelial barrier hypothesis and the development of allergic and autoimmune diseases. Allergo J 31, 18–31 (2022). https://doi.org/10.1007/s15007-022-5033-8. IPF: 1.946

Satitsuksanoa P, Angelina A, Palomares O, Akdis M. Mechanisms in AIT: Insights 2021. Allergol Select. 2022 Nov 21;6:259-266. doi: 10.5414/ALX02300E. IPF: 4.2

Agache I, Akdis CA, Akdis M, Brockow K, Chivato T, Del Giacco S, Eiwegger T, Eyerich K, Giménez-Arnau A, Gutermuth J, Guttman-Yassky E, Maurer M, Ogg G, Ong PY, O'Mahony L, Schwarze J, Warner A, Werfel T, Palomares O, Jutel M. EAACI Biologicals Guidelines-Omalizumab for the treatment of chronic spontaneous urticaria in adults and in the paediatric population 12-17 years old. Allergy. 2022 Jan;77(1):17-38. doi: 10.1111/all.15030. IPF: 14.71

Agache I, Sampath V, Aguilera J, Akdis CA, Akdis M, Barry M, Bouagnon A, Chinthrajah S, Collins W, Dulitzki C, Erny B, Gomez J, Goshua A, Jutel M, Kizer KW, Kline O, LaBeaud AD, Pali-Schöll I, Perrett KP, Peters RL, Plaza MP, Prunicki M, Sack T, Salas RN, Sindher SB, Sokolow SH, Thiel C, Veidis E, Wray BD, Traidl-Hoffmann C, Witt C, Nadeau KC. Climate change and global health: A call to more research and more action. Allergy. 2022 May;77(5):1389-1407. doi: 10.1111/all.15229. Review. IPF: 14.71

Angelina A, Pérez-Diego M, Maldonado A, Rückert B, Akdis M, Martín-Fontecha M, Akdis CA, Palomares O. The cannabinoid WIN55212-2 suppresses effector T-cell responses and promotes regulatory T cells in human tonsils. Allergy. 2022 Mar;77(3):1029-1032. doi: 10.1111/all.15160. IPF 14.71

Ardicli O, Carli KT, Satitsuksanoa P, Dreher A, Cusini A, Hutter S, Mirer D, Rückert B, Jonsdottir HR, Weber B, Cervia C, Akdis M, Boyman O, Eggel A, Brüggen MC, Akdis CA, van de Veen W. Exposure to avian coronavirus vaccines is associated with increased levels of SARS-CoV-2-cross-reactive antibodies. Allergy. 2022 Dec;77(12):3648-3662. doi: 10.1111/all.15441. IPF: 14.71

Cabanillas B, Valdelvira R, Akdis CA., Monkeypox outbreak in Europe, UK, North America, and Australia: A changing trend of a zoonotic disease. Allergy. 2022 Aug;77(8):2284-2286. doi: 10.1111/all.15393. IPF: 14.71

Cabanillas B, Novak N, Akdis CA. The form of PEG matters: PEG conjugated with lipids and not PEG alone could be the specific form involved in allergic reactions to COVID-19 vaccines. Allergy. 2022 Jun;77(6):1658-1660. doi: 10.1111/all.15187. IPF: 14.71

Celebi Sozener Z, Ozdel Ozturk B, Cerci P, Turk M, Gorgulu Akin B, Akdis M, Altiner S, Ozbey U, Ogulur I, Mitamura Y, Yilmaz I, Nadeau K, Ozdemir C, Mungan D, Akdis CA. Epithelial barrier hypothesis: Effect of the external exposome on the microbiome and epithelial barriers in allergic disease. Allergy. 2022 May;77(5):1418-1449. DOI: 10.1111/all.15240. IPF: 14.71

Celebi Sozener Z, Cevhertas L, Satitsuksanoa P, van de Veen W, Jansen K, Secil D, Sin BA, Akdis CA, Akdis M, Mungan D. Innate lymphoid cell subsets in obese asthma patients: Difference in activated cells in peripheral blood and their relationship to disease severity. Allergy. 2022 Sep;77(9):2835-2839. doi:10.1111/all.15378. IPF: 14.71

Celebi Sozener Z, Özbey Yücel Ü, Altiner S, Ozdel Oztürk B, Cerci P, Türk M, Gorgülü Akin B, Akdis M, Yilmaz I, Ozdemir C, Mungan D, Akdis CA. The External Exposome and Allergies: From the Perspective of the Epithelial Barrier Hypothesis. Front Allergy. 2022 Jul 8;3:887672. doi: 10.3389/falgy.2022.887672. IPF: 14.71

Chantveerawong T, Sangkangjanavanich S, Chiewchalermsri C, Pradubpongsa P, Mitthamsiri W, Jindarat S, Wang M, Akdis M, Sokolowska M, Akdis CA, Sangasapaviliya A, Boonpiyathad T. Increased circulating CRTH2+ Tregs are associated with asthma control and exacerbation. Allergy. 2022 Feb;77(2):681-685. doi: 10.1111/all.15145. IPF: 14.71

D'Amato G, Akdis CA., Desert dust and respiratory diseases: Further insights into the epithelial barrier hypothesis. Allergy. 2022 Dec;77(12):3490-3492. doi: 10.1111/all.15392. IPF: 14.71

Delgado-Dolset MI, Obeso D, Rodríguez-Coira J, Tarin C, Tan G, Cumplido JA, Cabrera A, Angulo S, Barbas C, Sokolowska M, Barber D, Carrillo T, Villaseñor A, Escribese MM. Understanding uncontrolled severe allergic asthma by integration of omic and clinical data. Allergy. 2022 Jun;77(6):1772-1785. doi: 10.1111/all.15192. IPF: 14.71

Della Bella E, Koch J and Baerenfaller K. Translation and emerging functions of non-coding RNAs in inflammation and immunity. Allergy 2022 77 (7), 2025-2037, doi: 10.1111/all.15234 IPF: 14.71

Fernandez-Santamaria R, Satitsuksanoa P. Engineered IL-10: A matter of affinity. Allergy. 2022 Mar;77(3):1067-1069. IPF:14.71. doi: 10.1111/all.15132. IPF: 14.71

Fieten KB, Drijver-Messelink MT, Cogo A, Charpin D, Sokolowska M, Agache I, Taborda-Barata LM, Eguiluz-Gracia I, Braunstahl GJ, Seys SF, van den Berge M, Bloch KE, Ulrich S, Cardoso-Vigueros C, Kappen JH, Brinke AT, Koch M, Traidl-Hoffmann C, da Mata P, Prins DJ, Pasmans SGMA, Bendien S, Rukhadze M, Shamji MH,

Couto M, Oude Elberink H, Peroni DG, Piacentini G, Weersink EJM, Bonini M, Rijssenbeek-Nouwens LHM, Akdis CA. Alpine altitude climate treatment for severe and uncontrolled asthma: An EAACI position paper. Allergy. 2022 Jul;77(7):1991-2024. doi: 10.1111/all.15242. IPF: 14.71

Fiorito S, Soligo M, Gao Y, Ogulur I, Akdis CA, Bonini S. Is the epithelial barrier hypothesis the key to understanding the higher incidence and excess mortality during COVID-19 pandemic? The case of Northern Italy. Allergy. 2022 May;77(5):1408-1417. DOI: 10.1111/all.15239. IPF:14.71

Fiorito S, Soligo M, Gao Y, Ogulur I, Akdis CA, Bonini S. Reply to: "COVID-19 pandemic and environment: Not only air pollution.". Allergy. 2022 Dec;77(12):3702-3703. DOI: 10.1111/all.15492. IPF: 14.71

Gao YD, Xepapadaki P, Cui YW, Stanic B, Maurer DJ, Bachert C, Zhang N, Finotto S, Chalubinski M, Lukkarinen H, Passioti M, Graser A, Jartti T, Kowalski M, Ogulur I, Shi ZW, Akdis M, Papadopoulos NG, Akdis CA. Effect of Haemophilus influenzae, Streptococcus pneumoniae and influenza vaccinations on infections, immune response and asthma control in preschool children with asthma. Allergy. 2022 Oct 13. DOI: 10.1111/all.15551. IPF: 14.71

Goshua A, Akdis CA, Nadeau KC. World Health Organization global air quality guideline recommendations: Executive summary. Allergy. 2022 Jul;77(7):1955-1960. doi: 10.1111/all.15224. IPF: 14.71

Hanif T, Ivaska LE, Ahmad F, Tan G, Mikola E, Puhakka T, Palomares O, Akdis CA, Toppila-Salmi S, Jartti T. Tonsillar transcriptional profiles in atopic and non-atopic subjects. Allergy. 2022 Jul 28. doi: 10.1111/all.15458. IPF: 14.71

Jansen K, Satitsuksanoa P, Wirz OF, Schneider SR, van de Veen W, Tan G, Sokolowska M, Message SD, Kebadze T, Glanville N, Mallia P, Akdis CA, Moniuszko M, Johnston SL, Nadeau K, Akdis M. T regulatory cells from atopic asthmatic individuals show a Th2-like phenotype. Allergy. 2022 Apr;77(4):1320-1324. doi: 10.1111/all.15193. IPF: 14.71

Jutel M, Torres MJ, Palomares O, Akdis CA, Eiwegger T, Untersmayr E, Barber D, Zemelka-Wiacek M, Kosowska A, Palmer E, Vieths S, Mahler V, Canonica WG, Nadeau K, Shamji MH, Agache I., COVID-19 vaccination in patients receiving allergen immunotherapy (AIT) or biologicals-EAACI recommendations. Allergy. 2022 Aug;77(8):2313-2336. doi: 10.1111/all.15252. IPF: 14.71

Klimek L, Agache I, Cooke E, Jutel M, Akdis CA, O'Hehir R. COVID-19 vaccines-The way forward. Allergy. 2022 Jan;77(1):15-16. doi: 10.1111/all.14995. IPF: 14.71

Korath ADJ, Janda J, Untersmayr E, Sokolowska M, Feleszko W, Agache I, Adel Seida A, Hartmann K, Jensen-Jarolim E, Pali-Schöll I. One Health: EAACI Position Paper on coronaviruses at the human-animal interface, with a specific focus on comparative and zoonotic aspects of SARS-Cov-2. Allergy. 2022 Jan;77(1):55-71. doi: 10.1111/all.14991. IPF: 14.71

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. IPF: 14.71

Lunjani N, Tan G, Dreher A, Sokolowska M, Groeger D, Warwyzniak M, Altunbulakli C, Westermann P, Basera W, Hobane L, Botha M, Gray C, Mankahla A, Gray C, Nadeau KC, Hlela C, Levin M, O'Mahony L, Akdis CA. Environment-dependent alterations of immune mediators in urban and rural South African children with atopic dermatitis. Allergy. 2022 Feb;77(2):569-581. doi: 10.1111/all.14974. IPF: 14.71

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. IPF: 14.71

Maurer D, Barletta E, Heider A, Stocker N, Wallimann A, Villiger M, Villiger B, Baerenfaller K, Akdis C, Kistler W. Immune-inflammatory proteome of elite ice hockey players before and after SARS-CoV-2 infection. Allergy 2022 77(1=, 3144-3147, doi: 10.1111/all.15405. IPF: 14.71

Maurer DJ, Liu C, Xepapadaki P, Stanic B, Bachert C, Finotto S, Gao YD, Graser A, Jartti T, Kistler W, Kowalski M, Lukkarinen H, Pasioti M, Tan G, Villiger M, Zhang L, Zhang N, Akdis M, Papadopoulos NG, Akdis CA. Physical activity in asthma control and its immune modulatory effect in asthmatic preschoolers. Allergy. 2022 Apr;77(4):1216-1230. doi: 10.1111/all.15105. IPF: 14.71

Mitamura Y, Schulz D, Oro S, Li N, Kolm I, Lang C, Ziadlou R, Tan G, Bodenmiller B, Steiger P, Marzano A, de Prost N, Caudin O, Levesque M, Stoffel C, Schmid-Grendelmeier P, Maverakis E, Akdis CA, Brüggen MC. Cutaneous and systemic hyperinflammation drives maculopapular drug exanthema in severely ill COVID-19 patients. Allergy. 2022 Feb;77(2):595-608. doi: 10.1111/all.14983. IPF: 14.71

Nadeau KC, Agache I, Jutel M, Annesi Maesano I, Akdis M, Sampath V, D'Amato G, Cecchi L, Traidl-Hoffmann C, Akdis CA. Climate change: A call to action for the United Nations. Allergy. 2022

Apr;77(4):1087-1090. doi: 10.1111/all.15079. IPF: 14.71

Orimo K, Tamari M, Takeda T, Kubo T, Rückert B, Motomura K, Sugiyama H, Yamada A, Saito K, Arae K, Kuriyama M, Hara M, Soyka MB, Ikutani M, Yamaguchi S, Morimoto N, Nakabayashi K, Hata K, Matsuda A, Akdis CA, Sudo K, Saito H, Nakae S, Tamaoki J, Tagaya E, Matsumoto K, Morita H. Direct platelet adhesion potentiates group 2 innate lymphoid cell functions. Allergy. 2022 Mar;77(3):843-855. doi: 10.1111/all.15057. IPF: 14.71

Pat, Y., Rückert, B., Ogulur, I., Yazici, D., Pérez-Diego, M., Küçükkase, O. C., Li, M., & Akdis, C. A. (2022). Differentiation of bronchial epithelial spheroids in the presence of IL-13 recapitulates characteristic features of asthmatic airway epithelia. Allergy. 2022 March 10; 77(7), 2229–2233. doi: 10.1111/all.15279. IPF: 14.71

Radzikowska, U. and Golebski, K. Sex hormones and asthma: The role of estrogen in asthma development and severity. Allergy. 2022 Oct 10. doi: 10.1111/all.15548. IPF: 14.71

Radzikowska, U, Baerenfaller, K, Cornejo-Garcia, JA, Karaaslan C, Barletta E, Sarac BE, Zhakparov D, Villasenor A, Eguiluz-Garcia I, Mayorga C, Sokolowska M, Barbas C, Barber D, Ollert M, Chivato T, Agache I, Escibese M. Omics technologies in allergy and asthma research: An EAACI position paper. Allergy. 17 June 2022; 77: 2888- 2908. doi: 10.1111/all.15412. IPF: 14.71

Sasaki M, Schwab C, Ramirez Garcia A, Li Q, Ferstl R, Bersuch E, Akdis CA, Lauener R; CK-CARE study group; Frei R, Roduit C. The abundance of Ruminococcus bromii is associated with faecal butyrate levels and atopic dermatitis in infancy. Allergy. 2022 Aug 2. doi: 10.1111/all.15440. IPF: 14.71

Schmidt V, Lalevée S, Traidl S, Ameri M, Ziadlou R, Ingen-Housz-Oro S, Barau C, de Prost N, Nägeli M, Mitamura Y, Meier-Schiesser B, Navarini AA, French LE, Contassot E, Brüggen MC. Intravenous immunoglobulins, cyclosporine, and best supportive care in epidermal necrolysis: Diverse effects on systemic inflammation. Allergy. 2022 Dec 4. doi: 10.1111/all.15608. IPF: 14.71

Sokolowska M, Rovati GE, Diamant Z, Untersmayr E, Schwarze J, Lukasik Z, Sava F, Angelina A, Palomares O, Akdis CA, O'Mahony L, Jesenak M, Pfaar O, Torres MJ, Sanak M, Dahlén SE, Woszczek G. Effects of non-steroidal anti-inflammatory drugs and other eicosanoid pathway modifiers on antiviral and allergic responses: EAACI task force on eicosanoids consensus report in times of COVID-19. Allergy. 2022 Aug;77(8):2337-2354. doi: 10.1111/all.15258. IPF: 14.71

Venter C, Meyer RW, Greenhawt M, Pali-Schöll I, Nwaru B, Roduit C, Untersmayr E, Adel-Patient K, Agache I, Agostoni C, Akdis CA, Feeney M, Hoffmann-Sommergruber K, Lunjani N, Grimshaw K, Reese I, Smith PK, Sokolowska M, Vassilopoulou E, Vlieg-Boerstra B, Amara S, Walter J, O'Mahony L. Role of dietary fiber in promoting immune health-An EAACI position paper. Allergy. 2022 Nov;77(11):3185-3198. doi: 10.1111/all.15430. IPF: 14.71

Vlieg-Boerstra B, de Jong N, Meyer R, Agostoni C, De Cosmi V, Grimshaw K, Milani GP, Muraro A, Oude Elberink H, Pali-Schöll I, Roduit C, Sasaki M, Skypala I, Sokolowska M, van Splunter M, Untersmayr E, Venter C, O'Mahony L, Nwaru BI. Nutrient supplementation for prevention of viral respiratory tract infections in healthy subjects: A systematic review and meta-analysis. Allergy. 2022 May;77(5):1373-1388. doi: 10.1111/all.15136. IPF: 14.71

Wirz OF, Jansen K, Satitsuksanoa P, van de Veen W, Tan G, Sokolowska M, Mirer D, Stanić B, Message SD, Kebadze T, Glanville N, Mallia P, Gern JE, Papadopoulos N, Akdis CA, Johnston SL, Nadeau K, Akdis M. Experimental rhinovirus infection induces an antiviral response in circulating B cells which is dysregulated in patients with asthma. Allergy. 2022 Jan;77(1):130-142. doi: 10.1111/all.14985. IPF: 14.71

Zhang L, Akdis CA. The Past, Present and Future of Allergic Diseases in China. Allergy. 2022 Jan 7. doi: 10.1111/all.15213. IPF: 14.71

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. 2022 Nov 24. DOI: 10.1111/all.15593. IPF: 14.71

López JF*, Bel imam M, Satitsuksanoa P, Lems S, Yang M, Hwang YK, Losol P, Choi JP, Kim SH, Chang YS, van de Veen W, Akdis M, Akdis CA. Mechanisms and biomarkers of successful allergen-specific immunotherapy. Asia Pacific Allergy. 2022 Oct 17;12(4). DOI: 10.5415/apallergy.2022.12.e45. IPF: 0

Dong, X., Ding, M., Zhang, J., Ogülür, I., Pat, Y., Akdis, M., Gao, Y., & Akdis, C. A. Involvement and therapeutic implications of airway epithelial barrier dysfunction in type 2 inflammation of asthma. Chin Med J (Engl). 2022 Feb 16;135(5):519-531. doi: 10.1097/CM9.0000000000001983. IPF : 6.133

Angelina A, Jiménez-Saiz R, Pérez-Diego M, Maldonado A, Rückert B, Akdis M, Martín-Fontecha M, Akdis CA, Palomares O. Cannabinoid WIN55212-2 impairs peanut-allergic sensitization and promotes the generation of allergen-specific regulatory T cells. Clin Exp Allergy. 2022 Apr;52(4):540-549. doi: 10.1111/cea.14092. IPF: 5.018

Cardoso-Vigueros C, von Blumenthal T, Rückert B, Rinaldi AO, Tan G, Dreher A, Radzikowska U, Menz G, Schmid-Grendelmeier P, Akdis CA, Sokolowska M. Leukocyte redistribution as immunological biomarker of corticosteroid resistance in severe asthma. Clin Exp Allergy. 2022 Oct;52(10):1183-1194. doi: 10.1111/cea.14128. IPF: 5.018

Jung YS, Sampath V, Prunicki M, Aguilera J, Allen H, LaBeaud D, Veidis E, Barry M, Erny B, Patel L, Akdis C, Akdis M, Nadeau K. Jung YS, Sampath V, Prunicki M, Aguilera J, Allen H, LaBeaud D, Veidis E, Barry M, Erny B, Patel L, Akdis C, Akdis M, Nadeau K. Characterization and regulation of microplastic pollution for protecting planetary and human health. Environ Pollut. 2022 Dec 15;315:120442. doi: 10.1016/j.envpol.2022.120442. IPF: 9.988

Peng YQ, Wu ZC, Xu ZB, Fang SB, Chen DH, Zhang HY, Liu XQ, He BX, Chen D, Akdis CA, Fu QL. Mesenchymal stromal cells-derived small extracellular vesicles modulate DC function to suppress Th2 responses via IL-10 in patients with allergic rhinitis. Eur J Immunol. 2022 Jul;52(7):1129-1140.
doi: 10.1002/eji.202149497. IPF: 6.688

Hurme P, Komulainen M, Tulkki M, Leino A, Rückert B, Turunen R, Vuorinen T, Akdis M, Akdis CA, Jartti T. Cytokine expression in rhinovirus- vs. respiratory syncytial virus-induced first wheezing episode and its relation to clinical course. Front Immunol. 2022 Nov 14;13:1044621. doi: 10.3389/fimmu.2022.1044621. IPF: 8.786

Karaaslan C, Mayorga C, Baerenfaller K and Escribese MM. Editorial: Systems Biology Approach to the Immunology of Asthma and Allergy. Front Immunol. 2022; 13: 857403, doi: 10.3389/fimmu.2022.857403. IPF: 8.786

Tynecka M, Janucik A, Niemira M, Zbikowski A, Stocker N, Tarasik A, Starosz A, Grubczak K, Szalkowska A, Korotko U, Reszec J, Kwasniewski M, Kretowski A, Akdis C, Sokolowska M, Moniuszko M, Eljaszewicz A. The short-term and long-term effects of intranasal mesenchymal stem cell administration to noninflamed mice lung. Front Immunol. 2022 Sep 16;13:967487. doi: 10.3389/fimmu.2022.967487. IPF: 8.786

Fieten KB, John SM, Nowak D. Secondary and Tertiary Prevention: Medical Rehabilitation. Handb Exp Pharmacol. 2022;268:449-470. doi: 10.1007/164_2021_511. IPF: 3.21

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 COVID-19 patients prior to PCR results and predicts their survival based on standard laboratory parameters in an observational study. Infect Dis Ther. 2022 Nov 4:1-19. doi: 10.1007/s40121-022-00707-8. IPF 6.119

Gao YD, Agache I, Akdis M, Nadeau K, Klimek L, Jutel M, Akdis CA. The effect of allergy and asthma as a comorbidity on the susceptibility and outcomes of COVID-19. Int Immunol. 2022 Mar 25;34(4):177-188. doi: 10.1093/intimm/dxab107. IPF: 5.071

Druszczyńska M, Godkowicz M, Kulesza J, Wawrocki S, Fol M. Cytokine Receptors-Regulators of Antimycobacterial Immune Response. Int J Mol Sci. 2022 Jan 20;23(3):1112. doi: 10.3390/ijms23031112.IPF:6.208

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. IPF: 14.29

Akdis CA. The epithelial barrier hypothesis proposes a comprehensive understanding of the origins of allergic and other chronic noncommunicable diseases. J Allergy Clin Immunol. 2022 Jan;149(1):41-44. doi: 10.1016/j.jaci.2021.11.010. IPF: 14.29

Ogulur, I., Pat, Y., Aydin, T., Yazici, D., Rückert, B., Peng, Y., Kim, J., Radzikowska, U., Westermann, P., Sokolowska, M., Dhir, R., Akdis, M., Nadeau, K., & Akdis, C. A. (2022). Gut epithelial barrier damage caused by dishwasher detergents and rinse aids. J. Allergy Clin. Immunol. 2023 Feb; 151(2): 469-484. doi: 10.1016/j.jaci.2022.10.020. IPF: 14.29

Khusial R, van Koppen S, Honkoop P, Rijssenbeek-Nouwens L, Fieten KB, Keij S, Drijver-Messelink M, Sont J. Patients' and Health Care Providers' Perceptions on mHealth Use After High-Altitude Climate Therapy for Severe Asthma: Mixed Methods Study. JMIR Form Res. 2022 Nov 22;6(11):e26925. doi: 10.2196/26925. IPF: 2.38

Komlósi ZI, van de Veen W, Kovács N, Szűcs G, Sokolowska M, O'Mahony L, Akdis M, Akdis CA. Cellular and molecular mechanisms of allergic asthma. Mol Aspects Med. 2022 Jun;85:100995. doi: 10.1016/j.mam.2021.100995. IPF: 16.337

Angelina A, Pérez-Diego M, López-Abente J, Rückert B, Nombela I, Akdis M, Martín-Fontecha M, Akdis C, Palomares O. Cannabinoids induce functional Tregs by promoting tolerogenic DCs via autophagy and metabolic reprograming. Mucosal Immunol. 2022 Jan;15(1):96-108. doi: 10.1038/s41385-021-00455-x. Epub 2021 Sep 21. IPF: 8.701

Akdis CA, Nadeau KC., Human and planetary health on fire. Nat Rev Immunol. 2022 Nov;22(11):651-652. doi: 10.1038/s41577-022-00776-3. IPF: 108.555

Fröhlich K, Brombacher E, Fahrner M, Vogele D, Kook L, Pinter N, Bronsert P, Timme-Bronsert S, Schmidt A, Bärenfaller K, Kreutz C, Schilling O. Benchmarking of analysis strategies for data-independent acquisition proteomics using a large-scale dataset comprising inter-patient heterogeneity. Nature Communications 2022 13, 2622, doi: 10.1038/s41467-022-30094-0. IPF: 17.694

Genuneit J, Jayasinghe S, Riggioni C, Peters RL, Chu DK, Munblit D, Boyle RJ, Du Toit G, Skypala I, Santos AF. EAACI Food Allergy Guidelines Expert Group, the EAACI Research, Outreach Committee Food Allergy Group. Protocol for a systematic review of the diagnostic test accuracy of tests for IgE-mediated food allergy. Pediatr Allergy Immunol. 2022 Jan;33(1):e13684. doi: 10.1111/pai.13684. IPF: 5.464

Messner, C. B., Demichev, V., Wang, Z., Hartl, J., Kustatscher, G., Mülleder, M., & Ralser, M. (2022). Mass spectrometry-based high-throughput proteomics and its role in biomedical studies and systems biology. Proteomics. IPF 5.4, 2022, Nov 18. doi.org/10.1002/pmic.202200013. IPF: 5.393

Pat, Y., Ogulur, I., Yazici, D., Mitamura, Y., Cevhertas, L., Küçükkase,

Articles in peer reviewed journals 2022 / Book chapters

O. C., Mesisser, S. S., Akdis, M., Nadeau, K., & Akdis, C. A. (2022). Effect of altered human exposome on the skin and mucosal epithelial barrier integrity. Tissue barriers. 2022 Oct 19;2133877. doi: 10.1080/21688370.2022.2133877. IPF: 4.613

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. ECML PKDD Workshop on Machine Learning for Pharma and Healthcare Applications 2022, doi: 10.3929/ethz-b-000565782

BOOK CHAPTERS

Akdis M. Allergen immunotherapy for allergic disease: Therapeutic mechanisms. Section Editor, Peter S Creticos, Deputy Editor, Anna M Feldweg. Wolters Kluwer, UpToDate, 2017-2022- Waltham, Massachusetts, USA. Electronic clinical resource.

Umit Sahiner, Mubeccel Akdis and Cezmi Akdis. Introduction to Mechanisms of Allergic Diseases. Section Editors, Robyn E. O`Hehir, Stephen T. Holgate, Gurjit K. Khurana Hershey, Aziz Sheikh. Elsevier, Allergy Essentials, 2022, USA, 1-24.

ABSTRACTS

Akdis M. Specific B cell responses in natural and induced B cell tolerance. World Immune Regulation Meeting XVI, Davos, Switzerland. 6-9 July 2022

Aguilera J, Cauwenberghs N, Smith E, Kaushik A, Ogulur I, Heider A, Akdis CA, Prunicki M, Nadeau K, Parsons ES. Symptomatology, immune changes, and proteomic alterations in subjects exposed to wildfire smoke. World Immune Regulation Meeting XVI (WIRM XVI), Davos, Switzerland 6-9 July 2022

Baerenfaller K, Translational regulation and translation of non-coding RNAs in T helper 1 cell differentiation and activation, World Immune Regulation Meeting XVI 2022, Davos, Switzerland, 6-9 July 2022

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. 16th MIM Introductory Course 2022, Online, 19-21 January 2022.

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. EAACI Immunology Winter School 2022, Online, 27-30 January 2022.

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. LS2 Annual Meeting 2022, Zurich, Switzerland, 21-22 April 2022.

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 2022, Davos, Switzerland, 6-9 July 2022.

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. 14th Advanced Proteomics European Summer School, Brixen/Bressanone, South Tirol, 31 July-6 August 2022

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. 15th MIM Retreat 2022, Wildhaus, Switzerland,18-20 September 2022

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. Graubünden Forscht 2022, Davos, Switzerland, 21-22 September 2022.

Bel imam M, Straumann A, Biedermann L, Schreiner P, Satitsuksanoa P, Schneider SR, Akdis M, van de Veen W. Identification of immunological biomarkers for the diagnosis and monitoring of eosinophilic esophagitis. 16th MIM Introductory Course, online, 19-21 January 2022.

Bel imam M, Straumann A, Biedermann L, Schreiner P, Satitsuksanoa P, Schneider SR, Akdis M, van de Veen W. Detection of food-antigen specific antibodies in the plasma of eosinophilic esophagitis patients. 16th World Immune Regulation Meeting (WIRM), Davos, Switzerland, 6-9 July 2022.

Bel imam M, Straumann A, Biedermann L, Schreiner P, Satitsuksanoa P, Schneider SR, Akdis M, van de Veen W. Insights on food-antigen specific antibodies in the plasma of eosinophilic esophagitis patients. 15th MIM retreat, Wildhaus, Switzerland, 18-20 September 2022.

Bel imam M, Straumann A, Biedermann L, Schreiner P, Satitsuksanoa P, Schneider SR, Akdis M, van de Veen W. Determining the presence of food-antigen specific total IgG and IgG4 antibodies in the plasma of eosinophilic esophagitis patients. Graubünden Forscht 2022, Davos, Switzerland, 21-22 September 2022.

Bel imam M, Straumann A, Biedermann L, Schreiner P, Satitsuksanoa P, Schneider SR, Akdis M, van de Veen W. Circulating food-allergen-specific of all IgG isotypes are elevated in eosinophilic esophagitis patients. World Allergy Congress (WAC), Istanbul, Turkey, 13-15 October 2022.

Chang I. Distinct gene expression profiles of G-Protein-Coupled Receptors on B cell subsets. WIRM 2022, Davos, Switzerland, 5-9 July 2022

Chang I. Differentially expressed gene profiles of histomine 1 receptor and histomine 2 receptor on B cell subsets. WAC 2022, Istanbul, Turkiye, 13-15 October 2022

Koch J, Imeri M, Schmelzer S, Westermann P, Heider A, Scheckel C, Baerenfaller K. Translational regulation of differentiating human Th1 cells. EACCI Winter School Digital, online, 27-30 January 2022.

Koch J, Westermann P, Imeri M, Schmelzer S, Froehlich K, Scheckel C, Baerenfaller K. Translational regulation T helper 1 cell differentiation. SIB days, Biel, Switzerland, 14-15 June 2022.

Koch J, Westermann P, Schmelzer S, Froehlich K, Heider A, Baerenfaller K.Characterization of Protein Prenylation in T helper 1 cell activation. WIRM 2022, Davos, Switzerland, 6-9 July 2022.

Pfeifer E, Koch J, Westermann P, Baerenfaller K. Characterization of T helper cell subsets. WIRM 2022, Davos, Switzerland, 6-9 July 2022.

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. CSHL meeting Translational Control 2022, Cold Spring Harbour, USA, 6-10 September 2022.

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. MIM retreat 2022, Wildhaus, Switzerland, 18-20 September 2022.

Kücükkase O, Ogulur I, Yazıcı D, Aydin T, Rückert B, Akdis M, Nadeau K, Akdis C. The supporting potential of nicotinamide (vitamin B3) and beta hydroxybutyrate (ketone body) on epithelial barrier integrity of human bronchial spheroids and gut on a chip models. World Immune Regulation Meeting XVI (WIRM XVI), Davos, Switzerland 6-9 July 2022.

Kücükkase O, Ogulur I, Yazıcı D, Aydin T, Rückert B, Akdis M, Nadeau K, Akdis AC. Nicotinamide supports gut epithelial barrier integrity in human organoids and gut on a chip models. EAACI Summer Symposium on Epithelial Barriers and Microbiome, Davos, Switzerland 28-29 July 2022

Maurer DJ, Barletta E, Heider A, Stocker N, Wallimann A, Villiger M, Villiger B, Bärenfaller K, Akdis CA, Kistler W. Immune-inflammatory proteome of elite ice hockey players before and after SARS-CoV-2 infection. WIRM 2022, Davos, Switzerland, 6-9 July 2022.

Maurer DJ, Barletta E, Heider A, Stocker N, Wallimann A, Villiger M, Villiger B, Bärenfaller K, Akdis CA, Kistler W. Immune-inflammatory proteome of elite ice hockey players before and after SARS-CoV-2 infection. Graubünden Forscht 2022, Davos, Switzerland, 21-22 September 2022.

Mitamura Y, Reiger M, Kim J, Xiao Y, Zhakparov D, Baerenfaller K, Brüggen MC, Brunner PM, Roqueiro D, Traidl-Hoffmann C, Akdis CA. Spatial transcriptomics combined with single-cell transcriptomics unravels the complex inflammatory cell network in atopic dermatitis Springtime School 2022, Copenhagen, Denmark, 25-26 April 2022.

Mitamura Y, Reiger M, Kim J, Xiao Y, Zhakparov D, Baerenfaller K, Brüggen MC, Brunner PM, Roqueiro D, Traidl-Hoffmann C, Akdis CA. Spatial transcriptomics combined with single-cell transcriptomics unravels the complex inflammatory cell network in atopic dermatitis EAACI annual congress 2022, Prague, Czech Republic, 1-3 July 2022.

Mitamura Y, Spatial transcriptomics combined with single-cell transcriptomics unravels the complex inflammatory cell network in atopic dermatitis. WIRM 2022, Davos, Switzerland, 6-9 July 2022

Mitamura Y, Single-cell seq, visium spatial seq, imaging mass cytometry and targeted proteomics for the investigation of atopic dermatitis lesions. EAACI Summer symposium on epithelial barriers and microbiome 2022, Davos, Switzerland, 28-29 July 2022

Lopez JF, Satitsuksanoa P, Van de Veen W, Akdis CA, Caraballo L, Zakzuk J, Akdis M. Immune regulatory behavior of B cells during Ascaris infection. World Allergy Congress (WAC) 2022, Istanbul, Turkey, 13-15 October 2022.

Ogulur I, Aydın T, Rückert B, Ozen A, Nadeau K, Akdis CA. The epithelial barrier damaging effects of professional dishwasher rinse aid on Caco-2 gastrointestinal epithelial cells. EAACI winter school 2022, Digital, 27-30 January 2022.

Ögülür I, Yazici D, Pat Y, Aydin T, Rückert B, Akdis M, Nadeau K, Akdis CA. Gut epithelial barrier damage by commonly used emulsifiers polysorbate-20 and polysorbate-80. World Immune Regulation Meeting XVI (WIRM XVI), Davos, Switzerland 6-9 July 2022

Ogulur I, Yazici D, Cagan E, Aydin T, Kucukkase OC, Li M, Do E, Simsek A, Kizmaz MA, Bozkurt T, Akdis M, Nadeau K, Budak F, Akdis CA. Novel biomarkers of disrupted gut permeability in severe COVID-19 patients. EAACI Summer Symposium on Epithelial Barriers and Microbiome, Davos, Switzerland 28-29 July 2022

Ogulur I, Yazici D, Pat Y, Aydin T, Rückert B, Akdis M, Nadeau K, Akdis CA. Gut epithelial barrier damage caused by commonly used emulsifiers polysorbate-20 and polysorbate-80. EAACI Summer Symposium on Epithelial Barriers and Microbiome, Davos, Switzerland 28-29 July 2022

Ogulur I, Yazici D, Cagan E, Aydin T, Kucukkase OC, Li M, Do E, Simsek A, Kizmaz MA, Bozkurt T, Akdis M, Nadeau K, Budak F, Akdis CA. Novel biomarkers of disrupted gut permeability in severe COVID-19 patients. 8. Kongress Graubünden forscht, Davos, Switzerland 21-22 September 2022.

Ogulur I, Yazici D, Pat Y, Aydin T, Rückert B, Akdis M, Nadeau K, Akdis CA. Gut epithelial barrier damage caused by commonly used emulsifiers polysorbate-20 and polysorbate-80. 8. Kongress Graubünden forscht, Davos, Switzerland 21-22 September 2022

Ogulur I, Yazici D, Cagan E, Aydin T, Kucukkase OC, Li M, Do E, Simsek A, Kizmaz MA, Bozkurt T, Akdis M, Nadeau K, Budak F, Akdis CA. Novel biomarkers of disrupted gut permeability in severe COVID-19 patients. World Allergy Congress (WAC), Istanbul, Türkiye, 13-15 October 2022.

Ogulur I, Yazici D, Pat Y, Aydin T, Rückert B, Akdis M, Nadeau K, Akdis CA. Gut epithelial barrier damage caused by commonly used emulsifiers polysorbate-20 and polysorbate-80. World Allergy Congress (WAC), Istanbul, Türkiye, 13-15 October 2022.

Ogulur I, Pat Y, Aydin T, Yazici D, Rückert B, Peng Y, Kim J, Radzikowska U, Westermann P, Sokolowska M, Dhir R, Akdis M, Nadeau K, Akdis CA. Gut epithelial barrier damage caused by dishwasher detergents and rinse aids. World Allergy Congress (WAC), Istanbul, Türkiye, 13-15 October 2022.
Ogulur I, Pat Y, Aydin T, Yazici D, Rückert B, Penq Y, Kim J, Radzikowska U, Westermann P, Sokolowska M, Dhir R, Akdis M, Nadeau

K, Akdis CA. Gut epithelial barrier damage and epithelitis caused by professional dishwashers and rinse aid. 2nd edition Type 2 Immunity in Homeostasis and Disease, Ghent, Belgium, 12-14 December 2022.

Pat, Y., Rückert, B., Ogulur, I., Yazici, D., Pérez-Diego, M., Küçükkase, O. C., & Akdis, C. A. Differentiation of airway organoids in the presence of IL-13 recapitulates characteristic features of asthmatic airway epithelia. EAACI winter school 2022, Digital, 27-30 January 2022.

Pat, Y., Rückert, B., Ogulur, I., Yazici, D., Pérez-Diego, M., Küçükkase, O. C., & Akdis, C. A. Differentiation of bronchial epithelial spheroids in the presence of IL-13 recapitulates characteristic features of type 2 asthmatic airway epithelia. EAACI hybrid congress 2022, Prague, Czech Republic, 01 - 03 July 2022.

Pat, Y., Rückert, B., Ogulur, I., Yazici, D., Pérez-Diego, M., Küçükkase, O. C., & Akdis, C. A. Differentiation of bronchial epithelial spheroids in the presence of IL-13 recapitulates characteristic features of asthmatic airway epithelia. World Immune Regulation Meeting XVI, Davos, Switzerland, 6-9 July 2022.

Pat, Y., Rückert, B., Ogulur, I., Yazici, D., Pérez-Diego, M., Küçükkase, O. C., & Akdis, C. A. Differentiation of bronchial epithelial spheroids in the presence of IL-13 recapitulates characteristic features of asthmatic airway epithelia. World Allergy Congress 2022, Istanbul, Türkiye, 13-15 October 2022.

Radzikowska, U. Rhinovirus-induced epithelial RIG-I inflammasome activation suppresses antiviral immunity and promotes inflammatory responses in virus-induced asthma exacerbations and COVID-19. Graubünden Forscht, Davos, Switzerland, 21-22-09.2022.

Radzikowska, U. Rhinovirus-induced epithelial RIG-I inflammasome activation suppresses antiviral immunity and promotes inflammatory responses in virus-induced asthma exacerbations and COVID-19. World Immune Regulation Meeting XVI, Davos, Switzerland, 06-09.07.2022.

Radzikowska U. The role of epithelial RIG-I inflammasome activation in suppressing antiviral immunity and promoting inflammatory responses in virus-induced asthma exacerbations and COVID-19. EAACI Immunology Winter School 2022, digital, 27-30.01.2022.

Radzikowska, U. Rhinovirus-induced epithelial RIG-I inflammasome activation suppresses antiviral immunity and promotes inflammatory responses in virus-induced asthma exacerbations and COVID-19. EAACI Summer Symposium on Epithelial Barriers and Microbiome, Davos, Switzerland, 28-29.07.2022

Radzikowska, U. Distinct metabolic reprogramming of airway epithelium in asthma in response to infection with rhinovirus. Cell Symposia Translational Immunometabolism, Basel, Switzerland, 26-28.06.2022.

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, Kebadze T, Jackson DJ, Edwards MR, Thiel V, Johnston SL, Akdis CA, Sokolowska M. Rhinovirus-induced epithelial RIG-I inflammasome activation suppresses antiviral immunity and promotes inflammatory responses in virus-induced asthma exacerbations and COVID-19. Swiss Young Immunologists Society (SYIS) 1st Annual Symposium 23rd May 2022

Satitsuksanoa P, van de Veen W, Tan G, Wirz O, Sokolowska M, Chang I, Nadeau K, Akdis M. Roles of allergen-specific B cells in food allergic children during oral immunotherapy and natural tolerance. EAACI Winter School Digital 2022, online, 27 - 30 January 2022.

Satitsuksanoa P, Bürgi L, Schneider S, van de Veen W, Nadeau K, Akdis M. Characterization of single allergen-specific IgE+ B cell from cow's milk allergic children. World Immune Regulation Meeting XVI, Davos, Switzerland, 6-9 July 2022.

Satitsuksanoa P, Bürgi L, Schneider S, van de Veen W, Nadeau K, Akdis M. Characterization of single allergen-specific IgE+ B cell from cow's milk allergic children during the oral immunotherapy. Grabünden forscht. Davos, Switzerland, 21-22 September 2022.

Satitsuksanoa P, an de Veen W, Tan G, Boonpiyathad T, Akdis M. The past, presence and future of allergen immunotherapy. 33rd European Veterinary Dermatology Congress, co-organized by the European Society of Veterinary Dermatology and European College of Veterinary Dermatology, Porto, Portugal. 29 September – 1 October 2022

Satitsuksanoa P, Bürgi L, Schneider S, van de Veen W, Nadeau K, Akdis M. Single allergen-specific IgE+ B cell analysis in cow's milk allergic children during the oral immunotherapy. World Allergy Congress 2022. Istanbul, Turkey, 13-15 October 2022.

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) 2022, Davos, Switzerland 6-9 July 2022

Sokolowska M, Rodriguez-Coira J,Boonpiyathad T, Eljaszewicz A, Radzikowska U, Globinska A, Castro Giner F, Ruchti F, Villaseñor A, Gomez-Casado C, Huang M, Sanchez-Solares J, Pablo Torres C; Obeso D; Saiz V; Ruiz- Leon B, Espinazo M, Escribese MM, Moreno-Aguilar C, Ruckert B, Dreher A, Morita H, Rinaldi A, Gschwend A, Helbling A, Negoias S, Hool SL, Borner U, Kwok W, Akdis M, Kahlert H, Berek N, Nandy A, Willers C, Barber D, Akdis CA.
Zhakparov D, Moriarty K, Schmid M, Roqueiro D, Baerenfaller K, SOS-ALL Consortium. Machine Learning Reveals Patterns in Transcriptomics and Clinical Datasets Associated with Atopic Dermatitis in African Children. WIRM, Davos, Switzerland, 6 - 9 July 2022.

SEMINAR AND CONGRESS TALKS

Akdis CA. AO CMF Bone Consotium Kick Off Meeting, 13 January 2022.

Akdis CA. T2 Education Module. The immunology of the Type 2 response. EAACI Knowledge Hub, 18 January 2022.

Akdis CA. Epithelial barrier hypothesis: Mechanisms and immunology: Complutense University Madrid, Spain, 21 January 2022.

Akdis CA. Epithelial barrier and allergic diseases. Department of Respiratory Diseases, Humanitas University, Milan, Italy, 3 February 2022.

Akdis CA. Epithelial barrier hypothesis. Helmholz-Munich Immunology Platform, 9 February 2022.

Akdis CA. Die epitheliale Barriere –Schlüssel zum Verständnis und Therapie von Allergien. Arzte Kongress Davos, 12 February 2022.

Akdis CA. Allergy China Issue. Online Presentation, 16 February 2022,

Akdis CA. What is Allergy. Post Graduate Course. University Zurich, Department of Clinical Immunology, 25 February 2022.

Akdis CA. Skin Barrier in Atopic Dermatitis. Skin Allergy Meeting. Koç University, Istanbul, Turkey, 26 February 2022.

Akdis CA. Epithelial barrier hypothesis, Immunology CMM Seminar Series. Karolinska University, Stockholm, Sweden, 2 March 2022.

Akdis CA. My life story. Bursa Anatolian Highschool Talks. Bursa, Turkey, 8 March 2022.

Akdis CA. Epithelial Barrier Hypothesis and Allergic Diseases. Uludağ Pediatry Congress, Bursa, Turkey, 12 March 2022.

Akdis CA. Epithelial barrier hypothesis and allergy and autoimmunity: 2 billion patients. Hacettepe University, Department of Internal Medicine, Ankara Turkey, 24 March 2022.

Akdis CA. Diseases related to epithelial barriers and microbiome. Future of medicine seminars. Uludağ University, Bursa, Turkey, 6 April 2022.

Akdis CA. Epithelial barriers and allergic diseases. Dutch Pediatric Allergy Society Conferenece, Rotterdam, The Netherlands, 8 April 2022.

Akdis CA. How to write and review top research articles. APAAACI, Junior Members, 11 April 2022.

Akdis CA. Epithelial Berriers, Allergy, Autoimmunity and Neuropsychiatric Diseases. Istanbul University, Cerrahpaşa Pediatry and Padietric Nurses Conference. 19 April 2022

Akdis CA. Epithelial Berrier Hypothesis, Allergy and Autoimmunity: Edinburgh, Scottland, 25 April 2022.

Akdis CA. Early immune response to bone materials. AO Consortium Meeting, Barcelona, Spain 3 May 2022.

Akdis CA. Severe Asthma Pathogenesis: Epithelial barrier hypothesis. AO Consortium Meeting, Korean Allergology Meeting, Soeul, Korea, 2 May 2022.

Akdis CA. Epithelial Barriers and Allergic Disease. Borstel Allergy Conference, Germany, 7 May 2022.

Akdis CA. Epithelial Barrier Hypothesis and development of allergic diseases. German Allergy Society (DGAKI), Berlin, Germany, 13 May 2022.

Akdis CA. Die Epithelbarriere – Der Schlüssel zum Verständnis der Pathogenese und Therapie von Allergien. Allergologie, im Kloster. Kloster Eberbach, Germany, 14 May 2022.

Akdis CA. Epithelial Barrier hypothesis: Understanding the Origins of Allergic Diseases. Allergy Asthma Immunology Conference in the honor of Prof. Dr. Marek Kowalski, Lodz, Poland, 23 June 2022.

Akdis CA. The Epithelial Barrier Hypothesis Understanding the Origins of Allergic Disease: Breaking The Wall. EAACI Annual Meeting. Prague 2 July 2022.

Akdis CA. Covid-19 papers published in Allergy. EAACI Journals Symposium, EAACI Annual Meeting, Prague, 2 July 2022.

Akdis CA. Allergy-Achievements. Editorial Board Meeting, EAACI Annual Meeting, Prague, 2 July 2022.

Akdis CA. How to write a first-class paper – tips and tricks, Junior Members and Affiliates Session, EAACI Annual Meeting, Prague, 3 July 2022.

Akdis CA. Epithelial Barrier Hypothesis: Mechanisms of Development of Allergy and autoimmunity. World Immune Regulation Meeting. Davos, 8 July 2022

Akdis CA. Opening Keynote Lecture. Epithelial Barriers, Allergic and Autoimmune Diseases, World Anatomy Congress, 5 August 2022.

Akdis CA. Epithelial Barrier Hypothesis, Allergic and Autoimmune Diseases, Argentinian Allergy Congress, 13 August 2022.

Akdis CA. Epithelial Barrier Hypothesis and Allergic Respiratory Diseases. European Respiratory Society Meeting, Barcelona, Spain, 5 September 2022.

Akdis CA. Epithelial Barrier Hypothesis and One Health. European Veterinary Congress, Porto, Portugal, 30 September 2022.

Akdis CA. EAACI Presidents Summit, Cagliari, Sardinia, 1-2 October 2022.

Akdis CA. Epithelial Barrier Hypothesis and Allergic Diseases. Japanese Allergy Congress, 8 October 2022.

Akdis CA. Airpollution and epithelial barriers. SynAir-G European Union Consortium Project. Kickoff meeting. Athens 11 October 2022.

Akdis CA. Epithelial Barrier Hypothesis and Allergic Diseases. World Allergy Congress, Istanbul, 20 October 2022.

Akdis CA. Epithelial Barrier Hypothesis and Allergic Diseases. EAACI, Isma-Rhina Congress, Istanbul, 5 November 2022.

Akdis CA. Epithelial Barrier Hypothesis and Allergic Diseases. Third Central and South European Type 2 Inflammation Forum, Athens 11 November 2022.

Akdis CA. Type 2 Immune Response and Asthma. Third Central and South European Type 2 Inflammation Forum, Athens 11 November 2022.

Akdis CA. The Epithelial Barrier Theory: "How to restore the allostatic load" «the cumulative burden of chronic stress and life events» EAACI Session in APAAACI Meeting, Manila 5 December 2022.

Akdis CA. Epithelial Barrier Hypothesis and Immune Regulation in Allergic Diseases 'Global Health Crisis'. Keynote Lecture. APAAACI Meeting, Manila 5 December 2022.

Akdis CA. How to write a first-class paper – tips and tricks and How to publish in high journals. JMA Session. APAAACI Meeting, Manila 6 December 2022.

Akdis CA. Epithelial Barier Theory for the development of Allergy and Autoimmunity. Japanese Immunology Society Congress. 8 December 2022.

Akdis CA. Epithelial Barier Theory for the development of Allergic and Autoimmune Diseases. Istanbul Unıversity Institute of Experimental Medicine Congress. 22 December 2022.

Akdis M. B cells and tolerance, Kazan Federal University, Kazan, Russia. 14 January 2022

Akdis M. Induction of immune tolerance by immunotherapy; role of B cells. Department of Biochemistry and Molecular Biology, Complutense University of Madrid, Spain. 21 January 2022

Akdis M. Rhino virus and Coid 19 infections; resembles and differences. 18. Uludağ Pediatric Winter Congress, Bursa, Turkiye. 13-16 March 2022
Akdis M. Breaking immune tolerance: role of rhinovirus infections in Asthma. Dutch Pediatric Allergology Symposium, Roterdam, Nederland. 7-8 April 2022

Akdis M. Induction of immune tolerance by Immunotherapy. Allergy Research Today meeting, Paris, France. 19 April 2022

Akdis M. B and Treg cells and induction of tolerance. World Allergy Organization (WAO) and British Society for Allergy and Clinical Immunology (BSACI), Edinburg, Scotland, UK.
25-27 April 2022

Akdis M. The influence of viruses and parasites on T and B cells. European Academy of Allergy and Clinical Immunology Hybrid Congress. Prague, Czech Republic. 1-3 July 2022

Akdis M. Specific B cell responses in natural and induced tolerance. WIRM XVI, Davos, Switzerland. 6-9 July 2022

Akdis M. Debate about allergen immunotherapy: human versus veterinary dermatology insights. 33rd European Veterinary Dermatology Congress, co-organized by the European Society of Veterinary Dermatology and European College of Veterinary Dermatology, Porto, Portugal. 29 September – 1 October 2022

Akdis M. Past, present and future immunotherapy. 33rd European Veterinary Dermatology Congress, co-organized by the European Society of Veterinary Dermatology and European College of Veterinary Dermatology, Porto, Portugal. 29 September – 1 October 2022

Akdis M. Allergen-specific B cell tolerance in food allergy. World Allergy Congress, Istanbul, Turkiye. 13-15 October 2022

Akdis M. The role of specific B cells in antigen-specific immunotherapy. Pediatric Allergy and Asthma Congress (CAAAD), Cyprus. 20-23 October 2022

Akdis M. Tolerance induction mechanisms for food immunotherapy; role of antigen specific B-cells. Allergy Academy Food Immunotherapy Seminar. Webinar program. 16 November 2022

Akdis M. B cell immune tolerance. Asia Pacific Association of Allergy, Asthma and Clinical Immunology (APAAACI) and the Philippine Society of Allergy, Asthma and Immunology (PSAAI), Manila, Philippines. 5-8 December 2022

Akdis M. Mechanisms of allergen-specific B cell responses in children with cows` milk oral immunotherapy-induced desensitisation, remission and natural outgrown milk allergy. VIB conference 'Type 2 Immunity in Homeostasis and Disease, partnership with Cell Press. Ghent, Belgium. 12-14 December 2022

Baerenfaller K, Translational regulation and translation of non-coding RNAs in T helper 1 cell differentiation and activation, World Immune Regulation Meeting XVI 2022, Davos, Switzerland, 6-9 July 2022

2022

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. 16th MIM Introductory Course 2022, Online, 19-21 January 2022.

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. EAACI Immunology Winter School 2022, Online, 27-30 January 2022.

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. LS2 Annual Meeting 2022, Zurich, Switzerland, 21-22 April 2022.

Barletta E. Introduction to Proteomics. Biomedical Data Mining Blockkurs FS 2021(BME351), Davos, Switzerland, 7-24 June 2022.

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. Graubünden Forscht 2022, Davos, Switzerland, 21-22 September 2022.

Bel imam M. Identification of immunological biomarkers for the diagnosis and monitoring of eosinophilic esophagitis. 16th MIM Introductory Course, online, 19-21 January 2022.

Bel imam M. Detection of food-antigen specific antibodies in the plasma of eosinophilic esophagitis patients. 16th World Immune Regulation Meeting (WIRM), Davos, Switzerland, 6-9 July 2022.

Bel imam M. Insights on food-antigen specific antibodies in the plasma of eosinophilic esophagitis patients. 15th MIM retreat, Wildhaus, Switzerland, 18-20 September 2022.

Bel imam M. Determining the presence of food-antigen specific total IgG and IgG4 antibodies in the plasma of eosinophilic esophagitis patients. Graubünden Forscht 2022, Davos, Switzerland, 21-22 September 2022.

Bel imam M. Circulating food-allergen-specific of all IgG isotypes are elevated in eosinophilic esophagitis patients. World Allergy Congress (WAC), Istanbul, Turkey, 13-15 October 2022.

Fieten KB. High altitude climate therapy – beneficial in allergies and asthma? Swiss Pulmonologists Congress Luzern 30 March - 1 April 2022

Fieten KB. Alpine altitude climate treatment for severe asthma. Dutch pulmonologists Congress "Op de hoogte van astma" Davos 16-18 March 2022

Koch J, Westermann P, Schmelzer S, Froehlich K, Heider A, Baerenfaller K.Characterization of Protein Prenylation in T helper 1 cell activation. Workshop at WIRM 2022, Davos, Switzerland, 6-9 July 2022.

Maurer DJ, Barletta E, Heider A, Stocker N, Wallimann A, Villiger M, Villiger B, Bärenfaller K, Akdis CA, Kistler W. Immune-inflammatory proteome of elite ice hockey players before and after SARS-CoV-2 infection. Graubünden Forscht 2022, Davos, Switzerland, 21-22 September 2022

Mitamura Y, Reiger M, Kim J, Xiao Y, Zhakparov D, Baerenfaller K, Brüggen MC, Brunner PM, Roqueiro D, Traidl-Hoffmann C, Akdis CA. Spatial transcriptomics combined with single-cell transcriptomics unravels the complex inflammatory cell network in atopic dermatitis Springtime School 2022, Copenhagen, Denmark, 25-26 April 2022.

Mitamura Y, Reiger M, Kim J, Xiao Y, Zhakparov D, Baerenfaller K, Brüggen MC, Brunner PM, Roqueiro D, Traidl-Hoffmann C, Akdis CA. Spatial transcriptomics combined with single-cell transcriptomics unravels the complex inflammatory cell network in atopic dermatitis EAACI annual congress 2022, Prague, Czech Republic, 1-3 July 2022.

Mitamura Y, Spatial transcriptomics combined with single-cell transcriptomics unravels the complex inflammatory cell network in atopic dermatitis. WIRM 2022, Davos, Switzerland, 6-9 July 2022

Mitamura Y, Single-cell seq, visium spatial seq, imaging mass cytometry and targeted proteomics for the investigation of atopic dermatitis lesions. EAACI Summer symposium on epithelial barriers and microbiome 2022, Davos, Switzerland, 28-29 July 2022

Ögülür I. Novel biomarkers of disrupted gut permeability in severe COVID-19 patients. World Immune Regulation Meeting XVI (WIRM XVI), Davos, Switzerland 6-9 July 2022

Satitsuksanoa P, van de Veen W, Tan G, Wirz O, Sokolowska M, Chang I, Nadeau K, Akdis M. Roles of allergen-specific B cells in food allergic children during oral immunotherapy and natural tolerance. EAACI Winter School Digital 2022, online, 27 - 30 January 2022.

Satitsuksanoa P, Bürgi L, Schneider S, van de Veen W, Nadeau K, Akdis M. Characterization of single allergen-specific IgE+ B cell from cow's milk allergic children. World Immune Regulation Meeting (WIRM) XVI, Davos, Switzerland, 6-9 July 2022.

Satitsuksanoa P, Bürgi L, Schneider S, van de Veen W, Nadeau K, Akdis M. Characterization of single allergen-specific IgE+ B cell from cow's milk allergic children during the oral immunotherapy. Grabünden forscht. Davos, Switzerland, 21-22 September 2022.

Satitsuksanoa P, Bürgi L, Schneider S, van de Veen W, Nadeau K, Akdis M. Single allergen-specific IgE+ B cell analysis in cow's milk allergic children during the oral immunotherapy. World Allergy Con-

gress 2022. Istanbul, Turkey, 13-15 October 2022.

Schneider S. Investigation of allergen specific B-cells in allergy concordant and discordant twins. Graubünden Forscht, Davos, Switzerland, 21-22 September 2022

Schneider S. Investigation of allergen specific B-cells in allergy concordant and discordant twins. World Allergy Conference (WAC), Istanbul, Turkey, 13-15 October 2022

Sokolowska M. Machine learning successfully detects COVID-19 patients prior to PCR results and predicts their survival based on standard laboratory parameters. Life Sciences in the 2020s: quantitation, integration and prediction, 20-22 April 2022, Zurich, Switzerland

Sokolowska M. Immunology of COVID-19: Mechanisms, clinical outcome, diagnostics, and perspectives. 16th Introductory Course in Microbiology and Immunology, ETH Zurich, January 19-21 2022

Sokolowska M. Environmental factors affecting epithelial barriers in asthma. Global Respiratory leadership Forum, AstraZeneca Innovation; 28-29 April 2022

Sokolowska M. Rhinovirus-induced epithelial RIG-I inflammasome in asthma and COVID-19. Swiss Young Immunologists Society (SYIS) 1st Annual Symposium 23rd May 2022

Sokolowska M. Metabolic checkpoints of pathogenic Th2 cells development. WORLD IMMUNE REGULATION MEETING – XVI., Davos, Switzerland, 6-9th July 2022

Sokolowska M. Epithelial cell responses in COVID-19 and rhinovirus infections. EAACI summer symposium on epithelial barriers and microbiome, Davos, Switzerland, 28-29th July 2022

Sokolowska M. Crosstalk of antiviral immunity and immune metabolism at the mucosal barriers. Global Allergy Forum. Davos, Switzerland,1-4th September 2022

Sokolowska M. The role of epithelium in allergic diseases. Czech and Slovak Allergology and Immunology Congress, Prague, Czech Republic 5-8th October 2022

Sokolowska M. Difference between SARS-COV-2 associated molecules in health and asthma. World Allergy Congress, Istanbul, Turkey 13-15th October 2022

Sokolowska M. Immunology and risk factors for severe illness in Covid-19. EAACI International Symposium on Molecular Allergology (ISMA) and the European Rhinallergy Meeting (RHINA), 4-5th November 2022 (online)

Sokolowska M. Novel mechanisms of allergic and viral inflammation in airway epithelium in asthma. Environmental Health and Lung Research School. Herrsching am Ammersee, Germany, 15-16 November 2022

Van de Veen W. Novel vaccine development and cross reactivities with Non-SARS COV-2. World Allergy Congress (WAC) 2022. Istanbul, Turkey, 13-15 October 2022.

Van de Veen W. The Role of B Cells in the Regulation of Allergic Immune Responses. Biomedicine Seminar. University of Zurich, Zurich, Switzerland. 8 November 2022.

Wallimann A. Antibiotic therapy for orthopedic device-related infection: Prolonged microbiome disturbances and systemic responses of relevance to bone health. WIRM 2022, Davos, Switzerland, July 6-9, 2022.

CHAIRS AT CONGRESSES

Akdis CA. Career Days. Turkish Immunology Society Seminar Series, 2 February 2022.

Akdis CA. Global Warming & Climate Change. Turkish Immunology Society Seminar Series, 18 May 2022.

Akdis CA. EAACI Prag Annual Meeting. Plenary Session, Prague, 2 July 2022.

Akdis CA. 16th World Immune Regulation Meeting, Davos 6-9 July 2022.

Akdis CA. World Immune Regulation Meeting. Opening Plenary Session, Davos, 6 July 2022.

Akdis CA. EAACI Epithelial Working Group Symposium. Environment, microbiome and allergic disease, 28-29 July 2022

Akdis CA. Immune Response to Allergens. World Allergy Congress, Istanbul, 20 October 2022.

Akdis CA. Type 2 Immune Response. Third Central and South European Type 2 Inflammation Forum, Athens 11 November 2022.

Akdis M. Plenary Session 3: T cell activation and immune response. WIRM XVI, Davos, Switzerland. 6-9 July 2022

Akdis M. Session 4: Medicine & Life Sciences. Graubünden forscht Conference, Davos, Switzerland. 21-22 September 2022

Akdis M. Plenary Session 3: Biologicals. World Allergy Congress, Istanbul, Turkiye. 13-15 October 2022

Akdis M. EAACI session at COP27: Asthma and Allergy - the perfect example for Climate Change and Health Outcome. COP27 UN Climate Conference. Sharm El Sheikh, Egypt. 28 October 2022

Baerenfaller K. Handling Large-Scale Complex Datasets: Integrati-

on, Modeling, Prediction. LS2 Annual Meeting 2022, Zurich, Switzerland, 20-22 April 2022.

Baerenfaller K. Plenary Session 12 Innate Immune Response, B cells and antibody synthesis. World Immune Regulation Meeting XVI 2022, Davos, Switzerland, 6-9 July 2022

Lopez JF, Mechanisms in asthma, allergy and immune regulation. World Immune Regulation Meeting (WIRM) 2022, Davos, Switzerland, 6-9 July 2022

Koch J, Poster Session 6 Transcriptomics. WIRM 2022, Davos, Switzerland, 6-9 July 2022

Ögülür I. COVID-19. World Immune Regulation Meeting XVI (WIRM XVI), Davos, Switzerland 6-9 July 2022

Ögülür I. Novel techniques for an extensive look at the defective epithelial barriers. EAACI Summer Symposium on Epithelial Barriers and Microbiome, Davos, Switzerland 28-29 July 2022

Ögülür I. Novel techniques for an extensive look at the defective epithelial barriers. EAACI Summer Symposium on Epithelial Barriers and Microbiome, Davos, Switzerland 28-29 July 2022

Radzikowska, U. Poster Session P1 Chair. World Immune Regulation Meeting XVI, Davos, Switzerland, 06-09.07.2022.

Satitsuksanoa P. B-cells and immune response.World Immune Regulation Meeting (WIRM) XVI, Davos, Switzerland, 6-9 July 2022.

Sokolowska M. Keynote Lecture: B-cell immunity in allergy and COVID-19. Scott Boyd. 20th EAACI Immunology Winter School "Basic Immunology Research in Allergy and Clinical Immunology, 27-30th January 2022

Sokolowska M. Practical Course: Treatment of patients with allergies in the context of biologicals, nutrition, infections, immunodeficiencies and cancer. 20th EAACI Immunology Winter School "Basic Immunology Research in Allergy and Clinical Immunology, 27-30th January 2022

Sokolowska M. Effects of microbiota on immune response in allergy prevention and therapy. EAACI/FOCIS Webinar and Sister Symposium, 30th May 2022

Sokolowska M. SYM 2 - Novel avenues of immunology in post-COVID era. European Academy of Allergy and Clinical Immunology (EAACI) Hybrid Annual Congress, Prague, Czech Republic, 1-3 July 2022

Sokolowska M. SYM 3 - Innate immune system in the mucosal diseases. European Academy of Allergy and Clinical Immunology (EAACI) Hybrid Annual Congress, Prague, Czech Republic, 1-3 July 2022

Sokolowska M. FT 12 - Flash Talks on primary immunodeficiencies, infection and allergy. European Academy of Allergy and Clinical Immunology (EAACI) Hybrid Annual Congress, Prague, Czech Republic, 1-3 July 2022

Sokolowska M. Session 6 Medicine & Life Sciences. 8th Congress Graubünden Forscht. Academia Raetica, Davos, Switzerland, 21-22 September 2022

Sokolowska M. Sym13: vaccine or vaccine hesitancy. World Allergy Congress, Istanbul, Turkey, 13-15 October 2022

Sokolowska M. PAS12: COVID-19-II. World Allergy Congress 13-15 October 2022, Istanbul, Turkey

Sokolowska M. Lifestyle and Environmental Changes and new allergens, EAACI ISMA-Rhina Digital, 4-5 November 2022

Van de Veen W. B cell responses and immune tolerance. World Immune Regulation Meeting (WIRM) XVI, Davos, Switzerland, 6-9 July 2022

Van de Veen W. Biologicals and molecular aspects in diagnosis and treatment. World Immune Regulation Meeting (WIRM) XVI, Davos, Switzerland, 6-9 July 2022

van de Veen W. on Epithelial Barriers and Microbiome. EAACI Summer Symposium on Epithelial Barriers and Microbiome. Davos, Switzerland. 28 - 29 July 2022

van de Veen W. Novel interactions between the epithelial barriers and microbiome. EAACI Summer Symposium on Epithelial Barriers and Microbiome. Davos, Switzerland. 28 - 29 July 2022

van de Veen W. COVID-19-I. World Allergy Congress (WAC) 2022. Istanbul, Turkey, 13-15 October 2022

Yasutaka M, Infections, microbiome and metabolism. WIRM 2022, Davos, Switzerland, 6-9 July 2022

Yasutaka M, T-cells in immune response. WIRM 2022, Davos, Switzerland, 6-9 July 2022

Yasutaka M, Models of epithelial barrier and microbiome. EAACI Summer symposium on epithelial barriers and microbiome 2022, Davos, Switzerland, 28-29 July 2022

Zhakparov D. Assesing Different Feature Selection Methods Applied to a Bulk RNA Serquencing Dataset with Regard to Biomedical Relevance. European Conference on Machine Learning and Principles and Practice of Knowledge Discovery in Databases (ECML-PKDD), Grenoble, France, 19 - 23 September 2022

Zhakparov D, Moriarty K, Schmid M, Roqueiro D, Baerenfaller K, SOS-ALL Consortium. Machine Learning Reveals Patterns in Transcriptomics and Clinical Datasets Associated with Atopic Dermatitis in African Children. WIRM, Davos, Switzerland, 6 - 9 July 2022.

LECTURES

Lectures at University of Zurich

Akdis C.
BCH301. Antibodies/B cells
BCH301. T cell receptors and MHC molecules

BCH301 Immune tolerance and immune regulation; Hypersensitivity reactions
BME351 Block course "Biomedical Data Mining"-lectures, seminars, workshops
Immunology Lectures SIAF

Akdis M.
BCH301. Antibodies/B cells
BCH301. T cell receptors and MHC molecules

Baerenfaller 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, 6 ECTS
636-0704-00L Computational Biology and Bioinformatics Seminar (ETH Zurich), duration: 2 hours
LSZGS, Lecture in 'Advanced Block Course: Computational Biology' of the Life Science Zurich Graduate School; Topic: Large data sets: Transcriptomics and Proteomics; duration: 3 hours
ETHZ: 636-0704-00L Computational Biology and Bioinformatics Seminar (ETH Zurich), duration: 2 hours
FHGR: CDS303 Data Science und Informatik in der Biologie, 4 ECTS

Mitamura Y.
In depth analyses of the pathogenesis of atopic dermatitis by spatial and single cell sequencing technologies, biomedicine seminar 2022, Zurich, Switzerland, 29 March 2022

Sokolowska M.
BCH301 Immune tolerance and immune regulation; Hypersensitivity reactions
BME351 Block course "Biomedical Data Mining"-lectures, seminars, workshops
Immunology Lectures SIAF

van de veen W.
BME 366 – Medical Immunology Course. Allergy Component. University of Zurich. 22.02.2022-16.03.2022

AWARDS

Akdis C. Jack Peppy's honorary Lecture: British Society of Allergy Clinical Immunology

Akdis C. APAACI award: Asia Pacific Society of Allergy Asthma Immunology. life time achievement award

Akdis C. Allergy Journal selected to top 10 Journals of Wiley out of 1700 Journals

Akdis C. Most Downloaded papers of wiley, 2 papers from SIAF

Akdis M. Schneider Stephen a member of immune regulation group. Received SIAF Science Day Award 1st Place. SIAF science day in Davos, Switzerland, 9. December 2022

Koch J. BioLegend Best Workshop Presentations Award. WIRM 2022, Davos, Switzerland, 6-9 July 2022.

Koch J. SIB days poster prize. SIB days, Biel, Switzerland, 14-15 June 2022.

Schneider S. SIAF Science Day Award 1st Place. SIAF science day in Davos, Switzerland, 9. December 2022

Sokolowska M. Distinguished Reviewer Award, Allergy, European Journal of Allergy and Clinical Immunology

Van de Veen W. Top Reviewer award 2022. Allergy - European Journal of Allergy and Clinical Immunology.

Wallimann A. Best Workshop Presentation. WIRM 2022, Davos, Switzerland, July 6-9, 2022.

DEGREES

Jansen K. PhD defense: The plasticity of T regulatory cells during human rhinovirus infection. University of Zurich, Switzerland. 19 May 2022.

Pat Y. Specialization in Medical Microbiology: Investigation of The Effect of Some Short Chain Fatty Acids Related to Probiotics on Respiratory Epithelial Barrier Function. Aydin Adnan Menderes University, Turkey. 12 May 2022.

Radzikowska U. PhD defense: Effects of house dust mite stimulation on inflammasome activation in human bronchial epithelium in asthma after rhinovirus infection. Medical University of Bialystok, Poland. 18 November 2022.

Sokolowska M. Habilitation in Immunology, Allergology and Pulmonology (Venia Legendi, PD): Eicosanoid signaling and regulation of NLRP3 inflammasome activation in the pathogenesis of severe asthma. University of Zur-ich, Switzerland. 30 March 2022.

Wallimann A. PhD defense: The Gut Microbiota and Bone: Microbial-Derived Components and Metabolites That Mediate Effects on Bone Health. University of Zurich, Switzerland. 11 April 2022.

PUBLIC SEMINARS

16.06.2022

Snitman J. "Advanced pulmonary in vitro platforms for ventilation & inhalation assay"

07.09.2022

Eidsmo L. The formation and function of resident T cells in human healthy and diseased skin.

Gyrd-Hansens M. Ubiquitin as a signalling platform in inflammation and immunity.

26.09.2022

Thyssen J. P. A mixed bag of AD studies from Copenhagen

28.07.2022 + 29.07.2022

SIAF Summer Symposium

Von Mutius E. The Hygiene Hypothesis

Shamji M. Innate immune cell interaction with tissue cells

Akdis CA The Epithelial Barrier Hypothesis

Elinav E. Molecular control of the gut epithelial barrier integrity

Gudmundsson G.H. Inducers of Host Defense Peptide expression improve the epithelial barrier integrity

Garn H. Side-directed release of differentially loaded extracellular vesicles by bronchial epithelial cells of healthy and asthmatic subjects

Gardarsson Fridrik R. Barriolides: Novel macrolides with epithelial barrier modulating properties but lacking antimicrobial potency

Kleuskens M. Activated human mast cells impair esophageal barrier: role of a possible bidirectional crosstalk

Kezic S. Nano-mechanical properties of corneocytes and skin barrier

Ruben D.G. Crosstalk between intestinal epithelial barrier and microbiota-derived shortchain fatty acids in the context of food allergy

Hideaki M. Inhaled laundry detergents induce eosinophilic airway inflammation through IL-33 and ILC2 activation

Ögülür I. Gut epithelial barrier damage caused by commonly used emulsifiers polysorbate-20 and
polysorbate-80

Zuurveld M. Ovalbumin induced epithelial activation directs moDC to instruct type 2 inflammation in Th cells which is differentially modulated by 2'FL and 3FL

Pat Y. Differentiation of bronchial epithelial spheroids in the presence of IL-13 recapitulates characteristic features of asthmatic airway epithelia

Mitamura Y. Single-cell seq, visium spatial seq, imaging mass cytometry and targeted proteomics for the investigation of atopic dermatitis lesions

Morelli M. An organ-on-a-chip screening platform to evaluate the intestinal epithelial response to microbial toxins and identify potential modulators

Yazici D. High Throughput Investigation of Epithelial Barrier Affecting Compounds with Gut-on-a-chip System

Afghani J. New Developments in Eczema Research: Skin Metabolome Sampling and Skin Bacterial Secretions; Oxygen Exposure and pH Stability

Rick E.M. Molecular Allergology between precision medicine and elucidation of pathomechanisms

Sindher S. B. Identification of Skin Epithelial Barrier Defects Using Nevisense Go

Roduit C. The use of electrical impedance spectroscopy to identify skin barrier impairment in children with atopic dermatitis

Zaiss M. Gut barrier and rheumatoid arthritis

Nadeau K. Immune response in epithelial barrier leaky individuals

Martens K. Epithelial barrier dysfunction contributes to mast cell degranulation and neutrophilic airway inflammation in vivo

Pospich R. T cells specific to skin bacteria are clonally propagated in lesional atopic dermatitis skin and mount a Th1 response

Traidl-Hoffmann C. Microbiome and epithelial barriers

Trompette A. Gut-derived short-chain fatty acids modulate skin barrier integrity by promoting keratinocyte metabolism and differentiation

Wenning A. S. The maternal microbiota drives embryonic epidermal formation and sets neonatal skin barrier

Annesi-Maesano I. Air pollution asthma and allergy in the exposome era

Jutel M. Asthma and the impact of biological treatments on microbiome and epithelial barrier

Himly M. Immune impact of particulates combined with biological matter at human alveolar epithelia

Hofer S. Direct SARS-CoV-2 inoculation of epithelia in the pulmonary alveolar region and the inflammatory response in COVID-19: Challenging the top-down virus migration and disease progression hypothesis

Raith M. The effects of environmental factors and nasal fluid on Bet v 1, the major birch pollen allergen

Sokolowska M. Epithelial cell responses in COVID-19 and rhinovirus infections

Pawankar R. Epithelial cells and chronic rhinosinusitis

Ögülür I. Novel biomarkers of disrupted gut permeability in severe COVID-19 patients

Golebski K. Dysregulated barrier function of nasal epithelium from long-COVID-19 patients: results of the Precision Medicine for more Oxygen-COVID-19 study

Radzikowska U. Rhinovirus-induced epithelial RIG-I inflammasome activation suppresses antiviral immunity and promotes inflammatory responses in virus-induced asthma exacerbations and COVID-19

Makrinioti H. Early wheeze relapse following a first wheezing episode is associated with peripheral blood MxA levels

Renz H. Models of epithelial barrier and microbiome

Palomares O. Novel molecular regulation of dendritic cells, microbiome and epithelial barriers

Chałubiński M. The effect of epithelium-derived alarmins IL-33, IL-25 and TSLP on the rhinoviral and coronaviral infections of the human lung vascular endothelium

Hülpüsch C. Skin microbiome and pH are associated with the development of severe radiodermatitis

Morel L. Interaction between the microbiome, epithelial cells and immune cells in the context of allergic airway inflammation

SIAF SCIENCE DAY

14.12.2022

Fieten K. Altitude Alpine Climate Treatment (AACT) for severe and uncontrolled asthma.

Radzikowska U. Usta usta with inflammasome.

Koch J. Investigating Th1 cells.

Barletta E. A Proteomic Special Winter Edition Quest

Chang I. Distinct gene expression profiles of G-Protein-Coupled Receptors on B cell subsets.

Schneider S. S. I. A. F.: Mission AI-ergen.

Alberch L. Nightmare before Christmas: Allergy.

Lopez J. All I want for Christmas is...Ascaris?!

Bel imam M. Discovering soluble biomarkers in EoE: are we getting closer.

Wawrocki S. Winter expedition and search for survivors/cells (delete as appropriate)

Yazici D. A story of the epithelium

Pat Y. The uncanny tale of the planet 0

Satitsuksanoa P. Tahe mysterious path of B cells beyond the horizontal.

Yang M. Winnie and friends: Winter role-playing game.

Zhakparov D. A Christmas Tale on Feature Selection.

Winner of the SIAF Sciene Day 2022: Stephan Schneider

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

Member of Collegium Internationale Allergologicum (CIA),

Member of European Academy of Allergy Clinical Immunology (EAACI),

Member of WP.1 in EU project

Scientific program Chair of EAACI

Baerenfaller K.
Group leader of the Swiss Institute of Bioinformatics (SIB)
Member of the SIB Board of Directors
Member of LS2, President of the LS2 Bioinformatics intersection
Member of European Reference Genome Atlas (ERGA)
Member of EAACI (European Academy of Allergy & Clinical Immunology)
Board member of Science City Davos
Editor of the Frontiers in Immunology Research Topic "Systems Biology Approach to the Immunology of Asthma and Allergy"

Messner C.
Review activity for Nature communications

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
Programme committee member, the Graduate School Graubunden, Graubünden Forscht 2022 Congress. Academia Raetica
Member of the scientific committee, World Immune Regulation Meeting 2022
Secretary of the scientific committee, European Academy of Allergy and Clinical Immunology (EAACI) Immunology Winterschool 2022
Member of the scientific committee, European Academy of Allergy and Clinical Immunology (EAACI) Summer Symposium on Epithelial Barriers and Microbiome
Expert Reviewer for Grant agencies: Medical Research Council, UK Research and Innovation (MRC-UKRI), German Research Foundation ("Deutsche Forschungsgemeinschaft", DFG), Estonian National Research Foundation
Heliyon, Cell Press, Associate Editor
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.
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

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

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

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

National and international collaborations

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 MD, 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 Researchgroup (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

Schweizerisches Institut für Allergie- und Asthmaforschung

Bilanz per 31. Dezember 2022

(inklusive Drittmittel)

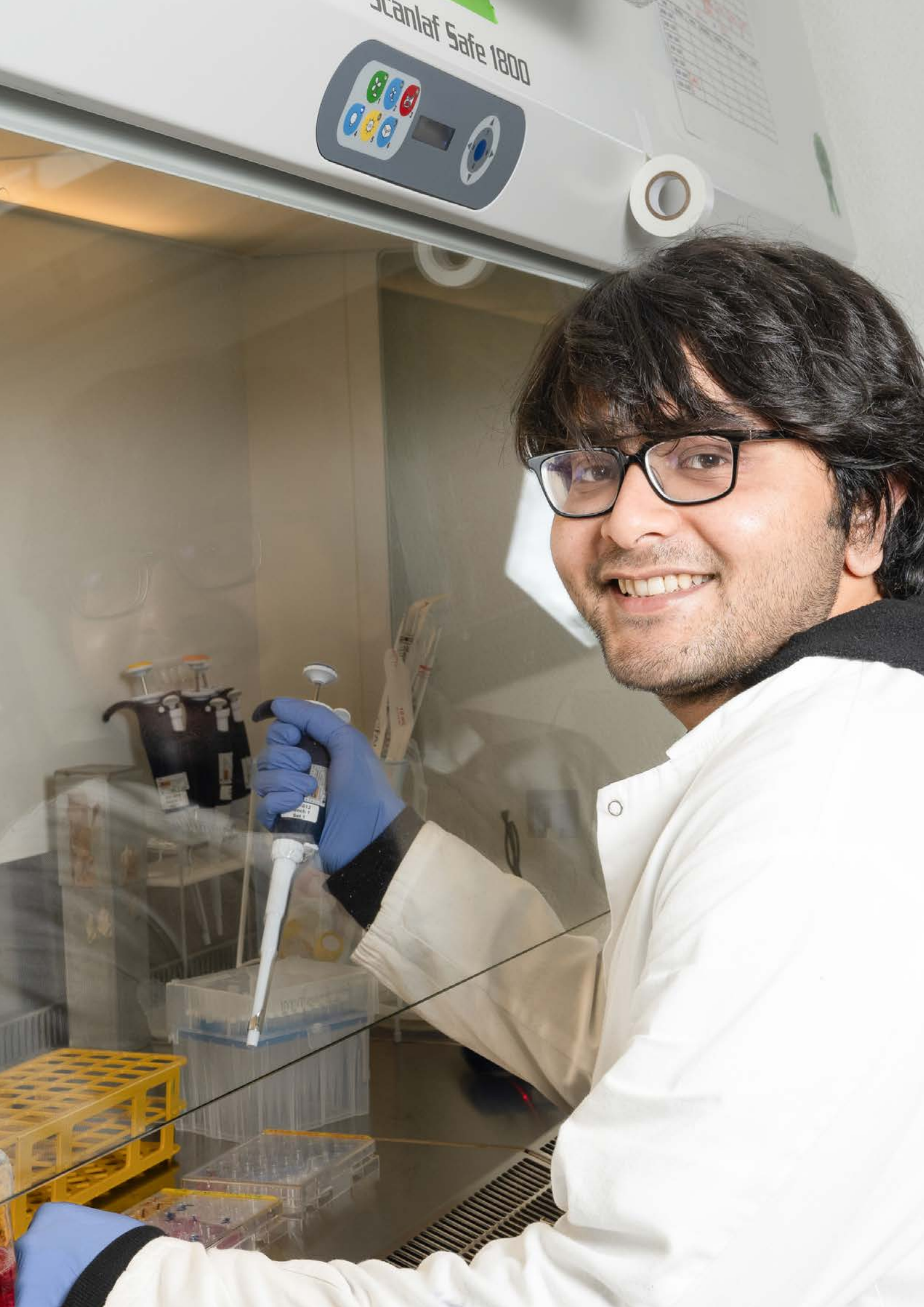
	31.12.2022	31.12.2021
	CHF	CHF
AKTIVEN		
Flüssige Mittel	1’817’392.46	1’540’605.87
Forderungen	187’894.99	83’477.54
Übrige kurzfristige Forderungen	40’708.24	27’637.60
Aktive Rechnungsabgrenzungen	217’552.34	293’039.90
	2’263’548.03	1’944’760.91
PASSIVEN		
Verbindlichkeiten	134’202.58	78’315.34
Kontokorrent SFI Stiftung	18’360.20	38’721.45
Übrige kurzfristige Verbindlichkeiten	16’628.95	15’721.45
Passive Rechnungsabgrenzungen	1’718’121.80	1’313’409.13
Rückstellungen	195’700.27	278’437.73
Eigenkapital	180’534.23	220’155.81
	2’263’548.03	1’944’760.91

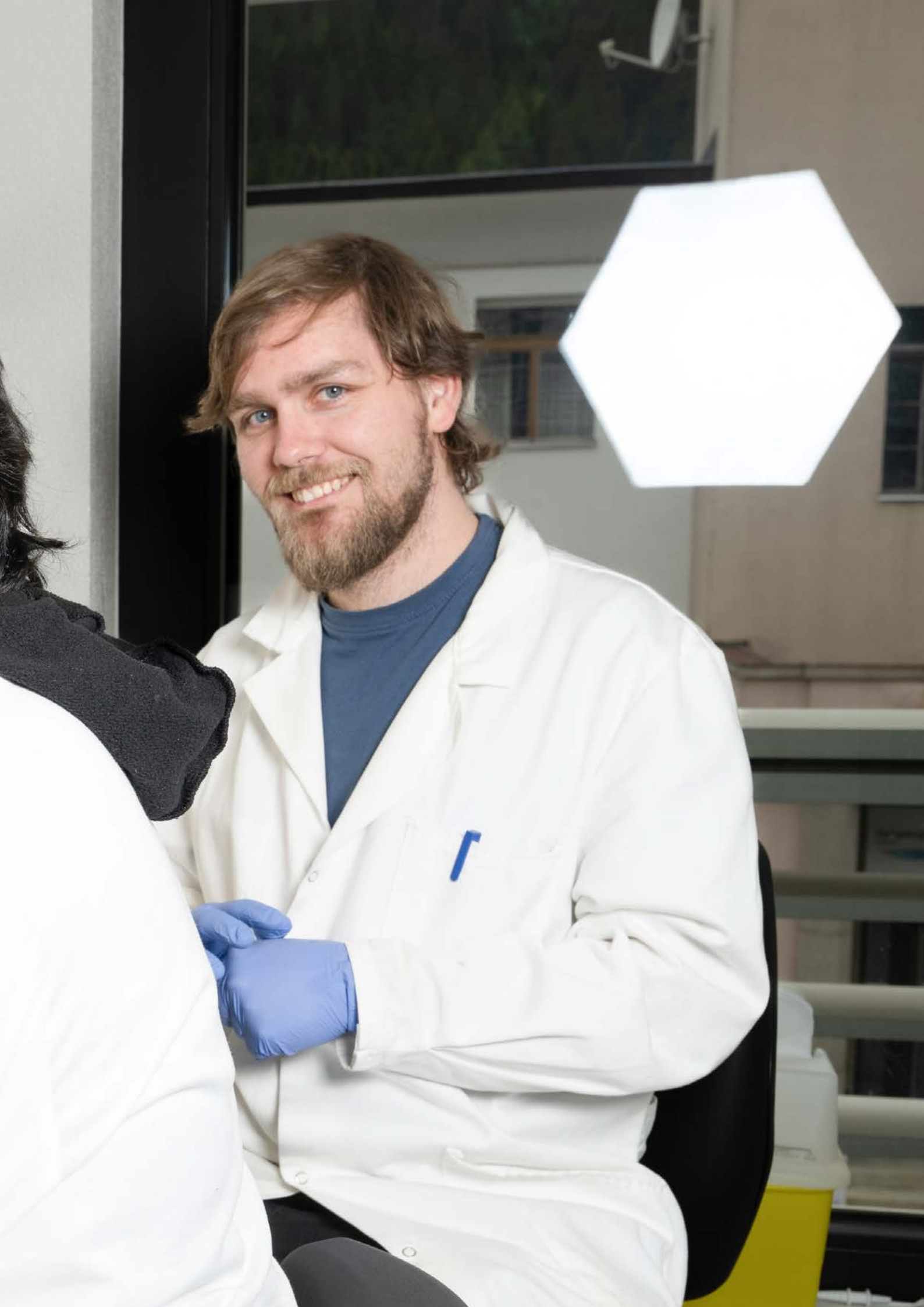
Schweizerisches Institut für Allergie- und Asthmaforschung

Betriebsrechnung 2022

(inklusive Drittmittel)

	Rechnung 2022	Budget 2022	Rechnung 2021
	CHF	CHF	CHF
ERTRAG			
Beitrag Bund Forschungsgesetz Art. 15	1’299’600.00	1’299’600.00	1’290’600.00
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	371’517.10	369’688.00	382’258.60
Beitrag Stiftung SFI	120’000.00	180’000.00	98’381.40
Beitrag Stiftung vormals Bündner Heilstätte Arosa	56’971.00	53’155.00	57’546.00
Beitrag Stiftungen/Drittmittel	154’108.25	0	158’261.85
Overheadbeiträge	132’558.00	112’830.00	0
Übriger Ertrag	14’958.95	3’000.00	3’759.20
Finanzertrag	0	0	257.10
Ausserordentlicher Ertrag	35’341.93	20’000.00	3’787.65
Auflösung von Rückstellungen	82’737.46	0	202’640.87
WIRM-Kongress	236’138.98	300’000.00	106’173.85
Drittmittel	2’591’731.69	2’988’935.00	2’066’611.90
	6’140’223.36	6’371’768.00	5’414’838.42
AUFWAND			
Personalaufwand	3’404’220.40	3’467’048.00	2’954’847.60
Verbrauchsmaterial	1’339’332.18	1’469’685.00	1’015’551.92
Raumaufwand	357’423.88	325’000.00	349’681.44
Unterhalt/Reparaturen/Ersatz	326’148.28	362’335.00	241’010.60
Investitionen	66’561.80	50’000.00	296’613.51
Sachversicherungen/Abgaben	9’735.00	10’000.00	9’935.75
Energie- und Entsorgungsaufwand	161’240.34	120’000.00	132’575.24
Verwaltungsaufwand	95’282.94	99’500.00	92’050.85
Werbeaufwand	10’938.61	0	5’982.15
Reisespesen	80’890.67	50’000.00	38’004.43
WIRM-Kongress	195’395.23	300’000.00	119’297.20
Übriger Betriebsaufwand	8’545.46	11’000.00	1’935.79
Abschreibungen	105’200.00	105’200.00	105’200.00
Finanzaufwand	18’561.58	1’000.00	9’518.60
Bildung von Rückstellungen	0	0	23’459.65
Ausserordentlicher Aufwand	368.57	1’000.00	19’173.69
	6’179’844.94	6’371’768.00	5’414’838.42
Ergebnis	- 39’621.58	0	0


Scanlaf Safe 1800



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