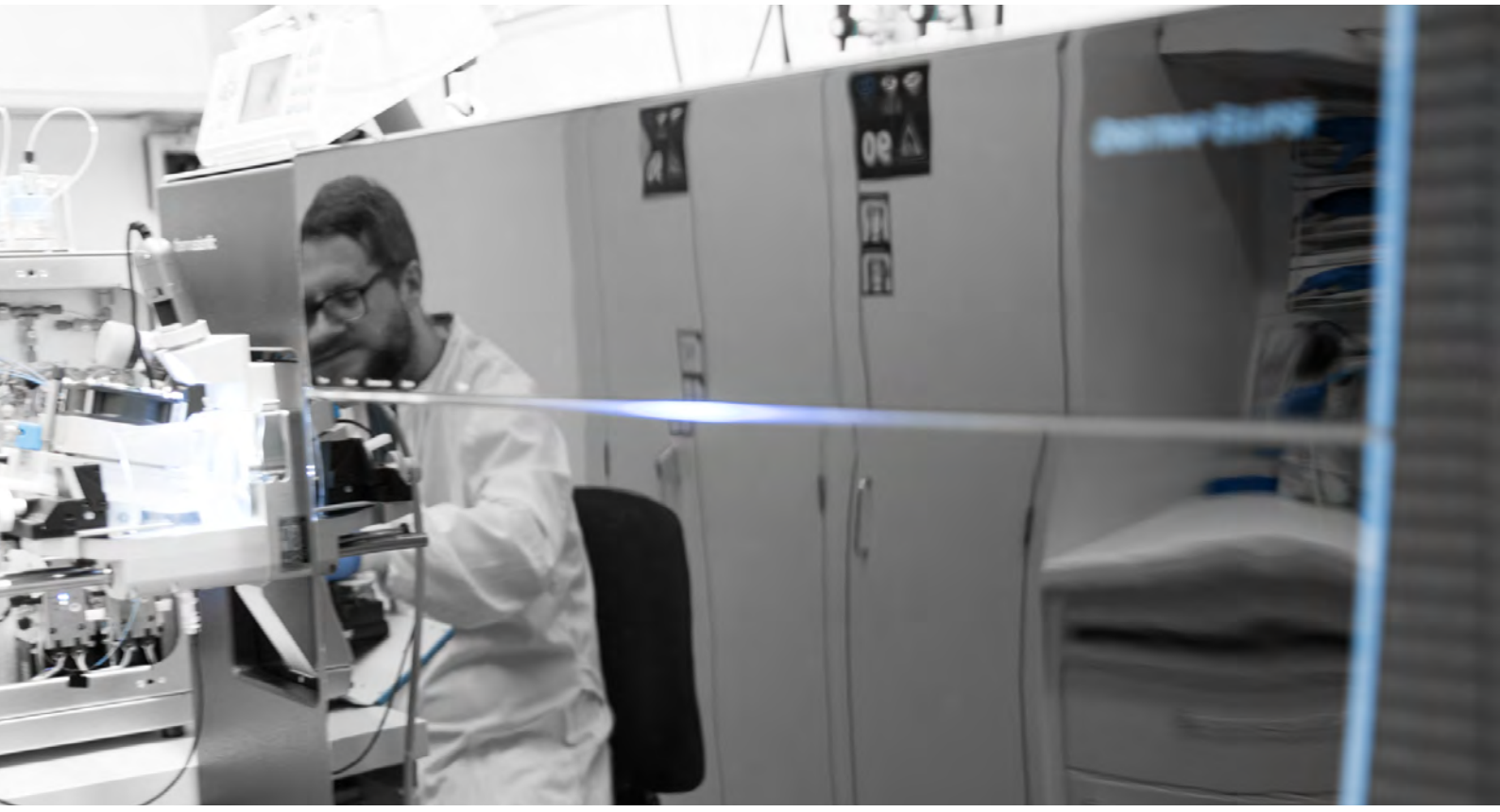
SIAF

Swiss Institute of Allergy and Asthma Research

ANNUAL REPORT 2021



University of Zurich[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. med. Cezmi A. Akdis

Das Schweizerische Institut für Allergie- und Asthmaforschung (SIAF) in seiner heutigen Form wurde 1988 von der Medizinischen Abteilung der Stiftung Schweizerisches Forschungsinstitut für Hochgebirgsklima und Medizin Davos (SFI) gegründet. 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.

Mit einem epidemischen Anstieg während der letzten sechs Jahrzehnte leidet mehr als 1 Milliarde Menschen an Nahrungsmittelallergien, Asthma, atopischer Dermatitis und allergischer Rhinitis mit einer Prävalenz von etwa 1,8 Millionen (23% der Bevölkerung) in der Schweiz. Lebensmittelallergien sind in Europa und den USA weit verbreitet und betreffen bis zu 10% der pädiatrischen Bevölkerung und 1-3% der erwachsenen Bevölkerung.

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.

2021 wurden 103 wissenschaftliche Arbeiten in begutachteten internationalen Fachzeitschriften mit “Impact Factor” veröffentlicht oder sind noch in Druck. 2021 erreichte das SIAF einen Gesamtwert des “Impact Factors” von 1'160.081 und einen Durchschnitt von 11.263 Punkten pro Publikation. Die neusten Ergebnisse wurden zudem in 28 Abstracts an verschiedenen Fachtagungen mitgeteilt. Unsere Mitarbeitenden wurden zu 105 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 28 verschiedenen Sessionen hatten SIAF-Mitarbeitende den Vorsitz. Zusätzlich übernehmen SIAF-Mitarbeitende 54 wissenschaftliche Ämter in internationalen Gesellschaften und internationalen Zeitschriften. Zudem hält Prof. C. A. Akdis seit 2018 das Amt des Chefredaktors der Fachzeitschrift Allergy inne. Als Folge seiner international höchst angesehenen wissenschaftlichen Publikationen wurde Prof. Dr. C. A. Akdis 2021 zum sechsten Mal von Thomson Reuters Clarivate in die Gruppe der meistzitierten Forscher aus allen wissenschaftlichen Fachbereichen weltweit aufgenommen. Das SIAF hat rund 1'540 Fachbeiträge veröffentlicht und gehört zu den meistzitierten Instituten weltweit. Die vom SIAF publizierten Artikel wurden 64'000 Mal zitiert.

Mit der Eröffnung des Medizincampus Davos Wolfgang 2019 wurde ein Meilenstein gesetzt. Mit den eigenständigen Partnern CK-CARE AG, HGK, Davos BioSciences AG und Cardio Care AG besteht eine sehr enge Zusammenarbeit. Die zusammen erarbeiteten Resultate kommen direkt in Therapie und Klinik zur Anwendung. So profitieren die Patienten von der translationalen Allergie- und Kardio-Forschung auf dem Campus, da die Behandlung jederzeit auf dem aktuellen Stand der wissenschaftlichen Erkenntnis ist. Ebenfalls im Campus beheimatet ist die von der Kühne-Stiftung geförderte Stiftungsprofessur, mit der gleichermassen im Bereich der bildgebenden Methode zur Analyse von Oberflächenmarker von Zellen im Gewebe eng zusammengearbeitet wird. Dank der Unterstützung durch die CK-CARE konnten seit 2009 mehr als 55 wissenschaftliche Mitarbeitende eingestellt und über 85 akademische Gäste im Austauschprogramm aufgenommen werden. Darüber hinaus wurden fast 330 Publikationen mit der institutionellen Zugehörigkeit des SIAF und der CK-CARE in namhaften Zeitschriften veröffentlicht.

Die Hypothese der epithelialen Barriere bietet ein umfassendes Verständnis der Entstehung von allergischen und anderen chronischen, nicht übertragbaren Krankheiten

Eine kürzlich durchgeführte weltweite Bestandsaufnahme ergab, dass mehr als 350'000 Industriechemikalien und -gemische für die Produktion registriert wurden und die meisten von ihnen als Schadstoffe in die Umwelt gelangen. Professionelle Geschirrspülmaschinen, verpackte Lebensmittelkonservierungsmittel und Emulgatoren, Waschmittel und Tenside, Feinstaub und Mikroplastik sollten die Hauptziele sein, um den Zustand der Welt und die Gesundheit von Mensch und Haustier zu verbessern.

Die Prävalenz vieler chronischer, nicht übertragbarer Krankheiten ist in den letzten 60 Jahren stark angestiegen und hat ein pandemisches Ausmass angenommen. Unsere Forschungen und Bemühungen, die Gründe für diesen Anstieg der Prävalenz zu erklären, haben zur Entwicklung der Epithelbarriere-Hypothese beigetragen. Die Epithelbarriere-Hypothese besagt, dass die Störung der Epithelbarrieren durch Wasch- und Geschirrspülmittel, Haushaltsreiniger, Tenside, Enzyme und Emulgatoren, die in der Lebensmittelindustrie verwendet werden, Zigarettenrauch, Feinstaub, Dieselabgase, Ozon, Nanopartikel und Mikroplastik zu Gewebeentzündungen und mikrobieller Dysbiose führen und eine Rolle bei vielen chronischen nicht übertragbaren Krankheiten spielen. Es ist notwendig, die Wissenschaft zu unterstützen und das Verständnis der Faktoren und molekularen Mechanismen, die mit undichten Epithelbarrieren in Verbindung gebracht werden, voranzutreiben und die politischen Entscheidungsträger über die schädlichen Auswirkungen der potenziell ursächlichen oder mitwirkenden Substanzen zu informieren.

Unsere Forschungen zu den epithelialen Barrieren begannen 1998 mit wichtigen Beiträgen und der Entwicklung der Epithelialbarriere-Hypothese. Diese Beiträge können als Hauptforschungstitel aufgelistet werden: Mechanismen des Absterbens von Haut- und Lungenepithelien und des Ekzems in der Haut und der Epithelablösung in der Lunge; Interaktion des Immunsystems mit Epithelzellen; Öffnung der Epithelbarrieren durch Zellen des Immunsystems und

Zytokine; Schädigung von Epithelzellen; Öffnung der Epithelbarrieren durch Detergenzien, Feinstaub, Tenside, Emulgatoren und Konservierungsmittel in verpackten Lebensmitteln.
Es gibt genügend epidemiologische Beweise beim Menschen und in Krankheitsmodellen, die zeigen, dass selbst Spuren von Stoffen, die derzeit als sicher gelten, die Epithelbarrieren schädigen und die Übertragung von Bakterien verstärken können. Bestimmte Bevölkerungsgruppen können aufgrund genetischer Faktoren einem höheren Risiko ausgesetzt sein. Daher kann der Verzicht auf diese Stoffe dazu beitragen, das Auftreten oder den Schweregrad bestimmter chronischer, nicht übertragbarer Krankheiten zu verringern. Zu den Strategien zur Verringerung von Krankheiten, die mit einer gestörten Epithelbarriere in Verbindung gebracht werden, gehört eine reduzierte Exposition oder die vollständige Vermeidung dieser möglicherweise ursächlichen Stoffe. Darüber hinaus könnte die Hypothese der Epithelschranke die Bedeutung eines wirksameren Screenings neuer, im täglichen Leben verwendeter Chemikalien aufzeigen, die Entwicklung sichererer Produkte anregen und die Identifizierung von Biomarkern zur Ermittlung und Überwachung von Personen mit dem Risiko einer Barrierestörung vorantreiben. Schliesslich sind Studien zur Entwicklung von präventiven oder therapeutischen Ansätzen mit Interventionen durch Änderungen der Lebensweise, der Ernährung und des Mikrobioms erforderlich.

Regulierung der Immunantwort durch antigenspezifische regulatorische B-Zellen und B-Gedächtniszellen
Asthma, atopische Dermatitis, Rhinitis und Nahrungsmittelallergien stellen mit einer Gesamtprävalenz von ca. 1,8 Millionen Patienten in der Schweiz ein grosses und stetig wachsendes Problem der öffentlichen Gesundheit dar. Nahrungsmittelallergien sind in Europa und den USA mit einer Prävalenz von bis zu 10% in der pädiatrischen Bevölkerung und 1-3% in der erwachsenen Bevölkerung weit verbreitet.
In den letzten Jahrzehnten hat diese Forschungsgruppe zusammen mit anderen Forschungsgruppen beträchtliche Fortschritte im Verständnis der Allergenverträglichkeit erzielt. Die IgE-vermittelte Allergie ist eine Typ-2-Immunantwort, die für die meisten Merkmale der allergischen Entzündung verantwortlich gemacht wird. Klinische Anzeichen einer Nahrungsmittelallergie werden nach der Aufnahme des Nahrungsmittels beobachtet und umfassen gastrointestinale Symptome, Urtikaria, Keuchen und in schweren Fällen eine systemische Anaphylaxie. Ein wichtiges Instrument zur Untersuchung des genetischen und umweltbedingten Einflusses auf komplexe Phänotypen allergischer Erkrankungen, wie z. B. Nahrungsmittelallergien, ist die detaillierte Untersuchung der Immunantwort zwischen diskordanten und konkordanten eineiigen und zweieiigen Zwillingen. Zwillingsstudien haben gezeigt, dass die Familienanamnese ein starker Risikofaktor für die Entwicklung von Allergien ist, was darauf hindeutet, dass die genetische Prädisposition wichtig ist, wenn auch nicht der einzige Faktor, der eine Rolle spielt. Dieser Ansatz bei zweieiigen Zwillingen schliesst einen Grossteil der umweltbedingten Verzerrungen aus, da Zwillingspaare im Allgemeinen einer ähnlichen Umwelt ausgesetzt sind. Parallel dazu wird die Untersuchung von diskordanten eineiigen Zwillingen Aufschluss über die Rolle von nicht-genetischen Faktoren geben. Solche Studien bei Nahrungsmittelallergien werden es ermöglichen, die genetischen und umweltbedingten Ursachen für allergenspezifische Immunantworten abzuschätzen, was bisher noch nicht durchgeführt wurde.

Immunologischer und molekularer Fingerabdruck von Krankheiten mit chronischer Atemwegseinschränkung: Asthma und chronisch obstruktive Lungenerkrankung
Chronisch obstruktive Atemwegserkrankungen sind weltweit für erhebliche Morbidität, Mortalität und Kosten im Gesundheitswesen verantwortlich. Konventionell wird davon ausgegangen, dass Asthma und COPD unterschiedlich sind, und in den Leitlinien werden unterschiedliche Behandlungsansätze empfohlen. In Wirklichkeit überschneiden sich die beiden Krankheiten jedoch erheblich. Auch wenn Asthma und COPD immer noch als zwei unterschiedliche obstruktive Atemwegserkrankungen angesehen werden, haben beide Krankheiten eine Komponente der Epithelfehlfunktion der Atemwege gemeinsam.
Es gibt mehrere Möglichkeiten, wie Umweltfaktoren auf die Epithelbarriere einwirken. Luftschadstoffe, Zigarettenrauch, Allergene, Viren, Bakterien und bakterielle Toxine sowie andere Partikel interagieren ständig mit den Epithelzellen der Atemwege und induzieren 1.) spezifische Stoffwechselveränderungen in diesen Zellen, 2.) dringen in das Epithel ein, 3.) führen zu einer Undichtigkeit der Barriere und 4.) aktivieren die Zellen des Immunsystems, was zu schweren chronischen Entzündungen führt. Kürzlich wurde von uns und anderen gezeigt, dass ein Defekt der Epithelbarriere eine wichtige Rolle in der Pathogenese dieser Krankheiten spielt.
Aufgrund der einzigartigen Kombination aus neuartiger Methodik, die in unserer Studie angewandt wird (systembiologischer Ansatz - Sequenzierung der nächsten Generation, Proteomik, Metabolomik, Mikrobiom-Sequenzierung, Mehrfarben-Durchflusszytometrie, Zellsortierung und konfokale Mikroskopie) und sehr gründlichen klinischen Merkmalen der Studienteilnehmer sowie der invasiven Diagnosemethoden erwarten wir: die Charakterisierung neuer Untergruppen von Asthma- und COPD-Patienten mit unterschiedlichen zugrundeliegenden epithelialen Barrierestörungen, die Unterscheidung der Biomarker verschiedener Endotypen von Asthma und COPD, Vorschläge für molekulare Ziele für neue Therapien im Epithel der Atemwege und die Beobachtung der Entwicklung der Endotypen während der Behandlung.

Profilfeld 5 – Life Science
Mit dem Entscheid der Regierung des Kantons Graubünden vom 5. September 2020 dem SIAF den Auftrag «...vom 1. August bis zum 31. Juli 2026 ein Zentrum für Proteomik mittels einer Sonderprofessur für das Profilfeld «Life Science» gemäss eingereichtem Konzept als «Leading House» ... aufzubauen und zu betreiben...» zu erteilen, konnte das Zentrum für Präzisions-Proteomik die nötigen Investitionen tätigen und den Betrieb aufnehmen. Die im eingereichten Konzept formulierte Forschungsausrichtung beruht einerseits in der Etablierung vor allem lokaler, aber auch nationaler und internationaler Kollaborationen zur Planung und Durchführung von Proteomik-Experimenten, und andererseits in der Umsetzung von Massenspektrometrie-Studien in SIAF-relevanten Themenfeldern.
Bei der Kollaboration mit lokalen Gruppen wurden zwei Pilotprojekte zusammen mit Forschenden aus dem AO Forschungsinstitut in Davos durchgeführt, wovon eines nun in die Projektphase

übergeht. Zusammen mit Prof. Dr. P. Schmid-Grendelmeier vom Universitätsspital Zürich und Prof. Dr. MC Brüggen von CK-CARE, dem Universitätsspital Zürich und der Hochgebirgsklinik Davos konnten wir erfolgreich ein Projekt bei LEO Pharma einreichen, im dem Massenspektrometer-Messungen eine grosse Rolle spielen werden, und das im Jahr 2022 starten wird. International konnten wir die Zusammenarbeit mit der Gruppe von Prof. Dr. O. Schilling von der Universität Freiburg in Deutschland weiterführen. Zudem laufen Projekte vor allem in der Forschungsgruppe Molekulare Allergologie am SIAF, in denen zum einen spezifisch nach allergenen Proteinen gesucht wird, die bei Nahrungsmittelallergien eine Rolle spielen, und zum anderen Anreicherungs- und Dektektionsmethoden zur Identifikation posttranslational modifizierter Proteine angewandt werden. Für die Interim Projekt-Leitung vor der Besetzung der Non-tenure-track Assistenzprofessur durch die Medizinischen Fakultät der Universität Zürich, die mit der Sonderprofessur im Profilfeld 5 verknüpft wurde, wurden Prof. Dr. C. Akdis und PD Dr. K. Bärenfaller eingesetzt. Die Assistenzprofessur wurde im Mai 2021 durch die Medizinische Fakultät ausgeschrieben, und nach der Empfehlung der Berufungskomission laufen momentan die Berufungsverhandlungen.

Computational Science - COVID-19

Im Jahr 2021 wurde in Zusammenarbeit zwischen der Fachhochschule Graubünden (FHGR) und dem SIAF intensiv an den Daten von Patientinnen und Patienten vom COVID-19-Spital in Zgierz, Polen, gearbeitet. Durch PD Dr. M. Sokolowska vom SIAF hatten wir Kontakt zu Ärztinnen und Ärzten in diesem Spital und ihren medizinischen Fragestellungen:

1) Kann man anhand der medizinischen Vorgeschichte und der Laborwerte früh eine Diagnose machen, ob ein Patient, eine Patientin SARS-CoV-2 positiv ist?

2) Kann man anhand der medizinischen Vorgeschichte und der Laborwerte eine Prognose zum Verlauf von COVID-19 machen?

Zusätzlich zu diesem Projekt wurde die DAViS-Expertise in der Analyse von biomedizinischen Daten in diversen kollaborativen Projekten mit Forschenden aus dem SIAF, dem AO Forschungsinstitut und dem Swiss Research Institute for Sports Medicine (SRISM) eingebracht, und verschiedene Manuskripte werden vorbereitet oder wurden bereits eingereicht. Ein weiteres Projekt war in Zusammenarbeit mit den kantonalen Ämtern für Lebensmittelsicherheit und Gesundheit, für Natur und Umwelt und für Militär und Zivilschutz und mit dem Gesundheitsamt und diente der Etablierung von Methoden zum Nachweis der Belastung von Abwasser mit SARS-CoV-2 RNA-Fragmenten mit PCR und mit der Sequenzierung dieser Fragmente zur Bestimmung der relativen Häufigkeit der verschiedenen Viren-Varianten. Das Highlight dieses Projekts wäre die Verfolgung der Ausbreitung der Omicron-Variante im Dezember 2021 Graubünden anhand der Abwasserdaten aus den sehr touristisch und sportlich geprägten Orten St. Moritz und Davos, und aus Lostallo und Landquart, die eine komplett andere Bevölkerungsdynamik aufweisen. Am 11./12. Dezember 2021 hat in St. Moritz der Alpine Ski World Cup der Damen und in Davos das Davos Nordic Langlauf-Weltcup-Rennen stattgefunden, was mit einer starken und internationalen Fluktuation von Personen einhergeht. Um diese Zeit herum wurden in den Abwasserproben der ARAs S-chanf (St. Moritz), Davos, Landquart und Lostallo virale RNA-Fragmente isoliert und am Functional Genomics Center Zurich (FGCZ) sequenziert. Das Mapping der Sequenzdaten und die Bestimmung der relativen Häufigkeit der SARS-CoV-2 Varianten erfolgte im DAViS-Team am SIAF durch Anwendung der V-PIPE pipeline. Die Daten zeigten interessanterweise einen starken Anstieg der Omicron-Variante (BA.1) im Dezember in St. Moritz und Davos, aber nicht in Lostallo oder Landquart. Dieses Projekt verdeutlicht, dass dank des DAViS-Projekts Expertise aufgebaut werden konnte, mit der auf neue, dringende Fragestellungen reagiert werden kann.

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.

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 der Universität Wuhan. PD Dr. K. Bärenfaller und PD Dr. M. Sokolowska sind Mitglieder des Lehrkörpers der UZH.

Aufgrund der Pandemie musste die fünfzehnte Durchführung des World Immune Regulation Meetings (WIRM) abermals als virtueller Kongress durchgeführt werden. Durch sehr gute Zusammenarbeit zwischen dem IT-Team des SIAF und der GroupConsulter AG konnte der Kongress erfolgreich vom 30. Juni bis 3. Juli 2021 durchgeführt werden. Über 500 Nachwuchsforscher sowie Senior-Wissenschaftler aus über 40 verschiedenen Länder hielten 97 Vorträge und trugen 179 Abstracts vor, tauschten sich über die neuesten Erkenntnisse in der Immunologie und zum aktuellsten Thema „COVID-19“ aus. Dieser globale Austausch von aktuellen Erkenntnissen hilft, neue Behandlungstherapien und neue Lösungsansätze für Patienten und Patientinnen zu entwickeln.

Das WIRM bietet jährlich eine perfekte Plattform, um die besten Forscher im Gebiet zu versammeln und die neuesten Entwicklungen zu diskutieren. Dieser globale Austausch von hochwertigen aktuellen Erkenntnissen hilft, neue Behandlungen zu entwickeln und neue Lösungsansätze zu finden. Das international ausgeschriebene WIRM zählt mittlerweile in Europa zu einem der angesehensten Kongresse seiner Art.

Vom 7. bis 25. Juni 2021 fand die zweite Auflage des Blockkur-

ses Biomedical Data Mining statt, aufgrund der Pandemie wieder vollständig online. Die verantwortlichen Dozenten waren PD Dr. K. Bärenfaller und PD Dr. M. Sokolowska, mit Unterstützung der Doktoranden J. Koch, D. Zhakparov, E. Barletta, A. Wallimann, 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 der CK-CARE betonen, welche uns patientenorientierte Forschung in der atopischen Dermatitis ermöglicht. Ich danke speziell Frau und Herr Kühne für Ihre Unterstützung, welche unsere Forschung zur Findung von nachhaltigen Lösungen für bessere Diagnosen und Behandlungen von Neurodermitis-Patienten ermöglicht. Dank dieser Unterstützung konnten im Institut viele Master-Diplome und PhD-Titel vergeben werden.

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. Nicht zuletzt gilt mein Dank den Behörden, die sich unermüdlich für die Forschung des SIAF interessieren und das Institut in jeder Hinsicht fördern.

Davos, Mai 2022

Report of the director

Prof. Dr. med. Cezmi A. Akdis

The Swiss Institute of Allergy and Asthma Research (SIAF) in its present form was founded in 1988 by the Medical Department of the Swiss Research Institute for High Altitude Climate and Medicine Davos Foundation (SFI). SIAF has been affiliated with the University of Zurich since 1996 and a member of the Life Science Zurich Graduate School, a joint educational project of the University of Zurich and ETH Zurich, since 2008. This affiliation enables SIAF to offer a fully comprehensive PhD education. In addition, SIAF is an active member of Academia Raetica and the Graduate School of the Canton of Graubünden.

With an epidemic increase during the last six decades, more than 1 billion people suffer from food allergies, asthma, atopic dermatitis and allergic rhinitis with a prevalence of about 1.8 million (23% of the population) in Switzerland. Food allergies are common in Europe and the US, affecting up to 10% of the pediatric population and 1-3% of the adult population.

The research at SIAF focuses on patient-relevant translational research and investigation of the immunological basis of allergic and asthmatic diseases, which creates starting points for new preventive and curative treatments for the benefit of those affected. The research is designed for direct cooperation with the clinics in Davos, the University of Zurich and other specialized institutes. In addition, SIAF is involved in the European network of national centers of excellence (GA2LEN project: Global Allergy and Asthma European Network of Excellence), in the European Academy of Allergology and Clinical Immunology (EAACI), in the American Academy of Allergy, Asthma and Immunology (AAAAI), and in the World Allergy Organization (WAO). EAACI is the world's largest academy for allergic diseases and plays an important role in science, continuing education, communications, and outreach. There is an intensive collaboration with Stanford University (Sean Parker Asthma and Allergy Center).

In 2021, 103 scientific papers were published or are still in press in peer-reviewed international journals with "Impact Factor". In 2021, SIAF achieved an overall "Impact Factor" score of 1,160.081 and an average of 11.263 points per publication. The latest results were also shared in 28 abstracts at various professional meetings. Our employees were invited to 105 different seminars and lectures at national and international congresses. Such invitations are important for the dissemination of the results obtained and for the international acceptance of the Institute's research. SIAF staff chaired 28 different sessions. In addition, SIAF staff members hold 54 scientific offices in international societies and international journals. In addition, Prof. C. A. Akdis has held the position of Editor-in-Chief of the journal Allergy since 2018. As a result of his highly regarded international scientific publications, Prof. Dr. C. A. Akdis was included in the group of most cited researchers from all scientific disciplines worldwide by Thomson Reuters Clarivate in 2021 for the sixth year in a row. SIAF has published over 1,540 papers and is one of the most cited institutes worldwide. Articles published by SIAF have been cited 64,000 times in Web of Science and more than 100'000 times in Google Scholar.

A milestone was set with the opening of the Davos Wolfgang Medical Campus in 2019. There is a very close collaboration with the independent partners CK-CARE AG, HGK, Davos BioSciences AG and Cardio Care AG. The results developed together are directly applied in therapy and clinic. Patients benefit from translational allergy and cardio research on the campus, as treatment is always based on the latest scientific findings. The campus is also home to the endowed professorship funded by the Kühne Foundation, with which close collaboration is equally being pursued in the field of imaging methods for analyzing surface markers of cells in tissue. Thanks to the support of CK-CARE, more than 55 scientific staff members have been hired since 2009 and more than 85 academic guests have been hosted in the exchange program. In addition, nearly 330 publications with the institutional affiliation of SIAF and CK-CARE have been published in prestigious journals.

The epithelial barrier hypothesis provides a comprehensive understanding of the development of allergic and other chronic noncommunicable diseases

A recent worldwide inventory revealed that more than 350,000 industrial chemicals and mixtures have been registered for production and most of them ended up as pollutants in the environment. Professional dishwashers, packaged food preservatives and emulsifiers, laundry detergents and surfactants, particulate matter and microplastic should be the main targets to improve the state of the world and human and domestic animal health. The prevalence of many chronic noncommunicable diseases has increased dramatically over the past 60 years and has reached pandemic proportions. Our research and efforts to explain the reasons for this increase in prevalence have contributed to the development of the epithelial barrier hypothesis. The epithelial barrier hypothesis states that disruption of epithelial barriers by laundry and dishwashing detergents, household cleaners, surfactants, enzymes and emulsifiers used in the food industry, cigarette smoke, particulate matter, diesel exhaust, ozone, nanoparticles, and microplastics lead to tissue inflammation and microbial dysbiosis and play a role in many chronic noncommunicable diseases. There is a need to support science and advance understanding of the factors and molecular mechanisms associated with leaky epithelial barriers and to inform policy makers about the adverse effects of potentially causative or contributory agents.

Our research has started on epithelial barriers in 1998 with major contributions and the development of the epithelial barrier hypothesis. These contributions can be listed as major research titles: mechanisms of skin and lung epithelial death and eczema in the skin and epithelial shedding in the lungs; interaction of the immune system with epithelial cells; opening of the epithelial barriers by immune system cells and cytokines; damage to epithelial cells opening of the epithelial barriers by detergents, particulate matter, surfactants, packaged food emulsifiers and preservatives. There is sufficient epidemiologic evidence in humans and in disease models to show that even trace amounts of substances currently considered safe can damage epithelial barriers and increase bacterial transmission. Certain populations may be at higher risk due to genetic factors. Therefore, elimination of these substances may help reduce the incidence or severity of certain chronic noncommunicable diseases. Strategies to reduce disease associated with a disrupted epithelial

barrier include reduced exposure or complete avoidance of these potentially causative agents. In addition, the epithelial barrier hypothesis may highlight the importance of more effective screening of new chemicals used in daily life, stimulate the development of safer products, and advance the identification of biomarkers to identify and monitor individuals at risk of barrier disruption. Finally, studies are needed to develop preventive or therapeutic approaches with interventions through lifestyle, dietary, and microbiome changes.

Regulation of the immune response by antigen-specific regulatory B cells and memory B cells

Asthma, atopic dermatitis, rhinitis, and food allergy represent a major and growing public health problem in Switzerland with a total prevalence of approximately 1.8 million patients. Food allergies are common in Europe and the USA with a prevalence of up to 10% in the pediatric population and 1-3% in the adult population.

In recent decades, this research group, along with other research groups, has made considerable progress in understanding allergen tolerance. IgE-mediated allergy is a type 2 immune response that is thought to be responsible for most features of allergic inflammation. Clinical signs of food allergy are observed after ingestion of the food and include gastrointestinal symptoms, urticaria, wheezing, and in severe cases, systemic anaphylaxis. An important tool for studying the genetic and environmental influence on complex phenotypes of allergic diseases, such as food allergy, is the detailed study of the immune response between discordant and concordant monozygotic and dizygotic twins. Twin studies have shown that family history is a strong risk factor for the development of allergy, suggesting that genetic predisposition is important, although not the only factor involved. This approach in fraternal twins eliminates much of the environmental bias, as twin pairs are generally exposed to similar environments. In parallel, the study of discordant monozygotic twins will provide insight into the role of nongenetic factors. Such studies in food allergy will allow the genetic and environmental causes of allergen-specific immune responses to be assessed, which has not yet been done.

Immunological and molecular fingerprinting of diseases with chronic airway limitation: asthma and chronic obstructive pulmonary disease

Chronic obstructive pulmonary disease is responsible for significant morbidity, mortality, and healthcare costs worldwide. Conventionally, asthma and COPD are thought to be distinct, and guidelines recommend different treatment approaches. In reality, however, there is considerable overlap between the two diseases. Although asthma and COPD are still considered two distinct obstructive airway diseases, both diseases share a component of respiratory epithelial dysfunction.

There are several ways in which environmental factors affect the epithelial barrier. Air pollutants, cigarette smoke, allergens, viruses, bacteria and bacterial toxins, and other particles constantly interact with airway epithelial cells and 1) induce specific metabolic changes in these cells, 2) invade the epithelium, 3) lead to barrier leakage, and 4) activate immune system cells, resulting in severe chronic inflammation. Recently, it has been shown by us and others that a defect in the epithelial barrier plays an important role in the pathogenesis of these diseases.

Due to the unique combination of novel methodology used in our study (systems biology approach - next generation sequencing, proteomics, metabolomics, microbiome sequencing, multicolor flow cytometry, cell sorting and confocal microscopy) and very thorough clinical characteristics of the study participants and invasive diagnostic methods, we expect: The characterization of new subgroups of asthma and COPD patients with different underlying epithelial barrier disorders, the differentiation of biomarkers of different endotypes of asthma and COPD, suggestions for molecular targets for new therapies in the airway epithelium, and the observation of the evolution of the endotypes during treatment.

Center for Precision Proteomics

With the decision of the government of the Canton of Graubünden on 5 September 2020 to award SIAF the contract to "...establish and operate a Center for Proteomics by means of a special professorship for the profile field "Life Science" according to the submitted concept as a "Leading House" ..." from 1 August 2020 to 31 July 2026 the Center for Precision Proteomics was able to make the necessary investments and start operations. The research orientation formulated in the submitted concept is based on the one hand on the establishment of mainly local, but also national and international collaborations for the planning and execution of proteomics experiments, and on the other hand on the implementation of mass spectrometry studies in SIAF-relevant topics.

In collaborations with local groups, two pilot projects have been carried out together with researchers from the AO Research Institute in Davos, one of which is now moving into the project phase. Together with Prof. Dr. P. Schmid-Grendelmeier from the University Hospital Zurich and Prof. Dr. M. Brüggen from CK-CARE, the University Hospital Zurich and the High Mountain Clinic Davos, we were able to successfully submit a project to LEO Pharma in which mass spectrometer measurements will play a major role and which will start in 2022. Internationally, we were able to continue our collaboration with the group of Prof. Dr. O. Schilling from the University of Freiburg in Germany. In addition, projects are underway primarily in the Molecular Allergology research group at SIAF, both to specifically search for allergenic proteins involved in food allergy and to apply enrichment and deprotection methods to identify post-translationally modified proteins. Prof. Dr. C.A. Akdis and PD Dr. K. Bärenfaller were appointed as interim project leaders prior to the filling of the non-tenure-track assistant professorship by the Medical Faculty of the University of Zurich, which was linked to the special professorship in profile field 5. The assistant professorship was advertised by the Faculty of Medicine in May 2021, and following the recommendation of the appointment committee, appointment negotiations are currently underway.

Computational Science - COVID-19

In 2021, in collaboration between the University of Applied Sciences Grisons (FHGR) and SIAF, we worked intensively on the data of patients from COVID-19 hospital in Zgierz, Poland. Through PD Dr. M. Sokolowska of SIAF, we had contact with physicians at this hospital. In addition to the project, DAViS expertise in biomedical data analysis has been contributed to various collaborative projects

with researchers from SIAF, the AO Research Institute, and the Swiss Research Institute for Sports Medicine (SRISM), and several manuscripts are being prepared or have already been submitted. Another project was in collaboration with the Cantonal Offices of Food Safety and Health, Nature and Environment, and Military and Civil Defense, and with the Department of Health, and was aimed at establishing methods to detect the presence of SARS-CoV-2 RNA fragments in wastewater with PCR and with sequencing of these fragments to determine the relative abundance of the different virus variants. The highlight of this project was the tracking of the spread of the Omicron variant in December 2021 Graubünden using wastewater data from the very touristy and sporty towns of St. Moritz and Davos, and from Lostallo and Landquart, which have completely different population dynamics. On December 2021, St. Moritz hosted the Women's Alpine Ski World Cup and Davos hosted the Davos Nordic Cross-Country Ski World Cup race, which is associated with a strong and international fluctuation of people. Around this time, viral RNA fragments were isolated in wastewater samples from the S-chanf (St. Moritz), Davos, Landquart and Lostallo ARAs and sequenced at the Functional Genomics Center Zurich (FGCZ). Mapping of the sequence data and determination of the relative abundance of SARS-CoV-2 variants was performed by the DAViS team at SIAF using the V-PIPE pipeline. Interestingly, the data showed a strong increase of the Omicron variant (BA.1) in December in St. Moritz and Davos, but not in Lostallo or Landquart. This project illustrates that, thanks to the DAViS project, expertise has been built up that can be used to respond to new, urgent issues.

Clinical service

The SIAF offers to Davos and all other interested clinics and practicing physicians special cellular immunological diagnosis. By means of the flow cytometric analysis of blood, bronchoalveolar lavage (BAL), but also other tissue fluids, the different immune cells and subpopulations are measured in their development, their proportions and their activation state.

Education, teaching, congresses

An important task has been fulfilled by the SIAF in the education of PhD students as well as in postgraduate studies. At the same time, the SIAF fulfills teaching obligations at the University of Zurich. These consist of various lecture courses 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 promotion rights in the Faculty of Mathematics and Natural Sciences and honorary professor at the Bezmialem University of Istanbul. Prof. C. A. Akdis and Prof. M. Akdis also hold an honorary professorship at the Tungren Hospital of Beijing University, at the Bursa-Uludag University and University of Wuhan. PD Dr. K. Bärenfaller and PD Dr. M. Sokolowska are members of the UZH teaching faculty.

In 2021, we taught the second edition of the block course Biomedical Data Mining, due to the pandemic again fully online. The responsible lecturers were PD Dr. K. Bärenfaller and PD Dr. M. Sokolowska, with assistance of the PhD students J. Koch, D. Zhakparov, E. Barletta, A. Wallimann, M. Huang and Y. Xiao. Background information on various functional genomics technologies and analysis tools was provided in 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 handed RNA sequencing result lists, and in various tasks they were asked to first analyze these lists using R, and then to put the results into context.

Due to the pandemic, the fifteenth World Immune Regulation Meeting (WIRM) had to be held as a virtual congress once again. Thanks to the excellent cooperation between the IT team of SIAF and GroupConsulter AG, the congress was successfully held from 30st June to 3rd July 2021. More than 500 junior researchers as well as senior scientists from over 40 different countries gave 97 presentations and contributed 179 abstracts, exchanged the latest findings in immunology and on the most current topic "COVID-19". This global exchange of current knowledge helps to develop new treatment therapies and new 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 Foundation Board and Foundation Board Committee for the support they have always provided. Last but not least, my thanks go to the authorities, who have taken a tireless interest in SIAF's research and have supported the Institute in every way.

Davos, May 2022

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 *
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
Crameri Sandra, 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
Wenger R.H., Prof. Dr., University Zurich, Zurich
Wilhelm P., City Mayor, Davos

SFI Foundation Council
Bezzola D., MSc, Academia Raetica, Davos
Borelli S., Prof. Dr. med., Dr. phil., Davos († 20.11.2021)
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
Müller H., dipl. Chem. HTL, Natural Research Society, Davos (- Juni 2021)
Ottmer B., MSc ETH Environmental Sc., WSL, SLF Davos
Pfister J., Dr., SCNAT, Bern
Ring J., Prof. Dr. Dr., Klinik am Biederstein, Munich

SIAF STAFF MEMBERS

2021

Scientific Staff

Ardiçli Özge	Master student *** (- Apr. 2021)
Ameri Milad	Bioinformatician ***
Barletta Elena	PhD student ***
Bel imam Manal	PhD student ***
Chang Iris	PhD student ***
Fernandez S. Ruben	PhD student *** (- Sept. 2021)
Ferstl Ruth	Post-doc, PhD ***
Fieten Karin	Post-doc, PhD ***
Heider Anja	Technician ***
Huang Mengting	PhD student **
Kim Juno	Bachelor student *** (- June 2021)
Koch Jana	PhD student ***
Küçükkase Ozan Can	PhD student **
Liu Manru	PhD student ***
Ma Siyuan	Post-doc, MD *** (- March 2021)
Maurer Debbie	PhD student ***
Meisser Sanne	Post-doc, MD ***
Mirer David	Technician ** (- Sept. 2021)
Mitamura Yasutaka	Junior Group Leader, MD, PhD *
Ögülür Ismail	Junior Group Leader, MD ***
Pat Yağız	Post-doc, MD *** (- Aug. 2021)
Perez Diego Mario	PhD student, ***
Radzikowska Urszula	PhD student ***
Rodriguez-Coira V. Juan	PhD student *** (- June 2021)
Rückert Beate	Head Technician */**
Satitsuksanoa Benz	Post-doc, PhD ***
Schneider Stephan	PhD student **
Stocker Nino	Technician ***
Wallimann Alexandra	PhD student ***
Wawrocki Sebastian	Post-doc, PhD ***
Westermann Patrick	Technician */***
Xiao Yi	PhD student ***
Yazici Duygu	PhD student ***
Zhakparov Damir	PhD student ***

Guest Scientists

Boersma Jolien Marleen, Wageningen University, The Netherlands
Komlosi Zsolt, Semmelweis University Budapest, Ungarn
Tynecka Marlena, Medical University of Bialystok, Poland
Schmelzer Schwindt Svenja, Heidelberg University, Germany
Martin-Fontecha Corrales Maria Mar, Complutense University of Madrid, Spain
Palomares Gracia Oscar, Complutense University of Madrid, Spain

Allergy Office

Alberch Gracia Laura	Managing Editor Allergy ****
Globinska Anna	Graphics Editor Allergy ****
Rüya Kiliç	Online Media Editor Allergy **** (- Sept. 2021)

Salary paid by

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

Prof. Dr. Cezmi A. Akdis, MD

The epithelial barrier hypothesis proposes a comprehensive understanding of the origins of allergic and other chronic non-communicable diseases

A steep increase in the prevalence of many chronic non-communicable diseases occurred during the last 60 years bringing them to a pandemic size. Our research and efforts to explain the reasons for this rise in their prevalence helped to develop the epithelial barrier hypothesis. The epithelial barrier hypothesis proposes that the disturbance of the epithelial barriers by laundry and dishwasher detergents, household cleaners, surfactants, enzymes and emulsifiers used in the food industry, cigarette smoke, particulate matter, diesel exhaust, ozone, nanoparticles, and microplastics cause tissue inflammation and microbial dysbiosis and play a role in many chronic non-communicable diseases. More than 350'000 new chemicals and mixtures have been registered for production after 1960s and most of them ended up with pollutants. There is a need to support science and advance the understanding of the factors and molecular mechanisms associated with leaky epithelial barriers and inform policymakers of the detrimental effects of the potential causal or contributing substances.

Since the 1960s, history has been marked by a pandemic increase in the prevalence of allergic, autoimmune, and neurodegenerative diseases, affecting over 2 billion individuals. After 2000, a new wave of diseases, such as food allergy, eosinophilic esophagitis, and drug-hypersensitivity and anaphylaxis grew into pandemic sizes. The first group contains diseases that show that the affected organ's local epithelial tissue is inflamed, such as asthma, atopic dermatitis, chronic rhinosinusitis, allergic rhinitis, eosinophilic esophagitis, inflammatory bowel and celiac diseases. The second group consists of metabolic and autoimmune diseases, which are associated with gut or lung epithelial barrier defects, such as obesity, diabetes mellitus, rheumatoid arthritis, multiple sclerosis, fatty liver, autoimmune hepatitis, systemic lupus erythematosus, ankylosing spondylitis, inflammatory bowel, and celiac disease. There have been detailed studies proposing how these diseases may be triggered or aggravated by distant inflammatory reactions in response to dysbiotic changes in the gut or lung immune cells and microbiome. In addition, increased intestinal barrier leakiness has been linked with neuropsychiatric disorders such as Parkinson's disease, Alzheimer's disease, stress-related psychiatric diseases, autism spectrum disorders, and chronic depression (Figure 1).

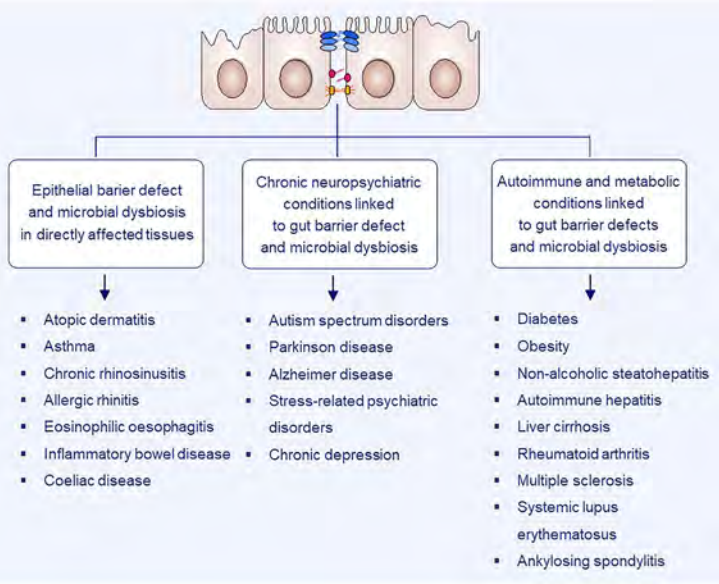


Figure 1. Diseases linked to epithelial barrier defects: Three groups of diseases are associated with epithelial barrier damage and microbial dysbiosis: i) Epithelial barrier defect and microbial dysbiosis in directly affected tissues; ii) Distant autoimmune and metabolic diseases linked to gut barrier defects and microbial dysbiosis; iii) Chronic neuropsychiatric conditions linked to a gut barrier defect and microbial dysbiosis

Because of urbanization and modernization, humans started to be exposed to numerous of toxins and chemicals after the 1960s (Figure 2).

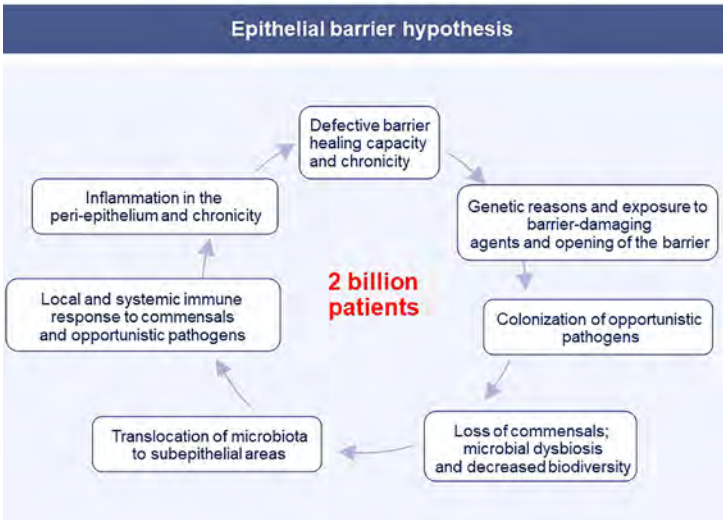


Figure 2. The physiopathology involved in the epithelial barrier hypothesis: The vicious cycle of chronic epithelial barrier dysfunction. Genetic defects in barrier-related molecules or exposure to epithelial barrier-damaging agents cause a disruption of the skin and mucosal tight junction barriers. A cascade of events develop that play a role in the pathogenesis of diseases associated with the epithelial barrier hypothesis.

A cascade of events have been proposed as pathogenetic mecha-

nisms linked to the epithelial barrier hypothesis (Figure 2). Microbial dysbiosis resulting from tissue colonization by opportunistic pathogens, followed by transepithelial translocation of opportunistic pathogens and commensals to the subepithelium. This results in stimulation of the immune system and subepithelial or submucosal inflammation. Decreased biodiversity develops, because of an adaptive immune response against commensals together with opportunistic pathogens and tissue inflammation. For example, anti-Staphylococcus aureus IgE response and S. aureus epithelial colonization are hallmarks of asthma, atopic dermatitis and chronic rhinosinusitis currently, which were not the case in the 1980s. A dysregulated subepithelial immune response, inflammation, and dysfunctional regeneration and remodeling occurs through the continuum and chronicity of the local inflammation. Epithelial basement membrane (Lamina reticularis) thickening and fibrosis are potentially a mucosal response to develop a secondary barrier following disruption of the primary epithelial barrier. The migration of inflamed cells from leaky barrier areas to other affected tissues and systemic low-level immune activation and microinflammation are potential factors in developing and exacerbating many chronic inflammatory diseases.

There is sufficient epidemiological evidence in humans and disease models demonstrating that even trace amounts of substances, currently considered safe, can damage epithelial barriers and increase bacterial translocation. Certain members of the population may be at greater risk due to genetic factors. Therefore, avoidance of these substances may be beneficial in reducing the occurrence or the severity of specific chronic, non-communicable diseases. Strategies to reduce illnesses associated with a disrupted epithelial barrier include reduced exposure or complete avoidance of these possibly causal substances. In addition, the epithelial barrier hypothesis may show the importance of more effective screening of new chemicals used in daily life, may stimulate the development of safer products, and may spur the identification of biomarkers to identify and monitor individuals at risk of barrier dysfunction. Finally, studies to develop preventive or therapeutic approaches with interventions through changes in lifestyle, diet, and microbiome are needed.

The epithelial barrier hypothesis proposes a comprehensive understanding of the origins of allergic and other chronic non-communicable diseases.
Akdis CA. J Allergy Clin Immunol. 2022 Jan;149(1):41-44.

Does the epithelial barrier hypothesis explain the increase in allergy, autoimmunity and other chronic conditions?
Akdis CA. Nat Rev Immunol. 2021 Nov;21(11):739-751.

Advances and highlights in biomarkers of allergic diseases.
Ogulur I, Pat Y, Ardicli O, Barletta E, Cevhertas L, Fernandez-Santamaria R, Huang M, Bel Imam M, Koch J, Ma S, Maurer DJ, Mitamura Y, Peng Y, Radzikowska U, Rinaldi AO, Rodriguez-Coira J, Satitsuksanoa P, Schneider SR, Wallimann A, Zhakparov D, Ziadlou R, Brüggen MC, van de Veen W, Sokolowska M, Baerenfaller K, Zhang L, Akdis M, Akdis CA. Allergy. 2021 Dec;76(12):3659-3686.
During the past years, there has been a global outbreak of allergic diseases, presenting a considerable medical and socioeconomical burden. A large fraction of allergic diseases is characterized by a type 2 immune response involving Th2 cells, type 2 innate lymphoid cells, eosinophils, mast cells, and M2 macrophages. Biomarkers are valuable parameters for precision medicine as they provide information on the disease endotypes, clusters, precision diagnoses, identification of therapeutic targets, and monitoring of treatment efficacies. The availability of powerful omics technologies, together with integrated data analysis and network-based approaches can help the identification of clinically useful biomarkers. These biomarkers need to be accurately quantified using robust and reproducible methods, such as reliable and point-of-care systems. Ideally, samples should be collected using quick, cost-efficient and noninvasive methods. In recent years, a plethora of research has been directed toward finding novel biomarkers of allergic diseases. Promising biomarkers of type 2 allergic diseases include sputum eosinophils, serum periostin and exhaled nitric oxide. Several other biomarkers, such as pro-inflammatory mediators, miRNAs, eicosanoid molecules, epithelial barrier integrity, and microbiota changes are useful for diagnosis and monitoring of allergic diseases and can be quantified in serum, body fluids and exhaled air. Herein, we review recent studies on biomarkers for the diagnosis and treatment of asthma, chronic urticaria, atopic dermatitis, allergic rhinitis, chronic rhinosinusitis, food allergies, anaphylaxis, drug hypersensitivity and allergen immunotherapy. In addition, we discuss COVID-19 and allergic diseases within the perspective of biomarkers and recommendations on the management of allergic and asthmatic patients during the COVID-19 pandemic.

Dysregulation of the epithelial barrier by environmental and other exogenous factors.
Mitamura Y, Ogulur I, Pat Y, Rinaldi AO, Ardicli O, Cevhertas L, Brüggen MC, Traidl-Hoffmann C, Akdis M, Akdis CA. Contact Dermatitis. 2021 Dec;85(6):615-626.
The "epithelial barrier hypothesis" proposes that the exposure to various epithelial barrier-damaging agents linked to industrialization and urbanization underlies the increase in allergic diseases. The epithelial barrier constitutes the first line of physical, chemical, and immunological defense against environmental factors. Recent reports have shown that industrial products disrupt the epithelial barriers. Innate and adaptive immune responses play an important role in epithelial barrier damage. In addition, recent studies suggest that epithelial barrier dysfunction plays an essential role in the pathogenesis of the atopic march by allergen sensitization through the transcutaneous route. It is evident that external factors interact with the immune system, triggering a cascade of complex reactions that damage the epithelial barrier. Epigenetic and microbiome changes modulate the integrity of the epithelial barrier. Robust and simple measurements of the skin barrier dysfunction at the point-of-care are of significant value as a biomarker, as recently reported using electrical impedance spectroscopy to directly measure barrier defects. Understanding epithelial barrier dysfunction and its mecha-

nism is key to developing novel strategies for the prevention and treatment of allergic diseases. The aim of this review is to summarize recent studies on the pathophysiological mechanisms triggered by environmental factors that contribute to the dysregulation of epithelial barrier function.

Cutaneous and systemic hyperinflammation drives maculopapular drug exanthema in severely ill COVID-19 patients.

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. Allergy. 2022 Feb;77(2):595-608.

Coronavirus disease-2019 (COVID-19) has been associated with cutaneous findings, some being the result of drug hypersensitivity reactions such as maculopapular drug rashes (MDR). The aim of this study was to investigate whether COVID-19 may impact the development of the MDR. Blood and skin samples from COVID-19 patients (based on a positive nasopharyngeal PCR) suffering from MDR (COVID-MDR), healthy controls, non-COVID-19-related patients with drug rash with eosinophilia and systemic symptoms (DRESS), and MDR were analyzed. We utilized imaging mass cytometry (IMC) to characterize the cellular infiltrate in skin biopsies. Furthermore, RNA sequencing transcriptome of skin biopsy samples and high-throughput multiplexed proteomic profiling of serum were performed. IMC revealed by clustering analyses a more prominent, phenotypically shifted cytotoxic CD8+ T cell population and highly activated monocyte/macrophage (Mo/Mac) clusters in COVID-MDR. The RNA sequencing transcriptome demonstrated a more robust cytotoxic response in COVID-MDR skin. However, severe acute respiratory syndrome coronavirus 2 was not detected in skin biopsies at the time point of MDR diagnosis. Serum proteomic profiling of COVID-MDR patients revealed upregulation of various inflammatory mediators (IL-4, IL-5, IL-6, TNF, and IFN-γ), eosinophil and Mo/Mac -attracting chemokines (MCP-2, MCP-3, MCP-4 and CCL11). Proteomics analyses demonstrated a massive systemic cytokine storm in COVID-MDR compared with the relatively milder cytokine storm observed in DRESS, while MDR did not exhibit such features. In conclusion, a systemic cytokine storm may promote activation of Mo/Mac and cytotoxic CD8+ T cells in severe COVID-19 patients, which in turn may impact the development of MDR.

Electrical impedance spectroscopy for the characterization of skin barrier in atopic dermatitis.

Rinaldi AO, Korsfeldt A, Ward S, Burla D, Dreher A, Gautschi M, Stolpe B, Tan G, Bersuch E, Melin D, Askary Lord N, Grant S, Svedenhag P, Tsekova K, Schmid-Grendelmeier P, Möhrenschlager M, Renner ED, Akdis CA. Allergy. 2021 Oct;76(10):3066-3079. doi: 10.1111/all.14842.

Allergic disorders such as atopic dermatitis (AD) are strongly associated with an impairment of the epithelial barrier, in which tight junctions and/or filaggrin expression can be defective. Skin barrier assessment shows potential to be clinically useful for prediction of disease development, improved and earlier diagnosis, lesion follow-up, and therapy evaluation. This study aimed to establish a method to directly assess the in vivo status of epithelial barrier using electrical impedance spectroscopy (EIS). Thirty-six patients with AD were followed during their 3-week hospitalization and compared with 28 controls. EIS and transepidermal water loss (TEWL) were measured in lesional and non-lesional skin. Targeted proteomics by proximity extension assay in serum and whole-genome sequence were performed. Electrical impedance spectroscopy was able to assess epithelial barrier integrity, differentiate between patients and controls without AD, and characterize lesional and non-lesional skin of patients. It showed a significant negative correlation with TEWL, but a higher sensitivity to discriminate non-lesional atopic skin from controls. During hospitalization, lesions reported a significant increase in EIS that correlated with healing, decreased SCORAD and itch scores. Additionally, EIS showed a significant inverse correlation with serum biomarkers associated with inflammatory pathways that may affect the epithelial barrier, particularly chemokines such as CCL13, CCL3, CCL7, and CXCL8 and other cytokines, such as IRAK1, IRAK4, and FG2, which were significantly high at admission. Furthermore, filaggrin copy numbers significantly correlated with EIS on non-lesional skin of patients. In conclusion, electrical impedance spectroscopy can be a useful tool to detect skin barrier dysfunction in vivo, valuable for the assessment of AD severity, progression, and therapy efficacy.

Allergic reactions to the first COVID-19 vaccine: A potential role of polyethylene glycol?

Cabanillas B, Akdis CA, Novak N. Allergy. 2021 Jun;76(6):1617-1618. doi: 10.1111/all.14711.

Sampath V, Rabinowitz G, Shah M, Jain S, Diamant Z, Jesenak M, Rabin R, Vieths S, Agache I, Akdis M, Barber D, Breiteneder H, Chinthrajah S, Chivato T, Collins W, Eiwegger T, Fast K, Fokkens W, O'Hehir RE, Ollert M, O'Mahony L, Palomares O, Pfaar O, Riggioni C, Shamji MH, Sokolowska M, Jose Torres M, Traidl-Hoffmann C, van Zelm M, Wang Y, Zhang L, Akdis CA, Nadeau KC. Vaccines and allergic reactions: The past, the current COVID-19 pandemic, and future perspectives. Allergy. 2021 Jun;76(6):1640-1660.

Vaccines are essential public health tools with a favorable safety profile and prophylactic effectiveness that have historically played significant roles in reducing infectious disease burden in populations, when the majority of individuals are vaccinated. The COVID-19 vaccines are expected to have similar positive impacts on health across the globe. While serious allergic reactions to vaccines are rare, their underlying mechanisms and implications for clinical management should be considered to provide individuals with the safest care possible. In this review, we provide an overview of different types of allergic adverse reactions that can potentially occur after vaccination and individual vaccine components capable of causing the allergic adverse reactions. We present the incidence of allergic adverse reactions during clinical studies and through post-authorization and post-marketing surveillance and provide plausible causes of these reactions based on potential allergenic components present in several common vaccines. Additionally, we review implications for individual diagnosis and management and vaccine manufacturing overall. Finally, we suggest areas for future research.

Cellular Allergy / Immunology

The cannabinoid WIN55212-2 restores rhinovirus-induced epithelial barrier disruption.
Angelina A, Martín-Fontecha M, Rückert B, Wawrzyniak P, Pérez-Diego M, López-Abente J, Akdis M, Akdis CA, Palomares O. Allergy. 2021 Jun;76(6):1900-1902.
Bronchial epithelial cells constitute the first physical barrier with mucociliary clearance and immunologic defence capacity against environmental inhaled insults. Disruption of tight junctions (TJs) and epithelial barrier dysfunction is a hallmark of chronic inflammatory airway diseases such as rhinitis, chronic rhinosinusitis with nasal polyposis or asthma. Rhinovirus infections induce the disruption of the airway epithelial barrier and the production of pro-inflammatory cytokines. Cannabinoids are lipid-derived mediators with anti-inflammatory properties in different disorders. Cannabinoid receptor 1 (CB1) agonists inhibited the development of arthritis by restoring the intestinal barrier in the in the pre-phase of arthritis. In the present study we uncovered a previously unknown capacity of the synthetic cannabinoid WIN55212-2 to help to restore the integrity of the airway epithelial barrier during rhinovirus infection, which might well pave the way for the future development of potential novel therapeutic approaches for different chronic inflammatory airway diseases.

Davos, May 2022

Prof. Dr. Mübeccel Akdis, MD, PhD

Role of B cells in oral tolerance.

The prevalence of food allergy has been increasing in recent decades and affects approximately 10% of the world population. Cow"s milk allergy (CMA) is a common disease in infants and children that shows a high rate of spontaneous resolution in early childhood until adolescence. In some cases, CMA can result in anaphylactic reactions and has long-term implications for growth and nutrition. Avoidance of all cow's milk products in daily life is a standard physicians` recommendation to patients. As an alternative to eliminating cow`s milk from the patient"s diet, oral allergen-specific immunotherapy (OIT) is an effective and curative treatment inducing clinical and immunologic tolerance to milk allergens in allergic patient. Understanding immune tolerance mechanisms to food allergens is crucial for further improving the existing treatments, and for the discovery of novel ways to prevent and treat food allergies. There are two major mechanisms which classify allergic reactions to cow"s milk and other food allergens; immunoglobulin E (IgE)-mediated and non-IgE-mediated. The development of IgE-mediated CMA is regulated by B cells through the production of allergen-specific IgE antibodies. Mechanisms driving B cells responses during allergy and development to tolerance remain to be elucidated. Hence, the investigation of B cell responses in food-allergic patients during OIT and in individuals who outgrow food allergy due to natural immune tolerance development may clarify mechanisms of induction and maintenance of food allergen tolerance. Natural outgrowth of food allergies represents a valuable model to study mechanisms of immune tolerance to food allergens. So far, there have been very few well-designed studies regarding the natural development of tolerance to food allergens. Reported rates of resolution (natural outgrowth) vary widely, likely attributable to methodological differences and study populations. Some food allergens are difficult to avoid and fortunately have a generally high likelihood of natural outgrowth, such as cow's milk and egg. Safely loosening the diet to include milk and egg for children has important nutritional and quality-of-life benefits. It was demonstrated that tolerant children, who outgrew their allergy developed higher frequencies of circulating CD4+CD25+ Treg cells and decreased in vitro proliferative responses to bovine beta-lactoglobulin compared to children who maintained clinically active allergy. Other food allergen sources, particularly peanuts and tree nuts, have a much lower spontaneous resolution rate and therefore require an efficient OIT approach. Molecular mechanisms of spontaneous outgrowth of food allergies have not been studied in detail and there is no report on the role of allergen-specific B cells in natural tolerance. Hoh et al. investigated B cell responses in peanut allergy and demonstrated that local class-switch recombination (CSR) to IgE in the gut directly has a major impact on the development of food allergen-specific IgE antibodies. Circulating IgE+ B cells display mostly immature plasmablast phenotype. Increased numbers of circulating IgE+ memory B cells and IgE+ plasmablasts are correlated with the presence of food allergy and may contribute to pathogenesis. Here, we have performed an indepth characterization of B cells specific for αS1-casein, the major allergen in cow"s milk, to analyse B cell changes related to the development of tolerance to cow"s milk allergy. We identify an increased frequency of allergen-specific B cells in OIT induced-cow"s milk tolerance and natural outgrowth-related immune tolerant individuals. Allergen-specific B cells predominantly express IgG4 after OIT and natural tolerance, with smaller numbers expressing IgG1 or IgE (Figure 1). Gene expression signatures associated with allergen-specific B cells were mostly downregulated after OIT, showing that allergen-specific B cells decrease their expression of 1456 genes and downregulate activation and proinflammatory gene expressions profile. Notably, secreted protein profiles of specific B cells were similar after OIT and NT, suggesting common but not identical mechanisms of food allergen tolerance (Figure 2).

We demonstrated a detailed characterization of the transcriptome, secreted proteins, and secreted specific antibodies of allergen-specific B cells in cow"s milk OIT-induced tolerance and NT individuals. Allergen-specific B cells show distinctive changes in induction of desensitization as well as induction of tolerance. The transcriptomic changes in specific B cells in OIT-induced tolerance are one step further silencing of genes of B cell activation after desensitization. More complete and more numerous gene expression mechanisms of suppression are exhibited in OIT-induced tolerance when compared to desensitized individuals. A proinflammatory environment is observed in allergen-specific B cells in allergic individuals due to 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 children that outgrow food allergy compared to OIT-induced tolerance. B cells appear to have one step further differentiation to pre-plasma stage with the expression of more innate immune receptors in NT. Breg cell-related genes are still active in OIT-induced tolerance with higher expression of IGHG4, IL10 and TGF-β genes. Altogether, our data demonstrated that allergen-specific B cells are induced during OIT and natural tolerance and that they have some major gene expression changes that suggest an important role in induction, and maintenance of immune tolerance to food antigens.

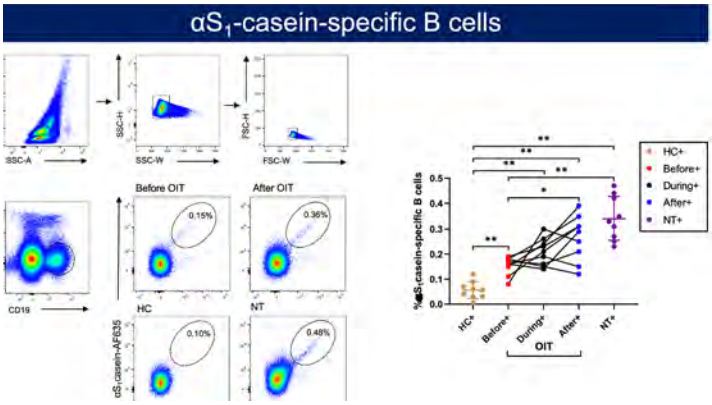


Figure. 1: The frequency of αS1-casein-specific B cells is increased after OIT in allergic patients and natural tolerance compared to healthy individuals. Flow cytometry plots in (A) are representative data coming from 4 samples; before OIT, after OIT, HC, and NT, respectively. (B)

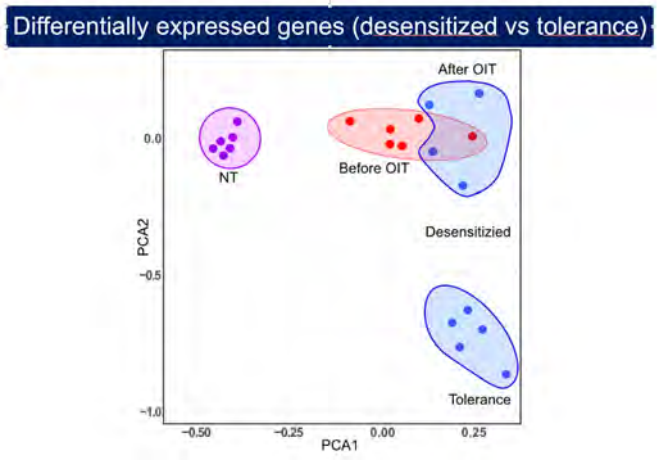


Figure 2: DGEs signatures in αS1-casein-specific B cells from after OIT (desensitized vs tolerance). (A) PCA plot of 200 DGEs separating allergic groups: before OIT vs after OIT (desensitized and tolerance) vs NT groups.

Mechanisms of allergen-specific 1 B cell tolerance in children with cow's milk-oral.

immunotherapy and natural outgrowth of milk allergy

Pattraporn Satitsuksanoa, Willem van de Veen, Ge Tan, Oliver Wirz, Kirstin Jansen, Milena Sokolowska, David Mirer, Anna Globinska, Tadech Boonpiyathad, Stephan R. Schneider, Elena Barletta, Hergen Spits, Iris Chang, Scott D. Boyd, Cezmi A. Akdis, Kari Nadeau, Mübeccel Akdis (Submitted to Nature Communication, under revision)

Antigen-specific memory B cells play a key role in the induction of immune tolerance to food allergens and clinical healing. Here, we characterized the role of allergen-specific B cells in immune tolerance induced by oral allergen-specific immunotherapy (OIT) and natural tolerance that developed in children who spontaneously outgrew cow"s milk allergy. Increased frequency of circulating milk allergen αS1-casein -specific B cells was observed after OIT and natural tolerance (NT). Milk desensitized subjects showed partial acquisition of tolerance phenotypic features induced tolerance, suggesting that desensitization is an earlier stage of tolerance. Immunoregulatory genes such as IL10RA and IGHG4 are significantly upregulated after OIT (desensitized and tolerance) versus NT. Secreted proteins from allergen-specific B cells revealed higher amounts of regulatory cytokines, IL-10 and TGF-β after OIT and NT. Taken together, allergen-specific B cells are essential elements in regulating food allergen tolerance in both OIT-received and naturally-resolved individuals.

Breaking of immune tolerance; Role of Rhinovirus infection.

Around 50-70% of upper respiratory tract infections are caused by human rhinoviruses (RV), making them the most common cause of viral-induced respiratory diseases and a major health care burden. RV infections are usually not life-threatening for healthy individuals and 30% of infections can be asymptomatic. Rhinoviruses replicate primarily in epithelial cells of the upper and lower respiratory tract. Together with phagocytes from mucosa-associated lymphoid tissues, these cells produce an array of proinflammatory cytokines, including type-I interferons (IFN). While type-I IFNs are essential mediators to induce antiviral immunity they also play an important role in B cell differentiation, antibody class-switch, and antibody secretion. B cells are constantly circulating through the body's tissues and are also present at the mucosal sites of the respiratory tract, where RV infections mainly take place. B cells represent the major cell population in tonsils, which represent the first line of defense and RV is often detected. B cells bind, uptake and proliferate in response to RV stimulation in vitro. B cell-mediated humoral immune response plays a central role in controlling RV infections. Neutralizing serum IgG and secretory IgA in the mucosa can be detected one to two weeks after infection, with a role of protection from re-infection. In addition, B cells transport lung-derived viral and bacterial antigens to secondary lymphoid organs in various murine models. While RV infections usually lead to mild symptoms in healthy adults, they can lead to complications in young children or in adults with underlying chronic respiratory diseases, particularly asthma. RV-induced wheezing in early life is strongly associated with the development of asthma during later childhood. Furthermore, RV infections are the main cause of asthma exacerbations. A bias towards non-virus neutralizing antibodies was found in asthmatic patients, but cellular aspects leading to this misdirected B cell response have not been studied in detail. Furthermore, bronchial epithelial cells and phagocytes such as monocytes and macrophages show a deficient production of type-I and type-III IFNs. Such decreased early antiviral response seems to result in reduced apoptosis of epithelial cells and increased viral load in asthmatic individuals, but the overall effect on circulating cells of the adaptive immune system in the periphery is not sufficiently understood. Given the frequent incidence of RV infections and the central role of humoral immunity during antiviral responses, it is surprising that the cellular side of this response was not yet addressed in more detail. Therefore, this study aimed to identify the underlying gene regulatory networks driving the B cell response during RV infection in vivo; to define the external stimulating factors driving this response; to address whether B cells directly interact with RV in vivo; and to discover potential B cell functions in addition to well-known antibody production. Furthermore, since responses to RV were described as less efficient in patients with chronic respiratory diseases, we addressed possible dysregu-

lation of circulating B cells and plasmablasts in asthmatics.
Here, we report early upregulation of an antiviral gene program followed by later upregulation of a pro-inflammatory response in B cells. B cells carried viral RNA after RV infection in vivo, suggesting direct interactions of B cells with infecting virions. Asthmatic subjects showed an elevated antiviral response and broad upregulation of antibody genes in B cells (Figure 3).

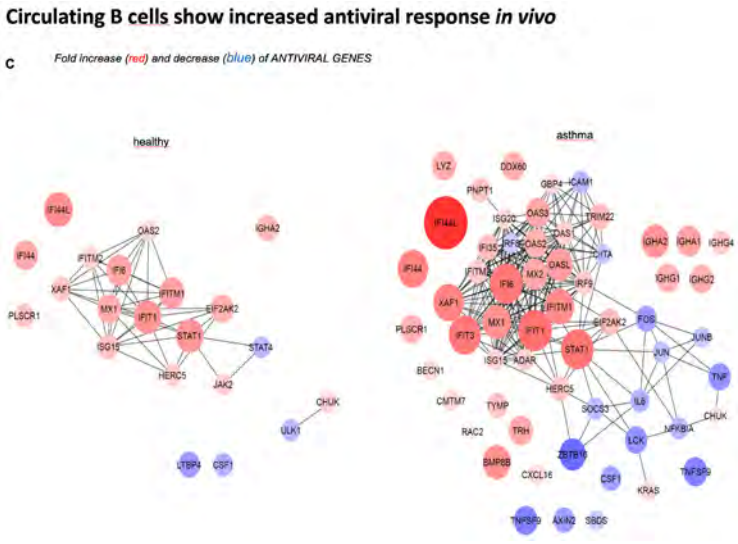


Figure 3: Extensive peripheral B cell response to RV infection in asthmatic individuals Satellite plot showing known interactions of upregulated gene families.

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.

Loss of regulatory capacity in T regulatory cells upon rhinovirus infection.

(Kirstin Jansen et al. J Allergy Clin Immunol. 2021 Oct;148(4):1016-1029.e16.)

Respiratory infections with rhinoviruses (RV) are strongly associated with the development and exacerbations of asthma and pose an additional health risk for allergic subjects. How RV infections and chronic allergic diseases are linked, and which role RV plays in the breaking of tolerance in T regulatory cells (Tregs) is unknown. Therefore, this study aims to investigate the effects of RV on Tregs. Tregs were isolated from asthmatic subjects and controls after experimental infection with RV16 and were analyzed with next-generation sequencing. Additionally, suppression assays, qPCRs, and protein quantifications were performed with Tregs after in vitro RV16 infection. RV16 induced a strong antiviral response in Tregs from asthmatic subjects and controls, including the upregulation of IFI44L, MX1, ISG15, IRF7, and STAT1. In asthmatic subjects, the inflammatory response was exaggerated and showed a dysregulated immune response compared to controls. Furthermore, asthmatic subjects failed to upregulate several immunosuppressive molecules such as CTLA4 and CD69 and upregulated the inflammasome related genes PYCARD and AIM2. Additionally, RV16 reduced the suppressive capacity of Tregs of healthy and asthmatic subjects in vitro and increased Th2-type cytokine production. Tregs from healthy and asthmatic subjects displayed an anti-viral response after RV infection and showed reduced suppressive capacity. This data suggest that Treg function might be altered or impaired during RV infections, which might play an important role in the association between RV and the development of asthma and asthma exacerbations.

T regulatory cells from atopic asthmatic individuals show a Th2-like phenotype.

Kirstin Jansen, Pattraporn Satitsuksanoa, Oliver F Wirz, Stephan R Schneider, Willem van de Veen, Ge Tan, Milena Sokolowska, Simon D Message, Tatiana Kebadze, Nicholas Glanville, Patrick Mallia, Cezmi A Akdis, Marcin Moniuszko, Sebastian L Johnston, Kari Nadeau, Mübeccel Akdis. Allergy. 2022 Apr;77(4):1320-1324.

B regulatory cells in allergy.

(Siyuan Ma et al. Immunol Rev. 2021 Jan;299(1):10-30.)

B cells have classically been recognized for their unique and indispensable role in the production of antibodies. Their potential as immunoregulatory cells with anti-inflammatory functions has received increasing attention during the last two decades. Herein, we highlight pioneering studies in the field of regulatory B cell (Breg) research. We will review the literature on Bregs with a particular focus on their role in the regulation of allergic inflammation.

Davos, May 2022

Molecular Allergology

PD Dr. Katja Bärenfaller, PhD

Molecular Allergology
PD Dr. Katja Baerenfaller

To code or not to code

The main focus of the PhD project of Jana Koch funded by "Stiftung vormals Bündner Heilstätte Arosa" is to better understand the molecular regulatory processes in Th cell differentiation and activation. To gain a molecular profile of these processes, Jana Koch has established an experimental workflow to characterize Th cells with cell cytometry, metabolic profiling using the Seahorse technology, as well as translatomics and transcriptomics. For the acquisition of transcriptomics data, total RNA is sequenced, and for the translatomics data the ribosome profiling method is applied. In ribosome profiling, the actually translated RNA stretches can be determined through an elaborate protocol in which those stretches of RNA are isolated and sequenced, which are located inside elongating ribosomes. After sequencing, a data analysis workflow was adopted in which the sequencing reads from the total RNA and from the ribosome profiling are mapped onto the genome. The integration of the transcriptomics and translatomics data can then provide information on the translational efficiencies of individual mRNAs and their change in different conditions. In addition, the data can be queried to search for transcription of long non-coding RNAs (lncRNAs), which are defined as RNAs that are typically longer than 200 nucleotides, function without major pre-processing, and do not contain open reading frames (ORFs) that code from more than 100 amino acids. Despite their annotation as non-coding, we do find ribosome footprints in short ORFs on lncRNA, which are indicative for the differential biosynthesis of peptides (Figure 1). Our current research efforts here focus on the detailed investigation of these exciting cases, and on expanding the established technologies to new scientific questions.

Figure 1: Mapping of ribosome profiling sequencing reads on lncRNAs

Our interest in the transcription of lncRNAs and in the translation of sORFs has also resulted in a review article, as more and more lncRNAs are identified, which contain short ORFs (sORFs) that get differentially translated under specific conditions. The peptides generated through translation of sORFs can have various regulatory functions (Figure 2). In addition, some interesting cases of sORF translation playing a role in inflammation and immunity have been discovered. For example, peptides including Mm47, MIEF1-MP, MOXI or mitoregulin were shown to play a role in mitochondrial processes, and the MIR155HG transcript, the miRNA that is processed from this transcript, and the peptides that are translated from this transcript have known functions in inflammatory diseases and cancer (Della Bella et al., 2022).

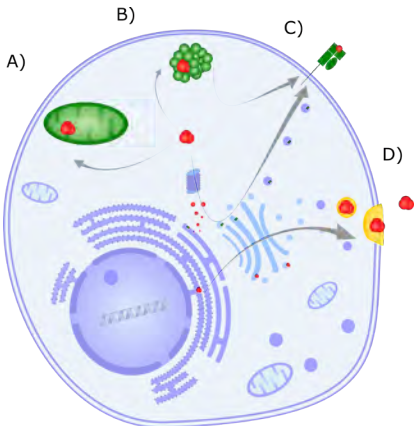


Figure 2: The various regulatory roles of sORF-encoded peptides as in Figure 2 of (Della Bella et al., 2022). Peptides can A) localize in different cellular compartments including mitochondria and play a role inflammasome activation, B) bind to protein complexes and affect their function, C) be processed and presented on MHC receptors, and D) be secreted and influence neighboring cells.

The DAViS Center goes 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. In 2021, the focus of our work in DAViS was to complete the analysis of the data obtained through the collaboration with the COVID-19 hospital in Zgierz, Poland, which was enabled through Milena Sokolowska, and to work together with various cantonal offices to analyze waste water samples for the presence of SARS-CoV-2 RNA fragments.

Identification of predictive diagnostic and prognostic COVID-19 feature subsets with machine learning

Filip Styrzynski, Damir Zhakparov, Marco Schmid, Damian Roqueiro, Zuzanna Lukasik, Julia Solek, Jakub Nowicki, Milosz Dobrogowski, Joanna Makowska*, Milena Sokolowska* and Katja Baerenfaller*, * Last-co-authors. Manuscript submitted.

A plethora of literature information on an increasing number of potentially important parameters including laboratory parameters and reported comorbidities and medications make it difficult to identify a reliable subset of significant diagnostic or prognostic features. We therefore implemented machine learning into clinical reasoning to arrive at a significant subsets of predictive features to address the main tasks:

1) Identification of diagnostic features to distinguish SARS-CoV-2 positive from negative patients based on laboratory parameters measured at admission to the hospital, and reported comorbidities and medications (dataset of 314 SARS-CoV-2 negative and 201 positive patients)

2) Identification of prognostic features on survival or death of 201 COVID-19 patients based on laboratory parameters measured at admission to the hospital and longitudinally during the course of the disease, and reported comorbidities and medications.

Using machine learning we found that diagnostic features to separate SARS-CoV-2 positive and negative patients are procalcitonin levels and complete blood counts. The subset of diagnostic features taken on admission to the hospital are inflammatory parameters, troponin I, blood cell counts, and age, while the progression of the laboratory parameters c-reactive protein, white blood cells and D-dimer over the course of the disease are predictive of a fatal disease outcome (Figure 3). Using machine learning we therefore managed to address a need of clinicians to identify a reliable subset of significant diagnostic or prognostic features.

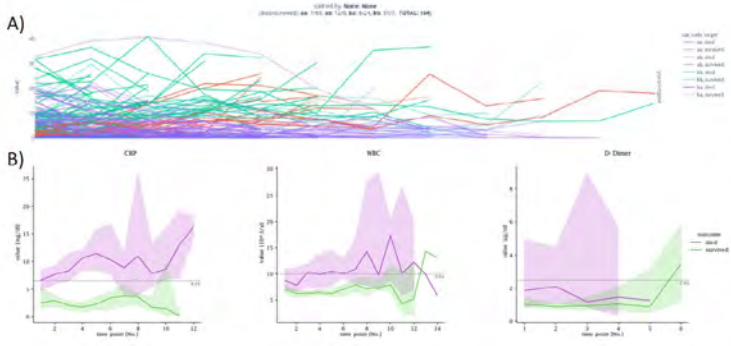


Figure 3: A) Laboratory parameters measured over the course of the disease with different numbers of measurements for different patients. B) The laboratory parameters measured during the course of the disease were clustered using SAX; the SAX-clustered longitudinal patterns of c-reactive protein (CRP), white blood cells (WBC) and D-Dimer distinguish deceased and surviving COVID-19 patients.

Arrival of Omicron (BA.1) in the canton of Grisons

In autumn 2020, the sampling of four waste water plants in the canton of Grisons was initiated to test for the presence of SARS-CoV-2 RNA fragments in the cantonal laboratory using RT-PCR, and the number of sampled waste water plants has in the meanwhile increased to 19 (https://www.gr.ch/DE/institutionen/verwaltung/ekud/anu/projekte/Abwasser/Oeff-AbwaReinAnl/SARS-CoV-2/Seiten/SARS-CoV-2.aspx). Together with the cantonal offices for Food Security and Animal Health, Nature and Environment, Military and Civil Protection, and Health, we also set up the sequencing of the RNA fragments that were enriched in the cantonal laboratory. For sequencing, the RNA is sent to the Functional Genomics Center Zurich and the raw reads are downloaded at SIAF. PhD student Yi Xiao from SIAF then used 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. To monitor the spread of the Omicron variant (BA.1), the waste water plants in Davos, St. Moritz, Landquart, and Lostallo were sampled, and the sequencing frequencies were increased in Davos and St. Moritz to assess the influence of international sports events such as the FIS Nordic World Cup in Davos and the Women's FIS Alpine Ski World Cup in St. Moritz on 11 and 12 December 2021. As shown in Figure 4 for Davos, there indeed was a pronounced increase in the prevalence of BA.1 from the beginning of December on, a pattern that was also observed for St. Moritz, but not in Lostallo and Landquart.

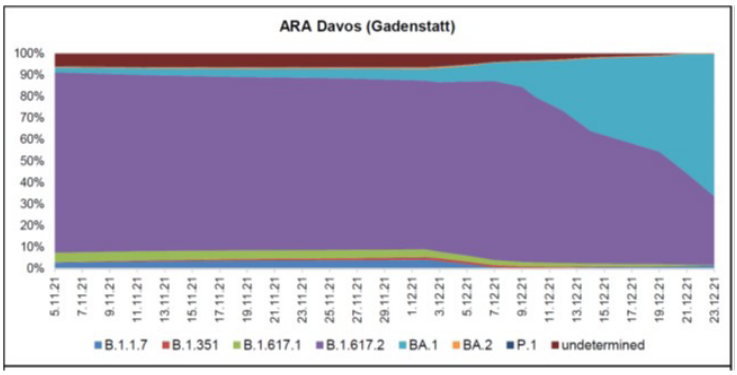


Figure 4: The relative prevalence of the different variants of SARS-CoV-2 in the waste water plant of Davos in November and December 2021; B.1.1.7 (alpha), B.1.351 (beta), B.1.617.1 (kappa), B.1.617.2 (delta), BA.1 (omicron), BA.2, P.1 (gamma)

The Center for Precision Proteomics and the Orbitrap ECLIPSE

The two major projects running at the Center for Precision Proteomics were the identification and quantification of the post-translational modifications phosphorylation, glycosylation and prenylation, and the detection of allergen proteins in food samples. For the identification of protein prenylation, proteins are first metabolically labelled in vivo through the addition of geranylgeranyl azide alcohol. The prenylated proteins are then enriched and identified with mass spectrometry. In the work by intern Svenja Schmelzer, Patrick Westermann and Jana Koch, a number of prenylated proteins could be identified. Interestingly, some of these have not previously been known to be prenylated, and some are differentially prenylated in different experimental conditions. For the identification of glycosylated and phosphorylated peptides in human plasma, PhD student Elena Barletta is currently setting up the experimental workflow. In her other main project, she is doing mass spectrometry measure-

ments for the detection of food allergen proteins using the Parallel Reaction Monitoring (PRM) method for which this type of instrument is ideally suited (Figure 5).

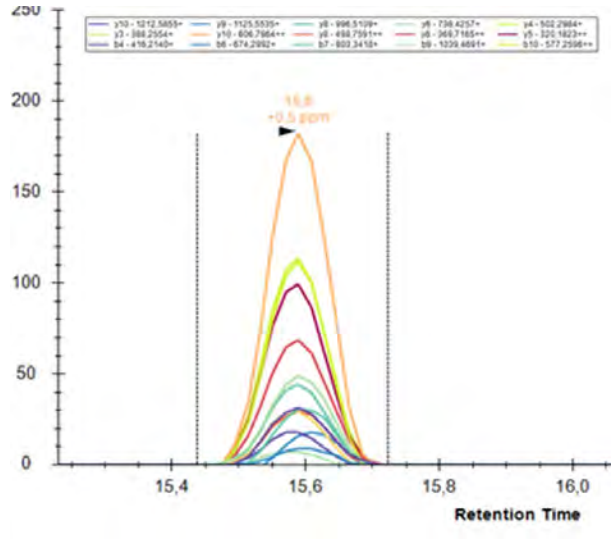


Figure 5: Parallel Reaction Monitoring spectrum for a Tropomyosin peptide

Global COVID-19 lockdown highlights humans as both threats and custodians of the environment.
Bates AE, Primack RB, Duarte CM, PAN-Environment Working Group*. (2021) Biol Conserv. Nov; 263: 109175.
Regulatory non-coding RNAs (ncRNAs) including small non-coding RNAs (sRNAs), long non-coding RNAs (lncRNAs), and circular RNAs (circRNAs) have gained considerable attention in the last few years. This is mainly due to their condition- and tissue-specific expression and their various modes of action, which suggests them as promising biomarkers and therapeutic targets. One important mechanism of ncRNAs to regulate gene expression is through translation of short open reading frames (sORFs). These sORFs can be located in lncRNAs, in non-translated regions of mRNAs where upstream ORFs (uORFs) represent the majority, or in circRNAs. Regulation of their translation can function as a quick way to adapt protein production to changing cellular or environmental cues, and can either depend solely on the initiation and elongation of translation, or on the roles of the produced functional peptides. Due to the experimental challenges to pinpoint translation events and to detect the produced peptides, translational regulation through regulatory RNAs is not well studied yet. In the case of circRNAs, they have only recently started to be recognized as regulatory molecules instead of mere artifacts of RNA biosynthesis. Of the many roles described for regulatory ncRNAs, we will focus here on their regulation during inflammation and in immunity.

Impact of DJ-1 and Helix 8 on the Proteome and Degradome of Neuron-Like Cells.
Kern U, Fröhlich K, Bedacht J, Schmidt N, Biniossek ML, Gensch N, Baerenfaller K, Schilling O. (2021) Cells, 10 (2): 404.

DJ-1 is an abundant and ubiquitous component of cellular proteomes. DJ-1 supposedly exerts a wide variety of molecular functions, ranging from enzymatic activities as a deglycase, protease, and esterase to chaperone functions. However, a consensus perspective on its molecular function in the cellular context has not yet been reached. Structurally, the C-terminal helix 8 of DJ-1 has been proposed to constitute a propeptide whose proteolytic removal transforms a DJ-1 zymogen to an active hydrolase with potential proteolytic activity. To better understand the cell-contextual functionality of DJ-1 and the role of helix 8, we employed post-mitotically differentiated, neuron-like SH-SY5Y neuroblastoma cells with stable over-expression of full length DJ-1 or DJ-1 lacking helix 8 (ΔH8), either with a native catalytically active site (C106) or an inactive site (C106A active site mutation). Global proteome comparison of cells over-expressing DJ-1 ΔH8 with native or mutated active site cysteine indicated a strong impact on mitochondrial biology. N-terminomic profiling however did not highlight direct protease substrate candidates for DJ-1 ΔH8, but linked DJ-1 to elevated levels of activated lysosomal proteases, albeit presumably in an indirect manner. Finally, we show that DJ-1 ΔH8 loses the deglycation activity of full length DJ-1. Our study further establishes DJ-1 as deglycation enzyme. Helix 8 is essential for the deglycation activity but dispensable for the impact on lysosomal and mitochondrial biology; further illustrating the pleiotropic nature of DJ-1.

Translation and emerging functions of non-coding RNAs in inflammation and immunity.
Della Bella, E, Koch, J, Baerenfaller, K. (2022) Allergy. 2022; 00: 1–13.
Regulatory non-coding RNAs (ncRNAs) including small non-coding RNAs (sRNAs), long non-coding RNAs (lncRNAs), and circular RNAs (circRNAs) have gained considerable attention in the last few years. This is mainly due to their condition- and tissue-specific expression and their various modes of action, which suggests them as promising biomarkers and therapeutic targets. One important mechanism of ncRNAs to regulate gene expression is through translation of short open reading frames (sORFs). These sORFs can be located in lncRNAs, in non-translated regions of mRNAs where upstream ORFs (uORFs) represent the majority, or in circRNAs. Regulation of their translation can function as a quick way to adapt protein production to changing cellular or environmental cues, and can either depend solely on the initiation and elongation of translation, or on the roles of the produced functional peptides. Due to the experimental challenges to pinpoint translation events and to detect the produced peptides, translational regulation through regulatory RNAs is not well studied yet. In the case of circRNAs, they have only recently started to be recognized as regulatory molecules instead of mere artifacts of RNA biosynthesis. Of the many roles described for regulatory ncRNAs, we will focus here on their regulation during inflammation and in immunity.

Davos, May 2022

Dr. Claudio Rhyner, PhD

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.

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.

Davos, May 2022

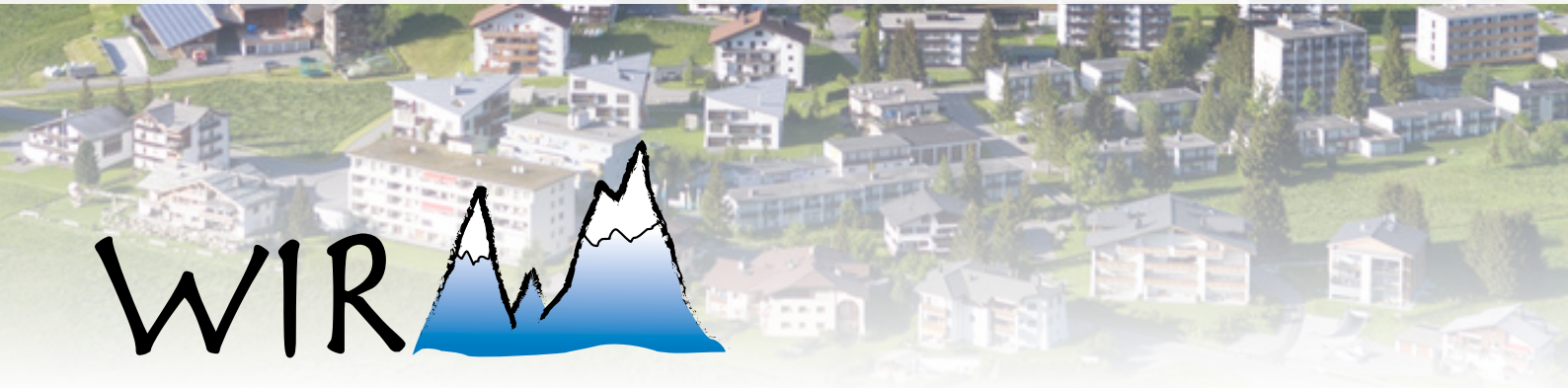
WORLD IMMUNE REGULATION MEETING XVI

6 - 9 July 2022 | Davos, Switzerland

„Immune Activation, Effector Functions and Immune Tolerance with a special focus on Autoimmunity and Allergy“

Register Now

www.wirm.ch



PD Dr. Milena Sokolowska, MD, PhD

Due to environmental and lifestyle changes, there is an increasing frequency of allergies and respiratory viral and bacterial infections. The last 2 years of pandemics of COVID-19 has been the most extreme demonstration 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. All of those factors impact the proper cross-talk between innate and the adaptive immunity 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 and provide new 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 respiratory infections

Rhinovirus-induced epithelial RIG-I inflammasome activation suppresses antiviral immunity and promotes inflammatory responses in virus-induced asthma exacerbations 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, Kebadze T, Jackson DJ, Edwards MR, Thiel V, Johnston SL, Akdis CA*, Sokolowska M*. *Last co-authors. Submitted.

Rhinoviruses (RV) and inhaled allergens, such as house dust mite (HDM) are the major agents responsible for asthma onset, exacerbations and progression to the severe disease, but the mechanisms of these pathogenic reciprocal virus-allergen interactions are not well understood. To address this, we analyzed mechanisms of airway epithelial sensing and response to RV infection using controlled experimental in vivo RV infection in healthy controls and patients with asthma and in vitro models of HDM exposure and RV infection in primary airway epithelial cells. We found that intranasal RV infection in patients with asthma led to the highly augmented inflammasome-mediated lower airway inflammation detected in bronchial brushes, biopsies and bronchoalveolar lavage fluid. Mechanistically, RV infection in bronchial airway epithelium led to retinoic acid-inducible gene I (RIG-I), but not via NLR family pyrin domain containing 3 (NLRP3) inflammasome activation, which was highly augmented in patients with asthma, especially upon pre-exposure to HDM (Figure 1).

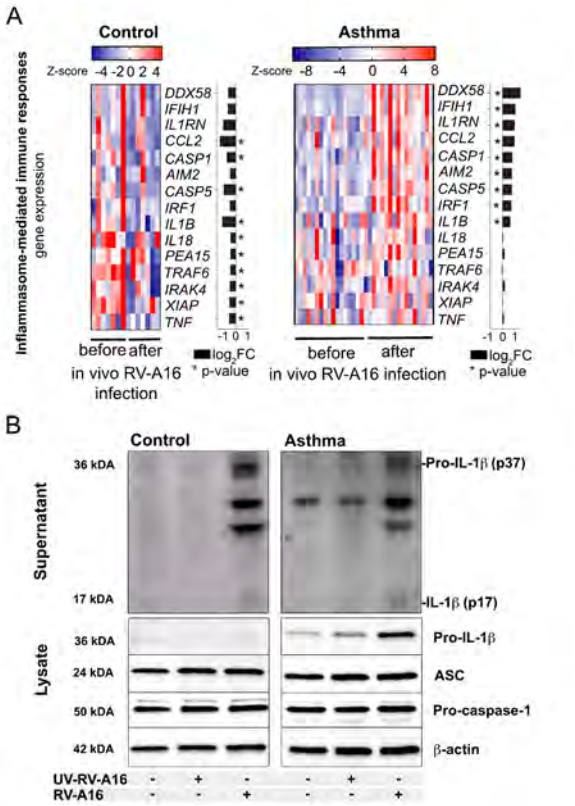


*Figure 1. Increased inflammasome activation in bronchial epithelium of patients with asthma. A) Genes encoding inflammasome-mediated immune responses in bronchial brushings after in vivo RV-A16 infection in controls and patients with asthma, *<0.05. B) IL-1γ, pro-IL-1γ, ASC, pro-caspase-1, and γ-actin in epithelium.*

This excessive activation of RIG-I inflammasomes was responsible for the impairment of antiviral type I/III interferons (IFN), prolonged

viral clearance and unresolved inflammation in asthma in vivo and in vitro. Pre-exposure to HDM amplifies RV-induced epithelial injury in patients with asthma via enhancement of pro-IL1β expression and release, additional inhibition of type I/III IFNs and activation of auxiliary proinflammatory and pro-remodeling proteins. Finally, in order to determine whether RV-induced activation of RIG-I inflammasome may play a role in the susceptibility to severe acute respiratory syndrome coronavirus (SARS-CoV-2) infection in asthma, we analyzed the effects of HDM exposure and RV/SARS-CoV-2 coinfection. We found that prior infection with RV restricted SARS-CoV-2 replication, but co-infection augmented RIG-I inflammasome activation and epithelial inflammation in patients with asthma, especially in the presence of HDM. Timely inhibition of epithelial RIG-I inflammasome activation may lead to more efficient viral clearance and lower the burden of RV and SARS-CoV-2 infections.

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

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. Submitted.

In the current pandemic, oversaturation of hospitals with patients with SARS-CoV-2 infection-like symptoms and an excess of hospitalized COVID-19 patients led to a global healthcare crisis. The aim of our study was to find a manageable set of decisive parameters that can be used to i) rapidly identify SARS-CoV-2 positive patients, ii) identify high-risk patients, and iii) recognize longitudinal warning signs of a possible fatal outcome. We trained several machine learning (ML) models using data on reported comorbidities, medications, symptoms, and laboratory parameters on hospital admission, and over the disease course in 201 SARS-CoV-2 positive and 314 SARS-CoV-2 negative subjects with a COVID-19-like clinical presentation. 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. Next, we determined that COVID-19 patients who on hospital admission were older, had higher procalcitonin, C-reactive protein, and troponin I together with lower hemoglobin and platelets/neutrophils ratio, were at highest risk of death from COVID-19. Finally, we identified patterns of changes in C-reactive protein, white blood cells, and D-Dimer that predicted the disease outcome. Interpretation: Our study provides sets of easily obtainable parameters that allow to assess a SARS-CoV-2 patient's status prior to RT-PCR results and the dynamics of the disease, based on which the hospital logistics and treatment can be planned.

Regulation of ACE2 mRNA and protein isoforms in viral and allergic inflammation.

Stocker N, Radzikowska U, Huang M, Ding M, Wawrzyniak P, Tan G, Akdis CA, Sokolowska M. In preparation.

SARS-CoV-2 infects airway epithelial cells mainly via the receptor angiotensin-converting enzyme 2 (ACE2). An association between COVID-19 and various endotypes of asthma is still unclear. ACE2 exists in various, differentially regulated mRNA and protein isoforms (Figure 2), which might affect SARS-CoV-2 infection and COVID-19 severity, but transcription, translation and posttranslational modifications of these isoforms have not been yet extensively studied. Here, we investigate the behavior of full length/long ACE2 and short ACE2 mRNA and protein isoforms in primary bronchial epithelial cells from control individuals and patients with asthma at baseline or upon in vitro infection with human rhinovirus 16 (HRV16), stimulation with the type 2 inflammatory cytokine, interleukin 13 (IL-13) or exposure to house dust mite (HDM) allergen.

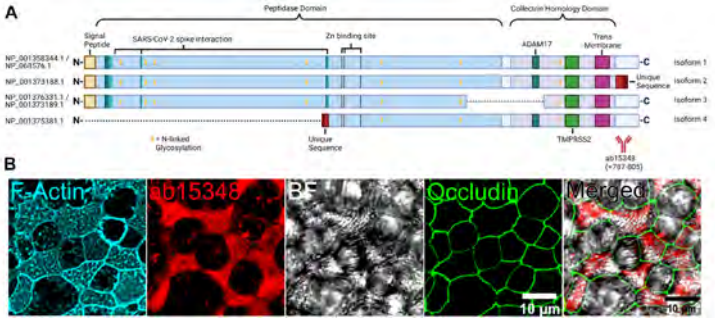


Figure 2. Expresssion of ACE2 isoforms in bronchial epithelium. A) Schematic presentation of ACE2 isoforms B) ACE2 localizes apically on the ciliated bronchial epithelial cells. Apical planar view on bronchial epithelial cells, stained with F-actin, ACE2 and Occludin, and transmitted light.

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 Feb 16.

Non-steroidal anti-inflammatory drugs (NSAIDs) and other eicosanoid pathway modifiers are among the most ubiquitously used medications in the general population. Their broad anti-inflammatory, antipyretic, and analgesic effects are applied against symptoms of respiratory infections, including SARS-CoV-2, as well as in other acute and chronic inflammatory diseases that often coexist with allergy and asthma. However, the current pandemic of COVID-19 also revealed the gaps in our understanding of their mechanism of action, selectivity, and interactions not only during viral infections and inflammation, but also in asthma exacerbations, uncontrolled allergic inflammation, and NSAIDs-exacerbated respiratory disease (NERD). In this context, we summarize here currently available knowledge, novel discoveries, and controversies regarding the use of NSAIDs 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.

SARS-CoV-2 candidate vaccines - composition, mechanisms of action and stages of clinical development.

Rodriguez-Coira R, Sokolowska M. Allergy. 2021 Jun;76(6):1922-1924.

We described here the approved COVID-19 vaccines and other candidates in the final stages of clinical trials. We explained briefly their modes of action, immunological mechanisms, as well as advantages and disadvantages of each type of vaccination platform.

EAACI statement on the diagnosis, management and prevention of severe allergic reactions to COVID-19 vaccines.

Sokolowska M, Eiwegger T, Ollert M, Torres MJ, Barber D, Del Giacco S, et all. Allergy. 2021 Jun;76(6):1629-1639.

This position paper of the European Academy of Allergy and Clinical Immunology (EAACI) clarifies that there is no contraindication to administer COVID-19 vaccines to allergic patients who do not have a history of an allergic reaction to any of the vaccine components. Importantly, as is the case for any medication, anaphylaxis may occur after vaccination in the absence of a history of allergic disease. Therefore, we provide a simplified algorithm of prevention, diagnosis and treatment of severe allergic reactions and a list of recommended medications and equipment for vaccine centres. We also describe potentially allergenic/immunogenic components of the approved vaccines and propose a workup to identify the responsible allergen.

2. Understanding immunometabolism in immune tolerance, allergy and asthma

The Importance of Metabolism for Immune Homeostasis in Allergic Diseases.

Rodriguez-Coira J, Villaseñor A, Izquierdo E, Huang M, Barker-Tejeda TC, Radzikowska U, Sokolowska M*, Barber D*. * Last co-authors. Front Immunol. 2021 Jul 28;12:692004.

There is increasing evidence that the metabolic status of T cells and macrophages is associated with severe phenotypes of chronic inflammation, including allergic inflammation. Metabolic changes in immune cells have a crucial role in their inflammatory or regulatory responses. This notion is reinforced by metabolic diseases influencing global energy metabolism, such as diabetes or obesity, which are known risk factors of severity in inflammatory conditions, due to the metabolic-associated inflammation present in these patients. Since several metabolic pathways are closely tied to T cell and macrophage differentiation, a better understanding of metabolic alterations in immune disorders could help to restore and modulate immune cell functions. Here, we summarized the main metabolic pathways of the cells involved in the allergic reaction with a focus on T cells and macrophages and describes different models and platforms of analysis used to study the immune system and its relationship with metabolism.

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

Rodriguez-Coira J, Villaseñor A, Gomez-Casado C, Sanchez-Solares J, Huang M, Pablo Torres C, Obeso D, Saiz V, Ruiz- Leon B, Espinazo M, Radzikowska U, Heider A, Tan G, Escribese MM, Moreno-Aguilar C, Akdis CA, Barber D *, Sokolowska M*. * Last co-authors. In preparation.

We performed a detailed untargeted and targeted metabolomic analysis of ex vivo sorted memory CD4+T effector cells and regulatory T cells in health and during type 2 inflammation in collaboration with the group of Domingo Barber in Spain. We found that memory effector T cells metabolism depended on amino acids and central carbon pathways, whereas memory T reg cells metabolism relied mostly on fatty acid oxidation and vitamin cofactors of FAO. We also determined that the high levels of some amino acids increased T cell receptor-induced glycolysis and oxidative phosphorylation in CD4+ T cells, while others efficiently limited CD4+T cell proliferation via transcriptional regulation of main responsible enzymes. Finally, we found that the lowest levels of intracellular amino acids were linked to the pathogenic subpopulations of effector T cells, including Th2a cells and impaired Treg cells in patients with the most severe forms of allergic diseases. It all suggests that there is a metabolic checkpoint of pathogenic type 2 cells development.

Viral infections induce metabolic reprogramming of airway epithelium in asthma.

Huang M*, Ding M*, Radzikowska U, Rodriguez-Coira J, Stocker N, Tan G, Heider A, Johnston S, Akdis CA, Sokolowska M#. * equally contributed. In preparation.

Human rhinovirus (RV-A16) plays a major role in exacerbation of asthma. However, limited studies focused on immunometabolic changes in airway epithelium in response to RV-A16. We aim to determine if there are any differences in mitochondrial respiration, oxidative phosphorylation (OXPHOS) and glycolysis in airway epithelium in response to RV-A16 infection in asthma as compared to health. We use in vitro cultures of human primary bronchial epithelial cells grown in air-liquid interphase (ALI), RNA-seq, qPCR, targeted-proteomics (OLINK), and Seahorse real time cell metabolic analysis, as well as we analyze samples from patients with asthma and healthy controls experimentally infected in vivo with RV-A16. So far we determined that bronchial epithelium of patients with asthma significantly differ in usage of various metabolic pathways as compared to healthy controls at baseline and after viral infection, which is partly connected with the efficiency of antiviral response and resolution of airway inflammation.

Trained immunity and tolerance in innate lymphoid cells, monocytes, and dendritic cells during allergen specific immunotherapy.

Eljaszewicz E., Ruchti F., Radzikowska U.; Globinska A., Boonpiyathad T.; Gschwend A., Morita H., Helbling A.; Arasi S.; Helga Kahlert, Berek N., et all. J Allergy Clin Immunol. 2021 May;147(5):1865-1877.

Despite the efficacy of allergen-specific immunotherapy (AIT), the role of trained immunity and tolerance in this process has not been elucidated. Here, we by performing a comprehensive longitudinal analysis of the systemic innate immune cell repertoire during the one-year course of AIT in allergic patients, we found that AIT induces changes in the composition and heterogeneity of circulating innate immune cells and brings them to the level observed in

healthy individuals. Monitoring of ILCs, monocytes, and DCs during AIT might serve as a novel biomarker strategy.

Can polyamine metabolism in T helper cell lineage commitment be a new target in allergy research?
Huang M, Rodriguez-Coira J. Allergy. 2022 Feb 21.
We summarized here how changes in polyamine metabolism impact T cell phenotype and lineage commitment. We also highlighted how these different metabolic profiles could be linked and used as biomarkers for T cell activity in allergic diseases.

Omics technologies in allergy research: EAACI position paper.
Radzikowska U, Baerenfaller K, Cornejo-Garcia JA, Karaaslan C, Barletta E, Sarac BE, Zhakparov D, Villaseñor A, Eguiluz-Gracia I, Mayorga C, Sokolowska M, et all. In revision.
In this EAACI position paper, we broadly reviewed current advances and applicability of omics techniques in allergy research, with a focus on methodology and data analysis, aiming to provide basic and clinical researchers with a desk reference in the field. We highlighted the potential of omics strategies in understanding disease pathophysiology and key tools to reach unmet needs in allergy precision medicine, such as successful patients' stratification, accurate disease prognosis, prediction of treatment efficacy, and successful prevention measures.

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.
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 (Figure 3).

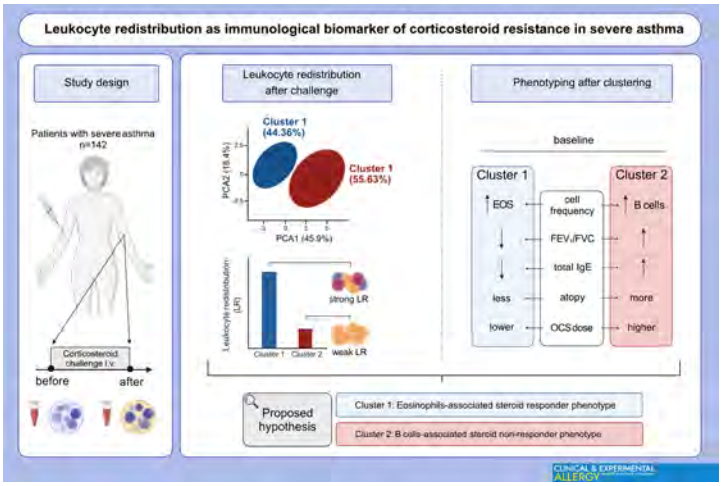


Figure 3. Leukocyte redistribution is an immunological marker of glucocorticosteoids insensitivity in severe asthma. Intravenous challenge with corticosteroids identified two clusters of patients with severe asthma, who had different leukocyte redistribution as analysed by the complete blood count and flow cytometry. Unbiased clinical phenotyping after clustering revealed that Cluster 1 and 2 patients varied slightly at baseline in clinical characteristics and in the need for systemic corticosteroids. LR might potentially serve as a biomarker of corticosteroid sensitivity to identify the biological reserve of the immune system.

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.

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, et all. Allergy. 2022 Feb 3.
In this position paper of the European Academy of Allergy and Clinical Immunology (EAACI), we described currently available European Alpine Altitude Climate Treatment (AACT) programs, which combine the physical characteristics of altitude with the avoidance of environmental triggers in the alpine climate, and a personalized multidisciplinary pulmonary rehabilitation approach.

Understanding uncontrolled severe allergic asthma by integration of omic and clinical data.
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. Allergy. 2021 Nov 28.
Here, we collaborated with the group of Maria Escribese on identification of a unique metabolic and proteomic serum fingerprint of patients with uncontrolled, severe asthma. Integration of clinical and experimental data led to a deeper understanding of the mechanisms underlying phenotype of severe asthma.

Davos, May 2022

Dr. Willem van de Veen, PhD

B cell immunology

B cells play a pivotal role in IgE-mediated allergies, as a result of their unique ability to produce allergen-specific IgE antibodies that sensitize mast cells and basophils by binding to their high affinity IgE receptors (FcεRI). Subsequent allergen crosslinking of FcεRI-bound IgE on mast cells and basophils initiates the release of pro-inflammatory mediators resulting in a type I hypersensitivity reaction. Immune regulatory functions of B cells, in particular mediated by regulatory B (Breg) cells, which produce anti-inflammatory cytokines, have also been described. Serological mechanisms of immune regulation by B cells include the prominent increase of IgG4 antibodies in serum observed in patients gaining immune tolerance, as seen during allergen-specific immunotherapy. Thus, B cells are fundamental in both induction of of allergies as well as developing tolerance to allergens. Our lab is interested in the different aspects of B cell immunology in the context of allergies and other immune pathologies.

Regulatory B cells, A to Z

Jansen K, Cevhertas L, Ma S, Satitsuksanoa P, Akdis M, van de Veen W. Allergy. 2021 Sep;76(9):2699-2715.

B cells play a central role in the immune system through the production of antibodies. During the past two decades, it has become increasingly clear that B cells also have the capacity to regulate immune responses through mechanisms that extend beyond antibody production. Several types of human and murine regulatory B cells have been reported that suppress inflammatory responses in autoimmune disease, allergy, infection, transplantation, and cancer. Key suppressive molecules associated with regulatory B-cell function include the cytokines IL-10, IL-35, and TGF-β as well as cell membrane-bound molecules such as programmed death-ligand 1, CD39, CD73, and aryl hydrocarbon receptor. Regulatory B cells can be induced by a range of different stimuli, including microbial products such as TLR4 or TLR9 ligands, inflammatory cytokines such as IL-6, IL-1β, and IFN-α, as well as CD40 ligation (Figure 1). This review provides an overview of our current knowledge on regulatory B cells. We discuss different types of regulatory B cells, the mechanisms through which they exert their regulatory functions, factors that lead to induction of regulatory B cells and their role in the alteration of inflammatory responses in different diseases.

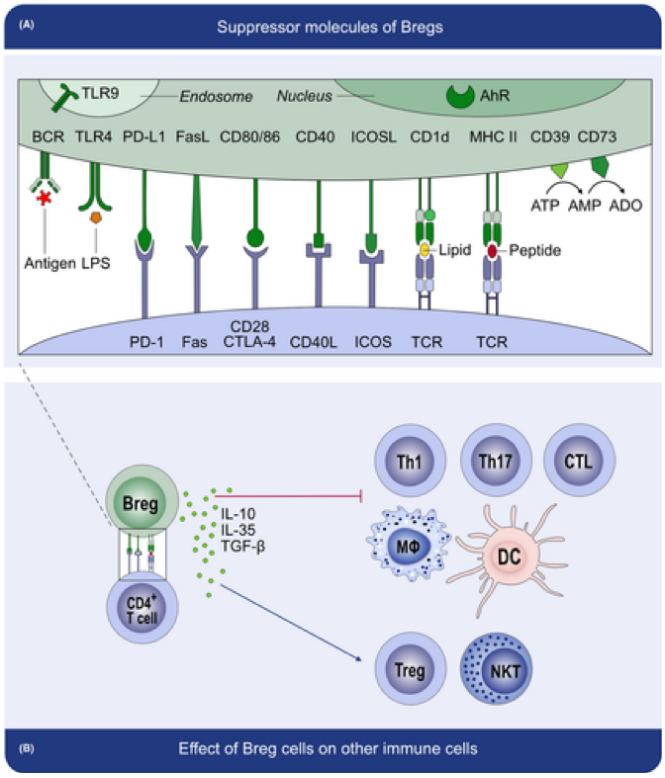


Figure 1 Breg cells and their suppressor molecules. (A) TLR ligation by the TLR4 ligand LPS and the TLR9 ligand CpG, as well as antigen-mediated BCR triggering and CD40 ligation can lead to Breg cell activation and the secretion of suppressive cytokines such as IL-10, IL-35, and TGF-β. Molecules expressed by Breg cells include BCR, CD80, CD86, PD-L1, CD40, FasL, ICOS-L, CD1d, MHC II, AHR, TLR9, and TLR4. Moreover, CD39 and CD73 are crucial enzymatic molecules in the ADO pathway and may contribute to the suppressive capacity of B cells. (B) The activation of macrophages and DCs is suppressed by Breg cells via the secretion of IL-10. Breg cells can also suppress Th1, Th17, and CTL responses. In contrast, Breg cells induce Treg cell expansion through the secretion of IL-10, TGF-β, and IL-35. In addition, CD1d which is expressed by certain Breg cells, activates NKT cells with a suppressive function. TLR, Toll-like receptor; LPS, lipopolysaccharide; PD-L1, Programmed death-ligand 1; BCR, B cell receptor; ICOS-L, inducible costimulator ligand; FasL, Fas ligand; MHC II, Major histocompatibility complex II; AHR, aryl hydrocarbon receptor; ADO, adenosine; DC, Dendritic cells; CTL, cytotoxic T lymphocyte; NKT, natural killer T cell. Jansen, et al. Allergy. 2021 Sep;76(9):2699-2715.

Biology and dynamics of B cells in the context of IgE-mediated food allergy

Satitsuksanoa P, Daanje M, Akdis M, Boyd SD, van de Veen W. Allergy. 2021 Jun;76(6):1707-1717.

An increasing number of people suffer from IgE-mediated food allergies. The immunological mechanisms that cause IgE-mediated food allergy have been extensively studied. B cells play a key role in the development of IgE-mediated food allergies through the production of allergen-specific antibodies. While this particular function of B cells has been known for many years, we still do not fully understand the mechanisms that regulate the induction and maintenance of allergen-specific IgE production. It is still not fully understood where in the body IgE class switch recombination of food

allergen-specific B cells occurs, and what processes are involved in the immunological memory of allergen-specific IgE responses. B cells can also contribute to the regulation of allergen-specific immune responses through other mechanisms such as antigen presentation and cytokine production. Recent technological advances have enabled highly detailed analysis of small subsets of B cells down to the single-cell level. In this review, we provide an overview of the current knowledge on the biology of B cells in relation to IgE-mediated food allergies (Figure 1).

IL-10 induces IgG4 production in NOD-scid Il2rγ null mice humanized by engraftment of peripheral blood mononuclear cells

Lacin Cevhertas*, Siyuan Ma*, Barbara Stanic, Urs Ochsner, Kirstin Jansen, Ruth Ferstl, Remo Frei, Obinna, Chijoke,Christian Münz, Liam O'Mahony, Mübeccel Akdis, Willem van de Veen. * Authors contributed equally. Allergy, 2021, 76: 3525-3529.

IgG4 antibodies are considered to have anti-inflammatory activity and may confer protection against anaphylaxis and allergic inflammation. The production of IgG4 by human B cells in vitro is strongly enhanced by IL-10. In vivo studies of the regulation of IgG4 have been handicapped by the fact that mice do not express this immunoglobulin isotype. The use of humanized mice allows the study of human immunoglobulin regulation including IgG4. Immunodeficient NOD-scid Il2rγnull (NSG) mice lack murine lymphocytes, including T, B and NK cells. This strain enables efficient engraftment of human hematopoietic progenitor cells (HPC) and peripheral blood mononuclear cells (PBMC). Here, we established a humanized mouse model to study the regulation of IgG4 production in vivo. To determine optimal conditions for B cell engraftment in NSG mice, engraftment of human leucocytes after intraperitoneal (IP) and intravenous (IV) injections of 5x106 and 20x106 PBMC were analyzed after 14 and 21 days in spleen. Engraftment of human cells was determined by flow cytometry. Expression of human (hu)CD45 was used for gating of human leukocytes (Figure 3A). The highest level of engraftment of huCD45+ cells was observed 21 days after IV injection of 20x106 PBMC. Human B lineage cells (gated as huCD45+CD19+) were detectable at low levels on day 14 in the IV group and in both the IV and IP group on day 21 (Figure 3 E,F). Total CD19+ B lineage cells, CD19+CD138- B cells and CD138+ plasma cells showed a similar pattern in which the highest level of engraftment, both as a percentage of huCD45+ cells and in absolute engrafted cell numbers, was observed with IV injection of 5x106 PBMC. Therefore, we concluded that the IV route with 5x106 PBMC was optimal for B lineage cell engraftment. Next, we assessed the effect of IL-10 on the B cell compartment and immunoglobulin production. All human immunoglobulin isotypes were detectable in serum of saline and IL-10 treated mice (Figure 2G). Interestingly, IL-10 induced a significant increase in the serum level of IgG4, while no significant changes were observed for IgG1, 2, 3, IgM, IgA and IgE. Our findings demonstrate that NSG mice can be utilized to study human B cell and immunoglobulin responses. 5X106 PBMC and application through IV injection were optimal for B cell and plasma cell engraftment. IL-10 stimulated the in vivo up-regulation of IgG4 production.

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

Manuscript under review. Preprint:

Although avian coronavirus infectious bronchitis virus (IBV) and SARS-CoV-2 belong to different genera of the Coronaviridae family, exposure to IBV may result in the development of cross-reactive antibodies to SARS-CoV-2 due to homologous epitopes. We aimed to investigate whether antibody responses to IBV cross-react with SARS-CoV-2 in poultry farm personnel who are occupationally exposed to aerosolized IBV vaccines.

We analyzed sera from poultry farm personnel, COVID-19 patients, and pre-pandemic controls. IgG levels against the SARS-CoV-2 antigens S1, RBD, S2, and N and peptides corresponding to the SARS-CoV-2 ORF3a, N, and S proteins as well as whole virus antigens of the four major S1-genotypes 4/91, IS/1494/06, M41, and D274 of IBV were investigated by in-house ELISAs. Moreover, live-virus neutralization test (VNT) was performed.

A subgroup of poultry farm personnel showed elevated levels of specific IgG for all tested SARS-CoV-2 antigens compared to pre-pandemic controls. Moreover, poultry farm personnel, COVID-19 patients, and pre-pandemic controls showed specific IgG antibodies against IBV strains. These antibody titers were higher in long-term vaccine implementers. We observed a strong correlation between IBV-specific IgG and SARS-CoV-2 S1-, RBD-, S2-, and N-specific IgG in poultry farm personnel compared to pre-pandemic controls and COVID-19 patients. However, no neutralization was observed for these cross-reactive antibodies from poultry farm personnel using the VNT.

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.

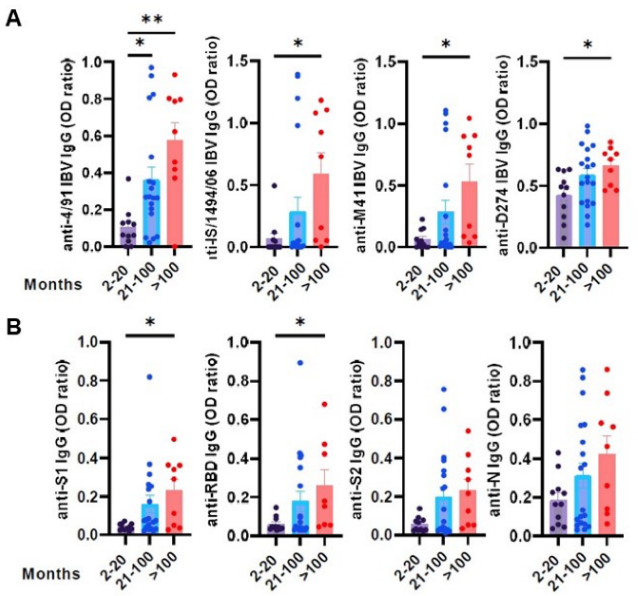


Figure 2. Long-term vaccine implementers have elevated IBV- and SARS-CoV-2-specific IgG. Specific IgG for IBV strains 4/91, IS/1494/06, M41 and D274 (A) and SARS-CoV-2 S1, RBD, S2 and N (B) were measured in serum samples of vaccine implementers with different durations of work experience (work experience in months is indicated on the x-axes.

The effect of measles on allergic sensitization in children

Tan Nguyen, Renske Schappin, Suzanne Pasmans, Rik de Swart, Willem van de Veen

Manuscript in preparation

Measles remains a significant cause of childhood morbidity and mortality, and causes more than 100,000 deaths globally each year. Hallmark of the disease is a generalized immune suppression that can last for several weeks to months after resolution of measles virus (MV) infection, resulting in increased susceptibility to opportunistic bacterial and viral infections. At the same time measles is associated with immune activation and induces strong MV-specific immune responses that confer life-long immunity. This apparent contradiction is known as the 'measles paradox'. Measles-associated loss of memory T cells, B cells and plasma cells may contribute to immune amnesia. In fact, acute measles apparently results in a partial "reset" of the adaptive immune system. Although in the majority of cases such a reset will be detrimental to the host, there may be exceptions to this rule. Especially in children with allergic disease and atopic sensitization, an immunological reset could potentially be beneficial. The immune amnesia effect resulting from measles infection indicates a broad, and non-specific elimination of the immunological memory. Measles infection in children who are sensitized to allergens could lead to a depletion of allergen-specific B- and T-lymphocytes, plasma cells and IgE antibodies. This may result in a reduction of allergic sensitization and the risk of allergies. We are currently carrying out a study in which we will assess whether MV infection results in a reduction of allergic sensitization.

To this end, total and allergen-specific IgE antibody levels will be analysed in paired plasma samples previously collected from unvaccinated children before and after measles. This will demonstrate whether there is a direct relation between MV infections and allergic sensitization. This is a retrospective cohort study that involves the analysis of biobanked plasma samples obtained from unvaccinated children aged four to 17 years old that were collected for a previous observational cohort study that was recently published. This observational cohort study was performed during a measles outbreak in the Orthodox Protestant community in the Netherlands. This study is currently ongoing and results are expected this year.

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

Manuscript in preparation

Understanding the mechanisms of tolerance induction to allergens is critical for the development of targeted therapies for the treatment of allergic disease. Beekeepers, who are frequently exposed to high-doses of bee venom allergens, represent a unique human in vivo model for studying these mechanisms. The aim of this study was to characterize the allergen-specific B cell repertoire in highly exposed healthy individuals and track its development over time. Blood samples were collected from 12 beekeepers before and during the beekeeping season over the course of up to 20 years. B cells specific for the major bee venom allergen phospholipase A2 (PLA) were identified through staining with fluorescently labelled PLA, and purified using fluorescence activated cell sorting. PLA-specific B cells were immortalized through transduction with BCL6 and BCL-XL, and expanded. Deep sequencing of the B cell repertoire was performed on expanded PLA-specific B cells as well as primary total B cells.

Frequencies of PLA-specific B cells were higher during the beekeeping season than before the season (Figure 3). PLA-specific clones were overrepresented within the IgE and IgG4 repertoire compared to other isotypes. Moreover, PLA-specific clonal lineages had increased V-gene mutations at the end of the season. Members of many PLA-specific clonal lineages were detected at multiple time points, which, in some individuals, were more than 20 years apart. PLA-specific clonal lineages contained members of different immunoglobulin heavy chain isotypes including IgG1, IgG2, IgG3, IgG4 and IgE. Within the clonal lineages that contained an IgE member, the members of other isotypes that showed the highest sequence similarity to the IgE member were most frequently IgG2 or IgG4 clones, indicating that IgE members may have undergone sequential class switch recombination through an IgG2 or IgG4 intermediate. Interestingly, clusters of PLA-specific clones with identical V and J gene usage and a CDR3 AA similarity of >90% were found in different beekeepers, indicating the existence of public antibody clonotypes against PLA.

Our study shows that allergen-specific clonal lineages in highly exposed non-allergic individuals persist for many years, are clonally expanded and show a large diversity. Moreover, allergen-specific clones expand and accumulate V-gene mutations in response to seasonal allergen exposure. PLA-specific IgE clones may develop

through an IgG2 or 4 intermediate and public PLA-specific antibody clonotypes exist. It remains to be determined which features of the B cell repertoire are indicative of allergen tolerance. Comparative analysis of the allergen-specific B cell repertoire of allergic individuals before and after allergen-specific immunotherapy is currently underway and will potentially help to identify key differences between healthy and allergic B cell responses.

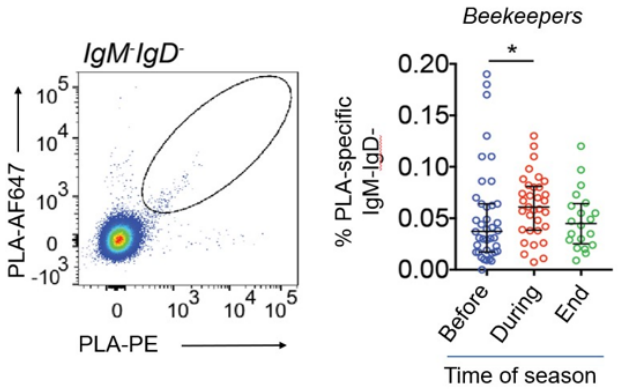


Figure 3. Frequencies of B cells specific for the major bee venom allergen phospholipase A2 transiently increase during the beekeeping season. PLA-specific B cells were stained with PLA-PE and PLA-AF647. Class-switched (IgM-IgD-) B cells were gated and B cells double positive for PLA-PE/647 were identified as PLA-specific cells. Frequencies of circulating PLA-specific class switched B cells increased during the beekeeping season.

Identification of immunological markers for monitoring disease activity in eosinophilic esophagitis

Manal Bel imam, Alex Straumann, Luc Biedermann, Philipp Schreiner, Pattraporn Satitsuksanoa, Stephan R. Schneider, Mübeccel Akdis, Willem van de Veen

Eosinophilic esophagitis (EoE) is a chronic immune-mediated inflammatory condition that showed increased prevalence during the past 2-3 decades. The mechanisms underlying EoE are not completely understood; however, several studies suggested the involvement of Th2 cytokines and antibody production. Also, food ingestion may play a role in EoE triggering, although several observations indicate that EoE is not an IgE-mediated food allergy. Rather, it has been observed that EoE patients have high levels of IgG4 in esophageal biopsies and of circulating food antigen-specific IgG4. This project aims to elucidate basic mechanisms underlying EoE in relation to antigen-specific B cell responses and to identify non-invasive biomarkers for early diagnosis and monitoring of EoE. Blood samples from EoE patients were collected at the Swiss EoE Clinics at the University Hospital Zurich. In total, 120 samples from patients with inactive, moderate-active and highly-active disease (assessed by endoscopic and histological findings) were processed and analyzed for food antigen-specific antibodies of all isotypes. In this preliminary analysis, cow's milk casein- and whey-specific total IgG and IgG4 levels in EoE patient's plasma were measured by enzyme-linked immunosorbent assay (ELISA). Among 120 samples, we could identify patients with highly positive, intermediate and low levels of casein and whey-specific IgG and IgG4 antibodies. Cow's milk allergen-specific antibodies were significantly increased in EoE patients compared to healthy controls. This analysis will allow us to identify patients with high levels of food antigen-specific antibodies, which will be further analyzed. From select patient we will isolate and characterize antigen-specific B cells and characterize them using single-cell transcriptomics. Moreover, this data will be correlated with disease severity, serum biomarkers and tissue infiltrating immune cells in esophageal biopsies.

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

Manuscript in preparation

Immune checkpoint inhibitor (ICI) therapies have been approved for treatment of malignant melanoma. Although a survival benefit and better overall response rate is observed in many patients, not all patients respond to these ICI treatments. Thus, identifying novel biomarkers is necessary to predict the response of patients and eligible patient selection for ICI treatment. Characterization of B cell phenotypes by their surface markers will improve the understanding of B cell immunity in melanoma and how ICI affects B cells. Therefore, we analyzed circulating B cells from healthy controls and in a cohort of patients (n=25) with metastatic melanoma before and after the administration of anti-PD1 and/or anti-CTLA4 mAbs from 2 different visits, representing early and late response. We detected statistically significant alterations of naïve B cell, switched B cell and IgA+ B cell frequencies in non-responding (n=12) patients during therapy. We observed BAFF (B cell activating factor) receptor expression was higher on all subsets of B cells in responders compared to non-responders at baseline and at early response. We also detected significantly higher serum BAFF in non-responders than responders at baseline. Consequently, our results suggest that ICIs treatment alters the B cell characteristics during ICIs therapy through the BAFF related receptor expression. Furthermore, soluble protein BAFF may represent a predictive biomarker for the response of metastatic melanoma patients to ICIs therapy.

Davos, May 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. 2021 Aug 17. doi: 10.1007/5584_2021_654. Online ahead of print. IPF 2.622

Agache I, Eguiluz-Gracia I, Cojanu C, Laculiceanu A, Del Giacco S, Zemelka-Wiacek M, Kosowska A, Akdis CA, Jutel M. Advances and highlights in asthma in 2021. Allergy. 2021 Nov;76(11):3390-3407. doi: 10.1111/all.15054. 34392546 Review. IPF 13.146

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 13.146

Agache I, Song Y, Posso M, Alonso-Coello P, Rocha C, Solà I, Beltran J, 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, Werfel T, Canelo-Aybar C, Palomares O, Jutel M. Efficacy and safety of dupilumab for moderate-to-severe atopic dermatitis: A systematic review for the EAACI biologicals guidelines. Allergy. 2021 Jan;76(1):45-58. doi: 10.1111/all.14510. IPF 13.146

Agache I, Akdis CA, Akdis M, Canonica GW, Casale T, Chivato T, Corren J, Chu DK, Del Giacco S, Eiwegger T, Flood B, Firinu D, Gern JE, Hamelmann E, Hanania N, Hernández-Martín I, Knibb R, Mäkelä M, Nair P, O'Mahony L, Papadopoulos NG, Papi A, Park HS, Pérez de Llano L, Pfaar O, Quirce S, Sastre J, Shamji M, Schwarze J, Palomares O, Jutel M. EAACI Biologicals Guidelines-Recommendations for severe asthma. Allergy. 2021 Jan;76(1):14-44. doi: 10.1111/all.14425. IPF 13.146

Agache I, Song Y, Alonso-Coello P, Vogel Y, Rocha C, Solà I, Santero M, Akdis C, Akdis M, Canonica GW, Chivato T, Del Giacco S, Eiwegger T, Fokkens W, Georgalas C, Gevaert P, Hopkins C, Klimek L, Lund V, Naclerio R, O'Mahony L, Palkonen S, Pfaar O, Schwarze J, Soyka MB, Wang Y, Zhang L, Canelo-Aybar C, Palomares O, Jutel M. Efficacy and safety of treatment with biologicals for severe chronic rhinosinusitis with nasal polyps: A systematic review for the EAACI guidelines. Allergy. 2021 Mar 8. 76(8):2337-2353. doi: 10.1111/all.14809. IPF 13.146

Agache I, Rocha C, Pereira A, Song Y, Alonso-Coello P, Solà I, Beltran J, Posso M, 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 P, O'Mahony L, Schwarze J, Werfel T, Canelo-Aybar C, Palomares O, Jutel M. Efficacy and safety of treatment with omalizumab for chronic spontaneous urticaria: A systematic review for the EAACI Biologicals Guidelines. Allergy. 2021 Jan;76(1):59-70. doi: 10.1111/all.14547. IPF 13.146

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-dupilumab for children and adults with moderate-to-severe atopic dermatitis. Allergy. 2021 Apr;76(4):988-1009. doi: 10.1111/all.14690. IPF 13.146

Angelina A, Martín-Fontecha M, Rückert B, Wawrzyniak P, Pérez-Diego M, López-Abente J, Akdis M, Akdis CA, Palomares O. The cannabinoid WIN55212-2 restores rhinovirus-induced epithelial barrier disruption. Allergy. 2021 Jun;76(6):1900-1902. doi: 10.1111/all.14707. IPF 5.018

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; 2021 Oct 28. doi: 10.1111/all.15160. IPF 13.146.

Bousquet J, Anto JM, Czarlewski W, Haahtela T, Fonseca SC, Iaccarino G, Blain H, Vidal A, Sheikh A, Akdis CA, Zuberbier T; ARIA group. Cabbage and fermented vegetables: From death rate heterogeneity in countries to candidates for mitigation strategies of severe COVID-19. Allergy. 2021 Mar;76(3):735-750. doi: 10.1111/all.14549. IPF 13.146

Bousquet J, Jutel M, Akdis CA, et all. ARIA-EAACI statement on asthma and COVID-19 (June 2, 2020). Allergy. 2021 Mar;76(3):689-697. doi: 10.1111/all.14471. IPF 13.146

Bousquet J, Anto JM, Bachert C, Haahtela T, Akdis CA, et all. ARIA digital anamorphosis: Digital transformation of health and care in airway diseases from research to practice. Allergy. 2021 Jan;76(1):168-190. doi: 10.1111/all.14422. IPF:13.146

Bousquet J, Agache I, Blain H, Jutel M, Akdis CA, et all. Management of anaphylaxis due to COVID-19 vaccines in the elderly. Allergy. 2021 Apr 2. doi: 10.1111/all.14838. Online ahead of print. PMID: 33811358. IPF 13.146

Bousquet J, Anto JM, Czarlewski W, Haahtela T, Fonseca SC, Iaccarino G, Blain H, Vidal A, Sheikh A, Akdis CA, Zuberbier T; ARIA group. Cabbage and fermented vegetables: From death rate heterogeneity in countries to candidates for mitigation strategies of severe COVID-19. Allergy. 2021 Mar;76(3):735-750. doi: 10.1111/all.14549. IPF 13.146

Cabanillas B, Akdis CA, Novak N. COVID-19 vaccine anaphylaxis: IgE, complement or what else? A reply to: "COVID-19 vaccine anaphylaxis: PEG or not?". Allergy. 2021 Jun;76(6):1938-1940. doi: 10.1111/all.14725. IPF 13.146

Cabanillas B, Akdis CA, Novak N. COVID-19 vaccines and the role of other potential allergenic components different from PEG. A reply

Articles in peer reviewed journals 2021

to: "Other excipients than PEG might cause serious hypersensitivity reactions in COVID-19 vaccines". Allergy. 2021 Jun;76(6):1943-1944. doi: 10.1111/all.14761. IPF 13.146

Cabanillas B, Akdis CA, Novak N. Allergic reactions to the first COVID-19 vaccine: A potential role of polyethylene glycol? Allergy. 2021 Jun;76(6):1617-1618. doi: 10.1111/all.14711. IPF 13.146

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. 2021 Nov 24. doi: 10.1111/all.15187. Online ahead of print. IPF 13.146

Cevhertas L, Ma S, Stanic B, Ochsner U, Jansen K, Ferstl R, Frei R, Chijioke O, Münz C, Zhang L, O'Mahony L, Akdis M, van de Veen W. IL-10 induces IgG4 production in NOD-scid Il2rγnull mice humanized by engraftment of peripheral blood mononuclear cells. Allergy. 2021 Nov;76(11):3525-3529. doi: 10.1111/all.15031. IPF 13.15

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. 2021 Oct 22. doi: 10.1111/all.15145. Online ahead of print. IPF 13.146

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. 2021 Nov 28. doi: 10.1111/all.15192. Online ahead of print. IPF 13.146

Du H, Dong X, Zhang JJ, Cao YY, Akdis M, Huang PQ, Chen HW, Li Y, Liu GH, Akdis CA, Lu XX, Gao YD. Clinical characteristics of 182 pediatric COVID-19 patients with different severities and allergic status. Allergy. 2021 Feb;76(2):510-532. doi: 10.1111/all.14452. IPF 13.146

Fernandez-Santamaria R, Satitsuksanoa P. Engineered IL-10: A matter of affinity. Allergy. 2021 Oct 9. doi: 10.1111/all.15132. Online ahead of print. IPF 13.146

Gao Y, Ding M, Dong X, Zhang J, Azkur AK, Azkur D, Gan H, Sun Y, Fu W, Li W, Liang H, Cao Y, Yan Q, Can C, Gao H, Brüggen M , van de Veen W, Sokolowska M, Akdis M, Akdis CA. Risk factors for severe and critically ill COVID-19 patients: a review. Allergy. 2021 Feb;76(2):428-455. doi: 10.1111/all.14657. IPF 13.146

Hagemann J, Onorato GL, Jutel M, Akdis CA, Agache I, et all. Differentiation of COVID-19 signs and symptoms from allergic rhinitis and common cold- An ARIA-EAACI-GA2 LENconsensus. Allergy. 2021 Aug;76(8):2354-2366. doi: 10.1111/all.14815. IPF 13.146

Jansen K, Cevhertas L, Ma S, Satitsuksanoa P, Akdis M, van de Veen W. Regulatory B cells, A to Z. Allergy. 2021 Sep;76(9):2699-271. doi: 10.1111/all.14763. Review. IPF 13.146

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. 2021 Dec 4. doi: 10.1111/all.15193. Online ahead of print. IPF 13.146

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 13.146

Klimek L, Novak N, Cabanillas B, Jutel M, Bousquet J, Akdis CA. Allergenic components of the mRNA-1273 vaccine for COVID-19: possible involvement of polyethylene glycol and IgG-mediated complement activation. Allergy. 2021 Nov;76(11):3307-3313. doi: 10.1111/all.14794. Review. IPF 13.146

Klimek L, Jutel M, Akdis CA, Bousquet J, Akdis M, Torres MJ, Agache I, Canonica GW, Del Giacco S, O'Mahony L, Shamji MH, Schwarze J, Untersmayr E, Ring J, Bedbrook A, Worm M, Zuberbier T, Knol E, Hoffmann-Sommergruber K, Chivato T. ARIA-EAACI statement on severe allergic reactions to COVID-19 vaccines - An EAACI-ARIA Position Paper. Allergy. 2021 Jun;76(6):1624-1628. doi: 10.1111/all.14726. IPF 13.146

Klimek L, Akdis CA, Jutel M, Zuberbier T, Bousquet J. Inhaled corticosteroids in early COVID-19-A tale of many facets. Allergy. 2021 Nov;76(11):3540-3542. doi: 10.1111/all.15041. IPF 13.146

Klimek L, Jutel M, Bousquet J, Agache I, Akdis CA, Hox V, Gevaert P, Tomazic PV, Rondon C, Cingi C, Toppila-Salmi S, Karavelia A, Bozkurt B, Förster-Ruhrmann U, Becker S, Chaker AM, Wollenberg B, Mösges R, Huppertz T, Hagemann J, Bachert C, Fokkens W. Management of patients with chronic rhinosinusitis during the COVID-19 pandemic-An EAACI position paper. Allergy. 2021 Mar;76(3):677-688. doi: 10.1111/all.14629. IPF 13.146

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. 2021 Jun 22:10.1111/all.14983. doi: 10.1111/all.14983. Online ahead of print. IPF 13.146

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 13.146

Lunjani N, Tan G, Dreher A, Sokolowska M, Groeger D, Wawrzyniak M, Altunbulakli C, Westermann P, Basera W, Hobane L, Bo-

tha 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. 2021 Jun 4. doi: 10.1111/all.14974. Online ahead of print. PMID: 34086351. IPF 13.146

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. 2021 Sep 21. doi: 10.1111/all.15105. PMID: 34547110. IPF 13.146

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. 2021 Sep 3. 2021;00:1–4. doi: 10.1111/all.15079. IPF 13.146

Novotny EN, White SJ, Wilson AD, Stefánsdóttir SB, Tijhaar E, Jonsdóttir S, Frey R, Reiche D, Rose H, Rhyner C, Schüpbach-Regula G, Torsteinsdóttir S, Alcocer M, Marti E. Component-resolved microarray analysis of IgE sensitization profiles to Culicoides recombinant allergens in horses with insect bite hypersensitivity. Allergy. 2021 Aug 11; 74(4):1147-1157. DOI: 10.1111/all.14556. IPF 13.146

Ogulur I, Pat Y, Ardicli O, Barletta E, Cevhertas L, Fernandez-Santamaria R, Huang M, Bel Imam M, Koch J, Ma S, Maurer DJ, Mitamura Y, Peng Y, Radzikowska U, Rinaldi AO, Rodriguez-Coira J, Satitsuksanoa P, Schneider SR, Wallimann A, Zhakparov D, Ziadlou R, Brüggen MC, van de Veen W, Sokolowska M, Baerenfaller K, Zhang L, Akdis M, Akdis CA. Advances and highlights in biomarkers of allergic diseases. Allergy. 2021 Sep 14. doi: 10.1111/all.15089. IPF 13.146

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. 2021 Aug 17. doi: 10.1111/all.15057. Online ahead of print. IPF 13.146

Pat Y, Ogulur I. The eptihelial barrier hypothesis: a 20-year journey. Allergy. 2021 Nov;76(11):3560-2. doi: 10.1111/all.14899. IPF 13.146

Pawankar R, Castells M, Akdis M, Nadeau K, Leung ASY. Women in science and medicine. Allergy. 2021 Dec;76(12):3578-3580. doi: 10.1111/all.14967. IPF 13.146

Pfaar O, Torres MJ, Akdis CA. COVID-19: A series of important recent clinical and laboratory reports in immunology and pathogenesis of SARS-CoV-2 infection and care of allergy patients. Allergy. 2021 Mar;76(3):622-625. doi: 10.1111/all.14472. IPF 13.146

Pfaar O, Klimek L, Jutel M, Akdis CA, et all. COVID-19 pandemic: Practical considerations on the organization of an allergy clinic-An EAACI/ARIA Position Paper. Allergy. 2021 Mar;76(3):648-676. doi: 10.1111/all.14453. IPF 13.146

Pfaller B, Yepes-Nuñez JJ, Agache I, Akdis CA, Alsalamah M, Bavbek S, Bossios A, Boyman O, Chaker A, Chan S, Chatzipetrou A, du Toit G, Jutel M, Kauppi P, Kolios A, Li C, Matucci A, Marson A, Bendien S, Palomares O, Rogala B, Szepfalusi Z, Untersmayr E, Vultaggio A, Eiwegger T. Biologicals in atopic disease in pregnancy: an EAACI position paper. Allergy. 2021 Jan;76(1):71-89. doi: 10.1111/all.14282. IPF 13.146

Rinaldi AO, Korsfeldt A, Ward S, Burla D, Dreher A, Gautschi M, Stolpe B, Tan G, Bersuch E, Melin D, Askary Lord N, Grant S, Svedenhag P, Tsekova K, Schmid-Grendelmeier P, Möhrenschlager M, Renner ED, Akdis CA. Electrical impedance spectroscopy for the characterization of skin barrier in atopic dermatitis. Allergy. 2021 Apr 8. doi: 10.1111/all.14842. Online ahead of print. PMID: 33830511. IPF 13.146

Sahiner UM, Layhadi JA, Golebski K, István Komlósi Z, Peng Y, Sekerel B, Durham SR, Brough H, Morita H, Akdis M, Turner P, Nadeau K, Spits H, Akdis C, Shamji MH. Innate lymphoid cells: The missing part of a puzzle in food allergy. 2021 Jul;76(7):2002-2016. doi: 10.1111/all.14776. Review. IPF 13.146

Sampath V, Rabinowitz G, Shah M, Jain S, Diamant Z, Jesenak M, Rabin R, Vieths S, Agache I, Akdis M, Barber D, Breiteneder H, Chinthrajah S, Chivato T, Collins W, Eiwegger T, Fast K, Fokkens W, O'Hehir RE, Ollert M, O'Mahony L, Palomares O, Pfaar O, Riggioni C, Shamji MH, Sokolowska M, Jose Torres M, Traidl-Hoffmann C, van Zelm M, Wang Y, Zhang L, Akdis CA, Nadeau KC. Vaccines and allergic reactions: The past, the current COVID-19 pandemic, and future perspectives. Allergy. 2021 Jun;76(6):1640-1660. doi: 10.1111/all.14840. IPF 13.146

Satitsuksanoa P, Daanje M, Akdis M, Boyd SD, van de Veen W. Biology and dynamics of B cells in the context of IgE-mediated food allergy. Allergy. 2021 Jun;76(6):1707-1717. doi: 10.1111/all.14684. IPF 13.146

Sokolowska M, Rovati GE, Diamant Z, Untersmayr E, Schwarze J, Lukasik Z, Sava F, Angelina A, Palomares O, Akdis C, O'Mahony L, Sanak M, Dahlen SE, Woszczek G. Current perspective on eicosanoids in asthma and allergic diseases - EAACI Task Force consensus report, part I. Allergy. 2021 Jan;76(1):114-130. doi: 10.1111/all.14295. IPF 13.146

Sokolowska M, Eiwegger T, Ollert M, Torres MJ, Barber D, Del Giacco S, Jutel M, Nadeau KC, Palomares O, Rabin RL, Riggioni C, Vieths S, Agache I, Shamji MH. EAACI statement on the diagnosis, management and prevention of severe allergic reactions to COVID-19 vaccines. Allergy. 2021 Jun;76(6):1629-1639. doi: 10.1111/all.14739. IPF 13.146

*Tynecka M, *Radzikowska U, Eljaszewicz E. IL-10-producing innate lymphoid cells: Did we find a missing piece of the pizzle? Allergy.

Articles in peer reviewed journals 2021

2021 Jun 16; 76(12):3849-3851. doi: 10.1111/all.14980 *equal fist authorship. IPF 13.146

Tramper-Stranders G, Ambrożej D, Arcolaci A, Atanaskovic-Markovic M, Boccabella C, Bonini M, Karavelia A, Mingomataj E, O' Mahony L, Sokolowska M, Untersmayr E, Feleszko W; EAACI Task Force on Conscious and Rational use of Antibiotics in Allergic Diseases. Dangerous liaisons: Bacteria, antimicrobial therapies, and allergic diseases. Allergy. 2021 Nov;76(11):3276-3291. doi: 10.1111/all.15046. IPF 13.146

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. 2021 Oct 9;00:1–16. doi: 10.1111/all.15136. Online ahead of print. IPF 13.146

Wang M, Bu X, Fang G, Luan G, Huang Y, Akdis CA, Wang C, Zhang L. Distinct expression of SARS-CoV-2 receptor ACE2 correlates with endotypes of chronic rhinosinusitis with nasal polyps. Allergy. 2021 Mar;76(3):789-803. doi: 10.1111/all.14665. IPF 13.146

Wawrzyniak P, Krawczyk K, Acharya S, Tan G, Wawrzyniak M, Karouzakis E, Dreher A, Jakiela B, Altunbulakli C, Sanak M, O'Mahony L, Nadeau K, Akdis CA. Inhibition of CpG methylation improves the barrier integrity of bronchial epithelial cells in asthma. Allergy. 2021 Jun;76(6):1864-1868. doi: 10.1111/all.14667. IPF 13.146

Wiehn E, Ricci C, Alvarez-Perea A, Perkin MR, Jones CJ, Akdis C, Bousquet J, Eigenmann P, Grattan C, Apfelbacher CJ, Genuneit J; Task Force 'Adherence to reporting guidelines in articles published in EAACI Journals: a systematic review' of the EAACI Working Group on Epidemiology. Adherence to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) checklist in articles published in EAACI Journals: A bibliographic study. Allergy. 2021 Dec;76(12):3581-3588. doi: 10.1111/all.14951. IPF 13.146

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 13.146

Zhang JJ, Cao YY, Tan G, Dong X, Wang BC, Lin J, Yan YQ, Liu GH, Akdis M, Akdis CA, Gao YD. Clinical, radiological, and laboratory characteristics and risk factors for severity and mortality of 289 hospitalized COVID-19 patients. Allergy. 2021 Feb;76(2):533-550. doi: 10.1111/all.14496. IPF 13.146

Zhang L, Akdis CA. The Past, Present and Future of Allergic Diseases in China. Allergy. 2022 Jan 7. doi: 10.1111/all.15213. IPF 13.146

Zhang L, Akdis CA. The inspirational journey of Chinese scholars in the field of allergy. Allergy. 2021 Feb;76(2):422-424. doi: 10.1111/all.14676. IPF 13.146

Zhou Y, Li Q, Pan R, Wang Q, Zhu X, Yuan C, Cai F, Gao YD, Cui Y. Regulatory roles of three miRNAs on allergen mRNA expression in Tyrophagus putrescentiae. Allergy. 2021 Sep 27. doi: 10.1111/all.15111. Online ahead of print. IPF 13.146

Shang J, Wang Q, Zhang H, Wang X, Wan J, Yan Y, Gao Y, Cheng J, Li Z, Lin J. The Relationship Between Diabetes Mellitus and COVID-19 Prognosis: A Retrospective Cohort Study in Wuhan, China. Am J Med. 2021 Jan; 134(1): e6–e14. Published online 2020 Jul 10. doi: 10.1016/j.amjmed.2020.05.033. IPF 4.529

Wang YM, Xu WJ, Xiang LL, Ding M, Zhang JJ, Lu JY, Xie BJ, Gao YD. Store-operated calcium entry-associated regulatory factor regulates airway inflammation and airway remodeling in asthma mice models. Am J Physiol Lung Cell Mol Physiol. 2021 Sep 1;321(3):L533-L544. doi: 10.1152/ajplung.00079.2020. PMID: 34231388. IPF 5.464

Jiang SY, Smith EM, Vo V, Akdis C, Nadeau KC. Non-immunoglobulin E-mediated allergy associated with Pfizer-BioNTech coronavirus disease 2019 vaccine excipient polyethylene glycol. Ann Allergy Asthma Immunol. 2021 Dec;127(6):694-696. doi: 10.1016/j.anai.2021.09.012. IPF 6.347

Bates AE, Primack RB, Duarte CM, PAN-Environment Working Group*. Global COVID-19 lockdown highlights humans as both threats and custodians of the environment. Biol Conserv. 2021. Nov; 263: 109175, doi: 10.1016/j.biocon.2021.109175. IPF 5.405

Wallimann A, Hildebrand M, Groeger D, Stanic B, Akdis CA, Zeiter S, Richards RG, Moriarty TF, O'Mahony L, Thompson K. An Exopolysaccharide Produced by Bifidobacterium longum 35624® Inhibits Osteoclast Formation via a TLR2-Dependent Mechanism. Calcif Tissue Int. 2021 May;108(5):654-666. doi: 10.1007/s00223-020-00790-4. IPF 3.423

Kern U, Fröhlich K, Bedacht J, Schmidt N, Biniossek ML, Gensch N, Baerenfaller K, Schilling O. Impact of DJ-1 and Helix 8 on the Proteome and Degradome of Neuron-Like Cells. Cells 2021, 10(2), 404. doi.org/10.3390/cells10020404. IPF 6.600

Ptaszynska-Kopczynska K, Eljaszewicz A, Marcinkiewicz-Siemion M, Sawicka-Smiarowska E, Tarasiuk E, Lisowska A, Tynecka M, Grubczak K, Radzikowska U, Janucik A, Moniuszko M, Charkiewicz K, Laudanski P, Sobkowicz B, Kaminski KA. Monocyte subsets in patients with cardiac resynchronization therapy. Cells 2021, 10(12), 3482. DOI: 10.3390/cells10123482. IPF 6.600

Angelina A, Pérez-Diego M, Maldonado A, Rückert B, Akdis M, Martín-Fontecha M, Akdis CA, Palomares O. The cannabinoid WIN55212-2 impairs peanut allergic sensitization and promotes the generation of allergen-specific regulatory T cells. Clin Exp Allergy.

2022 Jan 7. doi: 10.1111/cea.14092. IPF 5.018.

Bousquet J, Pfaar O, Agache I, Bedbrook A, Akdis CA, et all. ARIA-EAACI care pathways for allergen immunotherapy in respiratory allergy. Clin Transl Allergy. 2021 Jun 9;11(4):e12014. doi: 10.1002/clt2.12014. IPF 5.871

Ding M, Dong X, Sun YL, Sokolowska M, Akdis M, van de Veen W, Azkur AK, Azkur D, Akdis CA, Gao YD. Recent advances and developments in COVID-19 in the context of allergic diseases. Clin Transl Allergy. 2021 Sep;11(7):e12065. doi: 10.1002/clt2.12065. PMID: 34582102. IPF 5.871

Ivaska LE, Silvoniemi A, Palomares O, Turunen R, Waris M, Mikola E, Puhakka T, Söderlund-Venermo M, Akdis M, Akdis CA, Jartti T. Persistent human bocavirus 1 infection and tonsillar immune responses. Clin Transl Allergy. 2021 Jul;11(6):e12030. doi: 10.1002/clt2.12030. IPF 5.871

Mitamura Y, Ogulur I, Pat Y, Rinaldi AO, Ardicli O, Cevhertas L, Brüggen MC, Traidl-Hoffmann C, Akdis M, Akdis CA. Dysregulation of the epithelial barrier by environmental and other exogenous factors. Contact Dermatitis. 2021 Dec; 85(6):615-26. doi:10.1111/cod.13959. IPF 6.600

Wallimann A, Magrath W, Thompson K, Moriarty T, Richards RG, Akdis CA, O'Mahony L, Hernandez CJ. Gut microbial-derived short-chain fatty acids and bone: a potential role in fracture healing. Eur Cell Mater. 2021 Apr 21;41:454-470. doi: 10.22203/eCM.v041a29. IPF 3.942

Cossarizza A, Chang HD, Radbruch A, Abrignani S, Addo R, Akdis M, et all. Guidelines for the use of flow cytometry and cell sorting in immunological studies (third edition). Eur J Immunol. 2021 Dec;51(12):2708-3145. doi: 10.1002/eji.202170126. IPF 5.179

Krug J, Kiefer A, Koelle J, Vuorinen T, Xepapadaki P, Stanic B, Chiriac MT, Akdis M, Zimmermann T, Papadopoulos NG, Finotto S. TLR7/8 regulates type I and type III interferon signalling in rhinovirus 1b-induced allergic asthma. Eur Respir J. 2021 May 6;57(5):2001562. doi: 10.1183/13993003.01562-2020. IPF 16.67

Costa S, Saguner AM, Gasperetti A, Akdis D, Brunckhorst C, Duru F. The Link Between Sex Hormones and Susceptibility to Cardiac Arrhythmias: From Molecular Basis to Clinical Implications. Front Cardiovasc Med. 2021 Feb 17;8:644279. doi: 10.3389/fcvm.2021.644279. IPF 4.79

Rodriguez-Coira J, Villaseñor A, Izquierdo E, Huang M, Barker-Tejeda TC, Radzikowska U, Sokolowska M, Barber D. The Importance of Metabolism for Immune Homeostasis in Allergic Diseases. The Importance of Metabolism for Immune Homeostasis in Allergic Diseases. Front Immunol. 2021 Jul 28;12:692004. doi: 10.3389/fimmu.2021.692004. IPF 6.429

Ma S, Satitsuksanoa P, Jansen K, Cevhertas L, van de Veen W, Akdis M. B regulatory cells in allergy. Immunol Rev. 2021 Jan;299(1):10-30. doi: 10.1111/imr.12937. IPF 13.939

Bousquet J, Czarlewski W, Zuberbier T, Mullol J, Blain H, Cristol JP, De La Torre R, Pizarro Lozano N, Le Moing V, Bedbrook A, Agache I, Akdis CA, Canonica GW, Cruz AA, Fiocchi A, Fonseca JA, Fonseca S, Gemicioğlu B, Haahtela T, Iaccarino G, Ivancevich JC, Jutel M, Klimek L, Kraxner H, Kuna P, Larenas-Linnemann DE, Martineau A, Melén E, Okamoto Y, Papadopoulos NG, Pfaar O, Regateiro FS, Reynes J, Rolland Y, Rouadi PW, Samolinski B, Sheikh A, Toppila-Salmi S, Valiulis A, Choi HJ, Kim HJ, Anto JM. Potential Interplay between Nrf2, TRPA1, and TRPV1 in Nutrients for the Control of COVID-19. Int Arch Allergy Immunol. 2021;182(4):324-338. doi: 10.1159/000514204. Review. IPF 2.917

Bousquet J, Czarlewski W, Zuberbier T, Mullol J, Blain H, Cristol JP, De La Torre R, Le Moing V, Pizarro Lozano N, Bedbrook A, Agache I, Akdis CA, Canonica GW, Cruz AA, Fiocchi A, Fonseca JA, Fonseca S, Gemicioğlu B, Haahtela T, Iaccarino G, Ivancevich JC, Jutel M, Klimek L, Kuna P, Larenas-Linnemann DE, Melén E, Okamoto Y, Papadopoulos NG, Pfaar O, Reynes J, Rolland Y, Rouadi PW, Samolinski B, Sheikh A, Toppila-Salmi S, Valiulis A, Choi HJ, Kim HJ, Anto JM. Spices to Control COVID-19 Symptoms: Yes, but Not Only….Int Arch Allergy Immunol. 2021;182(6):489-495. doi: 10.1159/000513538. IPF 2.917

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. 2021 Nov 12:dxab107. doi: 10.1093/intimm/dxab107. Online ahead of print. IPF 4.813

Peng YQ, Chen DH, Xu ZB, Fang SB, He BX, Liu XQ, Akdis CA, Fu QL. IL-33 receptor expression on myeloid and plasmacytoid dendritic cells after allergen challenge in patients with allergic rhinitis. Int Immunopharmacol. 2021 Dec;101(Pt B):108233. doi: 10.1016/j.intimp.2021.108233. IPF 4.56

Li N, Mirzakhani H, Kiefer A, Koelle J, Vuorinen T, Rauh M, Yang Z, Krammer S, Xepapadaki P, Lewandowska-Polak A, Lukkarinen H, Zhang N, Stanic B, Zimmermann T, Kowalski ML, Jartti T, Bachert C, Akdis M, Papadopoulos NG, Raby BA, Weiss ST, Finotto S. Regulated on Activation, Normal T cell Expressed and Secreted (RANTES) drives the resolution of allergic asthma. iScience. 2021 Sep 25;24(10):103163. doi: 10.1016/j.isci.2021.103163. IPF 5.458

Maintz L, Welchowski T, Hermann N, Brauer J, Kläschen AS, Fimmers R, Schmid M, Bieber B, CK-CARE Study Group, Schmid-Grendelmeier P, Traidl-Hoffmann C, Akdis CA, Lauener R, Brüggen MC, Rhyner C, Bersuch E, Renner E, Reiger M, Dreher A, Hammel G, Luschkova D, Lang C. Machine Learning-Based Deep Phenotyping of Atopic Dermatitis: Severity-Associated Factors in Adolescent and Adult Patients. JAMA Dermatol. 2021 Dec 1;157(12):1414-1424. Doi: 10.1001/jamadermatol.2021.3668. IPF 10.3

Warren CM, Snow TT, Lee AS, Shah MM, Heider A, Blomkalns A, Betts B, Buzzanco AS, Gonzalez J, Chinthrajah RS, Do E, Chang

Articles in peer reviewed journals 2021

I, Dunham D, Lee G, O'Hara R, Park H, Shamji MH, Schilling L, Sindher SB, Sisodiya D, Smith E, Tsai M, Galli SJ, Akdis C, Nadeau KC. Assessment of Allergic and Anaphylactic Reactions to mRNA COVID-19 Vaccines With Confirmatory Testing in a US Regional Health System. JAMA Netw Open. 2021 Sep 1;4(9):e2125524. doi: 10.1001/jamadermatol.2021.3668. IPF 8.483

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 10.793

Eljaszewicz A, Ruchti F., Radzikowska U, Globinska A, Boonpiyathad T, Gschwend A, Morita H, Helbling A, Arasi S, Kahlert H, Berek N, Nandy A, Akdi Ms, Willers C, Moniuszko M, Akdis CA, Sokolowska M. Trained immunity and tolerance in innate lymphoid cells, monocytes, and dendritic cells during allergen specific immunotherapy. J Allergy Clin Immunol. 2021 May;147(5):1865-1877. doi: 10.1016/j.jaci.2020.08.042. IPF 10.793

Jansen K, Wirz OF, van de Veen W, Tan G, Mirer D, Sokolowska M, Satitsuksanoa P, Message SD, Kebadze T, Glanville N, Mallia P, Skiepko R, Eljaszewicz A, Moniuszko M, Cardoso C, Gern JE, Papadopoulos NG, Akdis CA, Johnston SL, Nadeau KC, Akdis M. Loss of regulatory capacity in Treg cells following rhinovirus infection. J Allergy Clin Immunol. 2021 Oct;148(4):1016-1029.e16. doi: 10.1016/j.jaci.2021.05.045. IPF 10.793

Sampath V, Abrams EM, Adlou B, Akdis C, Akdis M, Brough HA, Chan S, Chatchatee P, Chinthrajah RS, Cocco RR, Deschildre A, Eigenmann P, Galvan C, Gupta R, Hossny E, Koplin JJ, Lack G, Levin M, Shek LP, Makela M, Mendoza-Hernandez D, Muraro A, Papadopoulous NG, Pawankar R, Perrett KP, Roberts G, Sackesen C, Sampson H, Tang MLK, Togias A, Venter C, Warren CM, Wheatley LM, Wong GWK, Beyer K, Nadeau KC, Renz H. Food allergy across the globe. J Allergy Clin Immunol. 2021 Dec;148(6):1347-1364. doi: 10.1016/j.jaci.2021.10.018. IPF 10.793

Satitsuksanoa P, van de Veen W, Akdis M. B cells in food allergy. J Allergy Clin Immunol. 2021 Jan;147(1):49-51. doi: 10.1016/j.jaci.2020.11.014. IPF 10.793

Fu W, Xu S, Dong X, Xie Q, Gao Y. Aspirin "Allergy"-Induced Thrombocytopenia: A Case Report. J Asthma Allergy. 2021 Mar 9;14:201-205. doi: 10.2147/JAA.S292567. IPF 4.258

Wallimann A, Magrath W, Pugliese B, Stocker N, Westermann P, Heider A, Gehweiler D, Zeiter S, Claesson MJ, Richards RG, Akdis CA, Hernandez CJ, O'Mahony L, Thompson K, Moriarty TF. Butyrate inhibits osteoclast activity In vitro and regulates systemic inflammation and bone healing in a murine osteotomy model compared to antibiotic-treated mice. Mediators Inflamm. 2021 Dec 10;2021:8817421. doi: 10.1155/2021/8817421. IPF 4.06

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. 2021 Aug 4:100995. doi: 10.1016/j.mam.2021.100995. Online ahead of print. IPF 14.235

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.; 2021. doi: 10.1038/s41385-021-00455-x. IPF 7.313.

Akdis CA. Does the epithelial barrier hypothesis explain the increase in allergy, autoimmunity and other chronic conditions? Nat Rev Immunol. 2021 Nov;21(11):739-751. doi: 10.1038/s41577-021-00538-7. Review. IPF 53.106

Acevedo N, Alashkar Alhamwe B, Caraballo L, Ding M, Ferrante A, Garn H, Garssen J, Hii CS, Irvine J, Llinás-Caballero K, López JF, Miethe S, Perveen K, Pogge von Strandmann E, Sokolowska M, Potaczek DP, van Esch BCAM. Perinatal and Early-Life Nutrition, Epigenetics, and Allergy. Nutrients. 2021 Feb 25;13(3):724. doi: 10.3390/nu13030724. IPF 5.717

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 6.377

Wawrzyniak M, Groeger D, Frei R, Ferstl R, Wawrzyniak P, Krawczyk K, Pugin B, Barcik W, Westermann P, Dreher A, Scharl M, Jutel M, Akdis CA, O Mahony L. Spermidine and spermine exert protective effects within the lung. Pharmacol Res Perspect. 2021 Aug;9(4):e00837. doi: 10.1002/prp2.837. IPF 2.794

Fan X, Xu ZB, Li CL, Zhang HY, Peng YQ, He BX, Liu XQ, Chen DH, Chen D, Akdis CA, Fu QL. Mesenchymal stem cells regulate type 2 innate lymphoid cells via regulatory T cells through ICOS-ICOSL interaction. Stem Cells. 2021 Jul;39(7):975-987. doi: 10.1002/stem.3369. Online ahead of print. IPF 6.022

Rostaher A, Rodriguez-Campos S, Deplazes P, Zwickl L, Akdis AC, Urwyler A, Wheeler DW, Audergon S, Fischer NM, Favrot C. Atopic dermatitis in West Highland white terriers - Part III: early life peripheral blood regulatory T cells are reduced in atopic dermatitis. Vet Dermatol. 2021 Jun;32(3):239-e63. doi: 10.1111/vde.12939. IPF: 1.697

BOOK CHAPTERS

in Global Atlas of Asthma, 2nd edition. Editors: Agache I, Akdis CA. Publisher: European Academy of Allergy and Clinical Immunology (EAACI), Date: 2021, Place of Publication: Zurich

Escribese MM, Baerenfaller K, Villaseñor A, Gomez-Casado C, Barber D. Omics

Jansen K., Akdis M. "The adaptive immune response in asthma - regulatory T and B cells"

Akdis CA." The defective bronchial epithelial barrier and epithelial barrier hypothesis in asthma"

Cezmi A. Akdis, Ioana Agache, Marek Jutel" Vision, roadmap and land-marking event"

Sokolowska M. "Metabolic pathways in asthma"

Willem van de Veen "The adaptive immune response in asthma - B cells"

Pediatric Allergy - Principles and Practice, 4th edition. Editors: Leung DYM, Akdis CA, Bacharier LB, Cunningham-Rundles C, Sicherer SH, Samspon HA. Publisher: Elsevier.

ABSTRACTS

Barletta E, Fröhlich K, Westermann P, Brüggen MC, Schmid-Grendelmeier P and Bärenfaller K. Mass spectrometry-based identification of allergen proteins involved in seafood related allergic reactions. WIRM 2021, Davos, Switzerland, 30 June - 3 July 2021.

Barletta E, Fröhlich K, Westermann P, Brüggen MC, Schmid-Grendelmeier P and Bärenfaller K. Mass spectrometry-based identification of allergen proteins involved in seafood related allergic reactions. LS2 Annual Swiss Proteomics Meeting, Montreux, Switzerland, 14 October 2021.

Barletta E, Fröhlich K, Westermann P, Brüggen MC, Schmid-Grendelmeier P and Bärenfaller K. Mass spectrometry-based identification of allergen proteins involved in seafood related allergic reactions. Swiss Symposium in Point of Care Diagnostics, Davos, Switzerland, 21 October 2021.

Barletta E, Fröhlich K, Westermann P, Brüggen MC, Schmid-Grendelmeier P and Bärenfaller K. Mass spectrometry-based identification of allergen proteins involved in seafood related allergic reactions. 2021 Skyline User Group Meeting, Washington, USA, 28 October 2021.

Huang M, Ding M, Radzikowska U, Rodriguez-Coira J, Stocker N, Tan G, Heider A, Akdis CA, Sokolowska M. Metabolic reprogramming of airway epithelium in response to house dust mite and human rhinovirus. World Immune Regulation Meeting 2021, Davos(digital), Switzerland, 30 Jun-3 July 2021.

Maurer DJ. Physical activity in asthma control and its immune modulatory effect in asthmatic preschoolers. WIRM 2021, Davos, Switzerland.

Mitamura Y. Cutaneous and systemic hyperinflammation drives maculopapular drug exanthema in severely ill COVID-19 patients EAACI congress 2021, Digital, 10-12 July 2021.

Mitamura Y. Correlations between Spatial gene expression, Skin barrier electric impedance, and Serum biomarkers in atopic dermatitis, WIRM, Davos, Switzerland. 30 June-3 July 2021.

Mitamura Y. Cutaneous and systemic hyperinflammation drives maculopapular drug exanthema in severely ill COVID-19 patients SSAI Annual congress 2021, Zurich, Switzerland. 19-20 August 2021.

Ogulur I., Kim J., Rückert B., Pat Y., Aydiner E.K., Baris S., Nadeau K., Ozen A., Akdis C.A. Single cell sequencing of peripheral mononuclear cells reveals CD55 deficiency with Hyper-activation of complement, Angiopathic thrombosis, and severe Protein-Losing Enteropathy-specific distinct signaling pathways. APAAACI 2021 International Conference, Online, 15-17 October 2021.

Ogulur I., Rückert B., Ozen A., Nadeau K., Akdis C.A. The epithelial barrier damaging effects of professional dishwasher rinse aid on Caco-2 gastrointestinal epithelial cells. APAAACI 2021 International Conference, Online, 15-17 October 2021.

Ogulur I., Kim J., Rückert B., Pat Y., Aydiner E.K., Baris S., Nadeau K., Ozen A., Akdis C.A. Single cell sequencing of peripheral mononuclear cells reveals CHAPLE-specific distinct signaling pathways. 6th European Congress of Immunology (ECI), Online, 1-4 Sptember 2021.

Ogulur I., Rückert B., Ozen A., Nadeau K., Akdis C.A. The epithelial barrier damaging effects of professional dishwasher rinse aid on Caco-2 gastrointestinal epithelial cells. 6th European Congress of Immunology (ECI), Online, 1-4 Sptember 2021.

Ogulur I., Kim J., Rückert B., Pat Y., Aydiner E.K., Baris S., Nadeau K., Ozen A., Akdis C.A. Single cell sequencing of peripheral mononuclear cells reveals CHAPLE-specific distinct signaling pathways. World Immune Regulation Meeting XV, Online, 30 June- 3 July 2021.

Ogulur I., Rückert B., Ozen A., Akdis C.A. The epithelial barrier damaging effects of professional dishwasher rinse aid on Cac-2 gastrointestinal epithelial cells. EAACI Hybrid Congress 2021, Madrid - Krakow, 10-12 July 2021.

Maurer DJ. »Athlete Fingerprinting« of Elite Ice Hockey Players and Cross-Country Skiers: Towards Personalized Sports Medicine. SEMS Congress, Magglingen, Switzerland, 21 - 22 October 2021.

Radzikowska U, Eljaszewicz A, Stocker N, Wawrzyniak P, Dreher A, Ding M, Tan G, Rodriguez-Coira J, Steiner S, Smolinska S, Gajdanowicz P, Pirozynski M, Kebadze T, Edwards MR, Jackson DJ, Williamson RA, Moniuszko M, Thiel V, Jutel M, O`Mahony L, Johnston SL, Akdis CA, Sokolowska M. Interaction of rhinovirus and SARS-CoV-2 infection with allergen exposure modifies antiviral response in airway epithelium in asthma. World Immune Regulation Meeting 2021, Davos, Switzerland, 30.06-03.07.2021

Radzikowska U, Ding M, Tan G, Zhakparov D, Peng Y, Wawrzyniak P, Wang M, Li S, Morita M, Altunbulakli C, Reiger M, Neumann AU, Lunjani N, Traidl-Hoffman C, Nadeau KC, O`Mahony L, Akdis CA, Sokolowska M. Distribution of SARS-CoV-2 receptors and associated molecules in health and disease. EAACI Immunologx Winter School 2021, Digitally, 22-24.01.2021.

Satitsuksanoa P. Characterization of B cells in food allergic children during oral immunotherapy and natural tolerance. EAACI winter school 2021, Digital, 22-24 January 2021.

Satitsuksanoa P. Characterisation of allergen-specific B cell tolerance in children with cow's milk-oral immunotherapy and natural outgrow of milk allergy. ECI 2021, Digital, 1-4 September 2021.

Satitsuksanoa P. In-depth characterization of allergen-specific B cells in children with cow's milk-oral immunotherapy and natural tolerance. WIRM 2021, Digital, 30 June-3 July 2021.
Sokolowska M. Immunology of COVID-19: Mechanisms, clinical outcome, diagnostics and perspectives. Habilitation Probevorlesung. UZH, Zurich, Switzerland, 01.011.2021

Sokolowska M. Crosstalk of innate and adaptive immunity on a metabolic level in respiratory diseases UZH Biomedicine Seminar. UZH, Zurich, Switzerland, 01.011.2021

Van De Veen W. In depth analysis of the bee venom allergen-specific B cell repertoire in immunotherapy-treated venom allergic individuals and naturally exposed healthy beekeepers. European Congress of Immunology, Digital, 1-4 September 2021.

Wallimann A. Short-Chain Fatty Acids and Antibiotics Affect Local and Systemic Processes Relevant for Bone Healing. Gut-bone axis meeting 2021, online meeting, 21-23 June 2021.

Wallimann A. Short-Chain Fatty Acids and Antibiotics Affect Local and Systemic Processes Relevant for Bone Healing. World microbe forum 2021, online meeting, 21-24 June 2021.

Wallimann A. Short-Chain Fatty Acids and Antibiotics Affect Local and Systemic Processes Relevant for Bone Healing. World Immune Regulation Meeting (WIRM) 2021, 30.06-03.07.2021

Wallimann A. Impact of Rifampicin-Levofloxacin on gut microbiome and Short-Chain Fatty Acid production in mice with bone fracture: consequences for bone health. ECCMID congress 2021, online meeting, 9-12 July 2021

SEMINAR AND CONGRESS TALKS

Akdis CA. Immunology of Covid-19, pathogenesis and risk factors of severe disease. Acibadem University, Istanbul, Turkey, 14 January 2021.

Akdis CA. Immune Pathogenesis of COVID-19. Koc University, Infectious Disease Center. KUISCID. Istanbul, Turkey, 18 January 2021.

Akdis CA. Asia Pacific Society of Allergy Asthma and Clinical Immunology (APAAACI). Motivational Conversation with Global Leaders, 21 January 2021.

Akdis CA. Immunology of Covid-19, pathogenesis and risk factors of severe disease. Transplantation Immunology and Genetics, Balkan EPT Meeting, virtual meeting, 23 January 2021.

Akdis CA. Epithelial Barrier Hypothesis. Davos Digital Forum, Health Edition, 28 January 2021.

Akdis CA. Epithelial Barrier Hypothesis. Istanbul University, Medical Faculty, Research Club, National Congress, 21 February 2021.

Akdis CA. Epithelial Barrier Hypothesis. Harold Nelson Memorial Lecture. AAAAI Annual Meeting, 27 February 2021.

Akdis CA. Immunology and Pathogenesis of COVID-19. Uludag, Internal Medicine Summit, Bursa, Turkey, 5 March 2021.

Akdis CA. Immunology of SARS-CoV-2. COVID-19 one year beyond. Koc University – Isbank, Center for Infectious Diseases, Online Symposium, 12 March 2021.

Akdis CA. Severe disease and immunopathogenesis of COVID-19. 17th National Uludag Pediatrics Congress, 13 – 14 March 2021.

Akdis CA. Hot-Topic-Lecture: Risk factors for severe and critically ill COVID-19 patients. 33. Mainzer Allergie Workshop organised by Allergieakademie der DGAKI, virtual meeting, 25 – 26 March 2021.

Akdis CA. Barrier hypothesis in the Development of Allergic and Autoimmune Diseases. Turkuvaz Magazine Webinar, 13 April 2021.

Akdis CA. Barrier hypothesis and novel techniques on epithelial cell biology. EU Horisons Project CURE, 13 April 2021.

Akdis CA. The basic of severe asthma – mechanisms. International Severe Asthma Forum - ISAF Digital 2021, 17 April 2021.

Akdis CA. Barrier hypothesis in the Development of Allergic and Autoimmune Diseases. Pediatric Allergy and Asthma Academy (CAAAD), 29 April 2021.

Akdis CA. Epithelial Barrier Hypothesis. Medipol University, Medical Faculty, Students Science Club, 10 May 2021.

Akdis CA. Epithelial Barrier hypothesis in the Development of Allergic and Autoimmune Diseases. Evolution Tree Science Society, Webinar, 16 May 2021.

Akdis CA. Epithelial Barrier Hypothesis for Alleric Diseases. IV National Congress on Clinical Immunology, Allergology and Immunorehabilitation, Ukraine, 19 May 20221.

Akdis CA. Epithelial Barrier hypothesis in the Development of Allergic and Autoimmune Diseases. EAACI Living Laboratory on Biodivrsity, Webinar, 22 May 2021.

Akdis CA. Epithelial Barrier hypothesis in the Development of Allergic and Autoimmune Diseases. Istanbul, Pediatrics Days, Turkey, 22 May 2021.

Akdis CA. Epithelial Barrier Hypothesis in Asthma and Autoimmunity. Rising Challenges in Immunology: Infectious and Autoimmune Diseases - digital conference, ABCAM, CA, USA, 17 June 2021.

Akdis CA. Epithelial Barrier Hypothesis in Asthma and Autoimmunity. Russian Allergology and Clinical Immunology Congress, virtual meeting, 23-24 June 2021.
Akdis CA. How to publish in high impact journas & how to write a first-class paper – tips and tricks. 6th Science Days organised by Austrian Society of Dermatology and Venereology, online & Schlosshotel Mondsee, 25-26 June 2021.

Akdis CA. Future direction of epithelial barrier research in the allergy field and immunology. JM Business Meeting EAACI, 28 June 2021.

Akdis CA. Epithelial barrier hypothesis and Environment Guidelines in Alllergy & Immunology. EAACI Annual Meeting, 12 July 2021.

Akdis CA. COVID-19 publications in Alllergy Journal. EAACI Annual Meeting, 12 July 2021.

Akdis CA. Epithelial Barriers, Allergy & Autoimmunity. SIAF Science Day, 5 August 2021.

Akdis CA. Epithelial barrier hypothesis to explain allergies, autoimmunity and other inflammatory diseases. XLIV Annual Congress AAAeIC (Asociación Argentina de Alergia e Inmunología Clínica), virtual meeting, 14-16 August 2021.

Akdis CA. Epithelial Barrier Hypothesis. European Congress of Immunology. 5 September 2021.

Akdis CA. Akdis M. Honorary Professors and Opening Lecture of 2021 Autumn Semester, 17 September 2021.

Akdis CA. Epithelial Barriers and Inflammation. Mexican Allergy and Clinical Immunology Congress, Mexico City, 23 September 2021.

Akdis CA. Epithelial Barrier Hypothesis. Blood Centers Online Meeting. 28 September 2021.

Akdis CA. National Lung Meeting. SIAF session: Pathogenesis in allergy and asthma. 8 October 2021.

Akdis CA. Regulation of the tight junction barrier. Summer School 2021 - The Skin Barrier, Leo Foundation Skin Immunology Research Center, University of Copenhagen, Denmark, 11-13 October 2021.

Akdis CA. Epithelial dysfunction and oxidative stress. National Congress of Allergy and Clinical Immunology, Antalya, Turkey, 13 - 17 October 2021.

Akdis CA. Role of IgE in diseases. National Congress of Allergy and Clinical Immunology, Antalya, Turkey, 13 - 17 October 2021.

Akdis CA. Point of care analyses of skin barrier integrity by electric impedance and its implications for skin diseases. 4th Swiss Symposium in Point-of-Care Diagnostics, Davos, Switzerland, 21 October 2021.

Akdis CA. Epithelial barrier hypothesis. International Eczema Council, Residents Meeting. 22 October 2021.
Akdis CA. Epithelial cells and asthma. Namacolin Meeting, USA, 23 October 2021.

Akdis CA. Pro & Con. Role of Allergy in Asthma, Nemacolin Meeting USA, 23 October 2021.

Akdis CA. Epithelial barrier hypothesis, allergy and other chronic diseases. 32nd International Congress of Biochemistry, Gaziantep, Turkey, 29 October 2021.

Akdis CA. Immune response to SARS-CoV-2. Medical Biology and Genetics Congress, Istanbul, 28 October 2021.

Akdis CA. Epithelial Barrier Hypothesis.15th Congress of Pediatric allergy and Asthma. Bodrum, Turkey, 1 November 2021.

Akdis CA. Epithelial cells and allergic disease. 2021 Annual Academic Online Meeting of Hubei Province Key Laboratory of Allergy and Immunology from 2 November 2021.

Akdis CA. Epithelial Barrier. International One Health Day. EAACI Webinar. 3 November 2021.

Akdis CA. Epithelial Barrier. American College Allergy and Clinical Immunology Congress. 7 November New Orleans, USA 2021.

Akdis CA. Novel insights into the development of allergy. Japanese Pediatric Meeting, Yokohama 13 November 2021.

Akdis CA. Highlights in Allergy and Respiratoty Disease. In the honor of Prof Carlos Baena Cagnani, Milano, 18 November 2021.

Akdis CA. CoMPEDIA and the organising committee of the VI Immunotherapy State of the Art course. Mexican Allergy Society. 18

2021

November 2021.

Akdis CA. COVID-19 immunology and immunopathogenesis. Thorax Society. 19 November 2021.

Akdis CA. Epithelial Barriers and Diseases. In vivo Plenatery Heath. 3 December 2021.

Akdis CA. Type 2 Response. Immunolog. Vienna Syposium. 4 December 2021.

Akdis CA. Career Days. Turkish Immunology Society. 15 December 2021.

Akdis M. Mechanisms of immune tolerance to allergens; Role of B regulatory cells. Virtual “Nature Café” on Immunity, virtual meeting organised by Nature Immunity and IMSUT, The Unversity of Tokyo, 28 January 2021.

Akdis M. Antigen-specific immune response in food allergy. Russian Allergology and Clinical Immunology Congress, virtual meeting, 23-24 June 2021.
Akdis M. Milk-specific Oral Immunotherapy. Food Allergy Symposium, Koc University, Istanbul, Turkey, 15 January. 2021.

Akdis M. Mechanisms of immune tolerance and the role of new B cell sunsets. Students club for science. CerrahPasa Medical Faculty, Istanbul, Turkey, 21 February 2021.

Akdis M. New findings on B cells. 17. International Uludağ Pediatric Winter Congress. Bursa, Turkey, 13 March 2021.

Akdis M. Immune regulation in specific B cells in food allergy, tolerance and outgrowing children. EAACI Hybrid Congress. Krakow, Poland, 11 July 2021.

Akdis M. Novel B Cell Subsets and their Role in Immune Regulation. 6th European Congress of Immunology. Belgrad, Serbia. 1 September 2021.

Akdis M. New mechanisms of Allergen-specific tolerance. UASK Hybrid Congress. Antalya, Turkey, 8 October 2021.

Akdis M. Induction of immune tolerance by immunotherapy. Summer School 2021 - The Skin Barrier, Leo Foundation Skin Immunology Research Center, University of Copenhagen, Denmark, 11-13 October 2021.

Akdis M. Meet the Professor, discussion in small groups. Summer School 2021 - The Skin Barrier, Leo Foundation Skin Immunology Research Center, University of Copenhagen, Denmark, 11-13 October 2021.

Akdis M. Mechanisms that break allergen-specific tolerance. National Congress of Allergy and Clinical Immunology, Ela Quality Hotel, Turkey, 13-17 October 2021.

Akdis M. B cell tolerance. National Congress of Allergy and Clinical Immunology, Ela Quality Hotel, Turkey, 13-17 October 2021.

Akdis M. Mechanisms break allergen-specific tolerance. XXVIII. International Allergy and clinical immunology Hybrid Congress. Antalya, Turkey, 14 October 2021.

Akdis M. B cells and immune tolerance. APAAACI 2021 International Conference Joint TAAACI. Taiwan, 15-17 October 2021.

Akdis M. Mechanisms inducing and breaking allergen-specific tolerance. 32th International Biochemistry Congress. Gaziantep, Turkey, 29 October 2021.

Akdis M. Novel developments in immune tolerance to allergens.15th Congress of Pediatric allergy and Asthma. Bodrum, Turkey, 1 November 2021.

Akdis M. Regulatory and the effector B cell subsets in Allergy and Cancer. AllergoOncology Working Group One-day Meeting online. 18 November 2021.
Akdis M. Mechanisms break allergen-specific tolerance. Turkish Thoracic Society's 24th Annual Congress. Turkey. 19 November 2021.

Akdis M. Role of B cells in food allergy. Australian and New Zealand Society for Immunology, 49th Annual Scientific Meeting. Online. 8 December 2021.

Baerenfaller K. Towards a molecular view on health and disease with Precision Proteomics, Symposium for Precision Proteomics of the UZH Medical Faculty, Online, 21 July 2021.

Baerenfaller K. Precision medicine in allergy and asthma in Davos. SIAF Summer Symposium - Recent Developments and Molecular Mechanics in Allergic Diseases and Asthma, Davos, Switzerland, 5 August 2021.

Baerenfaller K. Allergien und Klimawandel, Vortrag für die Berufsmaturitätsklasse des Bildungszentrum Gesundheit und Soziales in Chur, Davos, 27. October 2021.

Baerenfaller K. A scientific career and survivorship bias, SIB PhD Training Network Retreat, Bienne/Biel, Switzerland, 6-7 December 2021.

Barletta E. Mass spectrometry-based identification of allergen proteins involved in seafood related allergic reactions. WIRM 2021, Davos, Switzerland, 30 June - 3 July 2021.

Barletta E. Mass spectrometry-based identification of allergen proteins involved in seafood related allergic reactions. LS2 Annual Swiss Proteomics Meeting, Montreux, Switzerland, 14 October 2021.

Barletta E. Mass spectrometry-based identification of allergen proteins involved in seafood related allergic reactions. 2021 Skyline User Group Meeting, Washington, USA, 28 October 2021.

Barletta E. Mass spectrometry-based identification of proteoforms involved in allergic diseases. SIB PhD Training Network Retreat, Biel, Switzerland, 6-7 December 2021.

Barletta E. Introduction to Proteomics. Biomedical Data Mining Blockkurs (BME351), Davos, Switzerland, 16 June 2021.

Barletta E. Introduction to Proteomics. Mantelstudium: Praktikum Allergologie Translational (17MAS003), Davos, Switzerland, 8 July 2021.

Huang M. Metabolic reprogramming of airway epithelium in response to house dust mite and human rhinovirus. World Immune Regulation Meeting 2021, Davos (digital), Switzerland, 30 Jun-3 July 2021.

Koch J. Translational regulation of differentiating human Th1 cells. Immune Regulation Meeting (WIRM) 2021, online, 30.06-03.07.2021.

Mitamura Y. Type 2 Immunity, World Immune Regulation Meeting (WIRM) 2021, online, 30.06-03.07.2021.

Satitsuksanoa P. Characterization of B cells in food allergic children during oral immunotherapy and natural tolerance. EAACI winter school 2021, Digital, 22-24 January 2021.

Satitsuksanoa P. Characterisation of allergen-specific B cell tolerance in children with cow's milk-oral immunotherapy and natural outgrow of milk allergy. ECI 2021, Digital, 1-4 September 2021.

Satitsuksanoa P. In-depth characterization of allergen-specific B cells in children with cow's milk-oral immunotherapy and natural tolerance. WIRM 2021, Digital, 30 June-3 July 2021.

Sokolowska M. Immunology of COVID-19: Mechanisms, clinical outcome, diagnostics and perspectives. Habilitation Probevorlesung, UZH, Zurich, Switzerland 01.12.2021.

Sokolowska M. Application of omics technologies in asthma. 24th Annual Turkish Thoracic Society Congress, 17-21st November 2021.

Sokolowska M. Crosstalk of innate and adaptive immunity on a metabolic level in respiratory diseases. UZH Biomedicine Seminar. UZH, Zurich 01.11.2021.

Sokolowska M. Allergen-specific T cell responses and immune metabolism. Swiss Institute of Allergy and Asthma Research (SIAF) Summer Symposium 06.08.2021.

Sokolowska M. Lipids and allergen-induced bronchoconstriction – how lipid mediators drive airway inflammation? EAACI Hybrid Annual Congress, Krakow, Poland 10-12 July 2021.

Sokolowska M. Respiratory epithelium in virus infection and in allergy. EAACI Hybrid Annual Congress, Krakow, Poland 10-12 July 2021.

Sokolowska M. Anti IL-4/13 and IL-33/TSLP- understanding immunological pathways of the new biological therapies. European Academy of Allergy and Clinical Immunology (EAACI) Hybrid Annual Congress, Krakow, Poland 10-12 July 2021.

Sokolowska M. Metabolic regulation of T cells in allergen tolerance during allergen specific immunotherapy. XV World Immune Regulation Meeting, Davos, Switzerland, 30 June-3 July, 2021.

Sokolowska M. Komórki ILC, DC i monocyty w mechanizmie immunoterapii alergenowej. XX Konferencja Alergia, Astma, Immunologia Kliniczna, Lodz, Poland, 17-19 June 2021.

Sokolowska M. The Influence of Allergens and Allergic Inflammation on SARS-CoV-2 and Other Viral Infections. Federation of Clinical Immunology Societies (FOCIS), 8-11 June, digital.

Sokolowska M. Distribution of SARS-CoV-2 receptors and associated molecules in health and disease XVII Congress of the Polish Society of Experimental and Clinical Immunology. 27-29 May, 2021, digital.

Sokolowska M. Trained immunity and tolerance in innate lymphoid cells, monocytes, and dendritic cells during allergen-specific immunotherapy. Tolerogenic Vaccinations Meeting. 6-8 APRIL 2021, digital.

Sokolowska M. Crosstalk of innate and adaptive immunity on a metabolic level in asthma and immune tolerance. Habilitation presentation UZH, Zurich, Switzerland 25th of January 2021.

Sokolowska M. Immunology of COVID-19 in the big data perspective. Microbiology and Immunology 15th Introductory Course. January 13-15, 2021, digital.

van de Veen W. In vivo follow up of antigen-specific B cell responses. SIAF Summer Symposium, Davos, Switzerland, 5 August 2021.

van de Veen W. Changes in B cell repertoire during allergen immunotherapy: a search for novel therapeutics. EAACI Hybrid Congress, Madrid - Krakow, 10-12 July 2021.

Wallimann A. Short-Chain Fatty Acids and Antibiotics Affect Local and Systemic Processes Relevant for Bone Healing. Gut-bone axis meeting 2021, online meeting, 21-23 June 2021.

CHAIRS AT CONGRESSES

Akdis CA. COVID-19 Pathogenesis, Immunology Teaches, Turkish Immunology Society. 20 January 2021.

Akdis CA. Type 2 immunity: challenges and opportunities. Virtual "Nature Café" on Immunity, virtual meeting organised by Nature Immunity and IMSUT, The Unversity of Tokyo, 28 January 2021.

Akdis CA. Innate Immune Response. 15th World Immune Regulation Meeting. Davos, Switzerland, 1 July 2021.

Akdis CA. Plenary Session, Immune Regulation. EAACI Annual Meeting 12 July 2021.

Akdis CA. SIAF Summer Symposium. 5 August 2021.

Akdis CA. Moderator, Meet the Professor, discussion in small groups. Summer School 2021 - The Skin Barrier, Leo Foundation Skin Immunology Research Center, University of Copenhagen, Denmark, 11-13 October 2021.

Akdis CA. Immuneregulation. National Congress of Allergy Congress, Antalya, Turkey, 13 - 17 October 2021.

Akdis M. T and B Cell Responses and Preparedness. 15th World Immune Regulation Meeting. Davos, Switzerland, 1 July 2021.

Akdis M. Immunological Mechanisms in Allergic Diseases and Immunotherapy. 6th European Congress of Immunology. Belgrade, Serbia, 1 September 2021.

Akdis M. Immune Pathways to Understanding Prevention. Sean N. Parker Center for Allergy and Asthma Research at Stanford University. San Francisco, USA, 23 September 2021.

Baerenfaller K. Immunity and Regeneration, World Immune Regulation Meeting (WIRM) XV, 30 June - 3 July 2021.

Baerenfaller K. SIAF Summer Symposium - Recent Developments and Molecular Mechanics in Allergic Diseases and Asthma, Davos, Switzerland, 5 August 2021.

Koch J. Allergy, Asthma and Respiratory Inflammatory Diseases II, World Immune Regulation Meeting (WIRM) 2021, online, 30.06-03.07.2021.

Mitamura Y. Type 2 Immunity, World Immune Regulation Meeting (WIRM) 2021, online, 30.06-03.07.2021.

Ogulur I. Hygiene Hypothesis in Immune Regulation. World Immune Regulation Meeting XV, Online, 30 June - 3 July 2021.

Radzikowska U. COVID-19 and immunology.World Immune Regulation Meeting 2021, Davos, Switzerland, 30.06-03.07.2021.

Satitsuksanoa P. B cell Subsets and Immune Regulation. WIRM 2021, Digital, 30 June-3July 2021.

Sokolowska M. Keynote Lecture: Integration of cellular and systemic immunometabolism: Immune Cells Are What We Eat. 19th EAACI Immunology Winter School "Basic Immunology Research in Allergy and Clinical Immunology" 22-24 January 2021.

Sokolowska M. Oral Abstract Session II. 19th EAACI Immunology Winter School "Basic Immunology Research in Allergy and Clinical Immunology" 22-24 January 2021.

Sokolowska M. Microbiome and metabolism poster session 19th EAACI Immunology Winter School "Basic Immunology Research in Allergy and Clinical Immunology" 22-24 January 2021.

Sokolowska M. Keynote Lecture: NLRC5: a new side of antigen presentation. Basic and Clinical Immunology Section Business Meeting. Monday 05 July 2021.

Sokolowska M. Biologicals: novel therapeutic approaches-OAS 02. European Academy of Allergy and Clinical Immunology (EAACI) Hybrid Annual Congress, Krakow, Poland 10-12 July 2021.
Sokolowska M. Cutting edge issues in allergy and clinical immunology-ePDS 06 European Academy of Allergy and Clinical Immunology (EAACI) Hybrid Annual Congress, Krakow, Poland 10-12 July 2021.

Sokolowska M. Metabolism of Inflammation and Immune Responses. XV World Immune Regulation Meeting, 30 June - 3 July 2021, digital.

Sokolowska M. Epithelial Cell Activation and Barrier Functions. XV World Immune Regulation Meeting, 30 June - 3 July 2021, digital.

van de Veen W. Interactive Workshops: Challenges in Allergy and Asthma – Management of adolescents and young adults with allergy and asthma. EAACI Hybrid Congress, Madrid - Krakow, 10-12 July 2021.

van de Veen W. B Cell and Antibody Responses to Viruses. World Immune Regulation Meeting XV, Digital, 30 June - 3 July 2021.

Wallimann A.Hygiene Hypothesis in Immune Regulation. World Immune Regulation Meeting (WIRM) 2021, online meeting, 30 June - 3 July 2021.

LECTURES

Lectures at University of Zurich

Akdis CA.
BCH301. Introduction to immunology, Cells and organs of the immune system, Immune tolerance, Immune effector functions and tissue inflammation

Akdis M.
BCH301. Adaptive immune response, B cells and antibodies, T cells and T cell receptor

Baerenfaller K.
Lecture in 'Advanced Block Course: Computational Biology' of the Life Science Zurich Graduate School; Topic: Large data sets: Transcriptomics and Proteomics
Lecture in BIO390 'Indroduction to Bioinformatics' ; Topic: Proteomics
BME351 Block course "Biomedical Data Mining"
17MAS003 Mantelstudium: Praktikum Allergologie translation

Sokolowska M.
BME351 Block course "Biomedical Data Mining"

AWARDS

Akdis CA. Harold Nelson Memorial Lecture American Academy of Allergy Asthma & Immunology. 2021.

Akdis CA. American College of Allergy & Clinical Immunology International Distinguished Fellow Award. June 2021.

Akdis CA. Honorary Professor in Uludag University Bursa, Turkey. 17 September 2021.

Akdis CA. German Allergy Association Erich Fuchs-Preis. September 2021.

Akdis CA. Nemacolin Gilbert Friday Memorial Lecture, West Virginia University, USA. 22 October 2021.

Akdis M. Fellow Award, EAACI, 2021.

Akdis M. Dr Nejat Eczacıbaşı Medicine Awards; Medical Science award, 2021.

Akdis M. FEBS National Lecture award, by The Federation of European Biochemical Societies. 32nd National congress. 27-30 October 2021.

Akdis M. Honorary Professor in Uludag University Bursa, Turkey. 17 September 2021.

Baerenfaller K. Winner of the 1st Ideation Campaign of SwissFood-Ecosystems and InnovationBooster, May 2021.

Koch J. SCNAT Registration fellowship, Basel Computational Biology Conference (BC2) in Basel, Switzerland, 13-15 September 2021.

Maurer DJ. SEMS Poster Award. SEMS Congress 2021 in Magglingen, Switzerland, 21 - 22 October 2021.

Ogulur I. Best Oral Abstract Award. APAAACI 2021 International Conference, 15-17 October 2021.

Satitsuksanoa P. The remarkable tale of magic allergen-specific B cells. 1st place at SIAF Science Day 2021, Digital, 16 December 2021.

Sokolowska M. Distinguished Reviewer Award, Allergy. 2021

Wallimann A. Best student oral presentation. Gut-bone axis meeting 2021, online meeting, 21-23 June 2021.

DEGREES

Sokolowska M. Board Certification in Internal Medicine/Fachärztin im Fachgebiet Innere Krankheiten. Medical Examination Centre, Poland. 15.04.2021

Ogulur I. Associate Professor, in Basic Immunology, from Interuniversity Board Presidency of Turkey, 29.09.2021

2021

PUBLIC SEMINARS

21.06.2021
Wirchov JC. Role of AIT in the treatment of asthma.

05.08.2021
SIAF Summer Symposium
Agache I. Asthma endotypes from bench to practice.
Renz H. Epigenetic regulation links gene-environment interactions in allergy and asthma.
Nadeau K. Pollution, climate change and allergic disease.
Shamji M. Innate lymphoid cells and allergy.
Palomares O. Novel vaccines and future treatments of allergic diseases.
Bärenfaller K. Precision Proteomics taking off in Davos.
Akdis M. Characterization of Treg cell and B cell responses in rhinovirus infection.
van de Veen W. In vivo follow up of antigen-specific B cell responses.
Sokolowska M. Allergen-specific T cell responses and immune metabolism.
Mitamura Y. In depth analyses of non-lesional and lesional AD skin by spatial and single cell sequencing technologies.
Akdis CA. Epithelial Barrier Hypothesis and future prospects.

SIAF SCIENCE DAY (online)
16.12.2021
Akdis CA. How to demonstrate your data in the best way in a presentation or a publication.
Koch J. Following footprints.
Radzikowska U. Christmas adventures of RIG-I: a real twist of fate.
Wallimann A. The effect of having Christmas dinner with in-laws on gut microbiota composition and possible consequences for bone health.
Barletta E. Who Framed Mr. Shrimp?... A Christmas Eve Mystery.
Zhakparov D. Data science is fun. Interactive analysis showcase.
Xiao Y. miRNA's Bizarre Adventure.
Satitsuksanoa P. The remarkable tale of magic allergen-specific B cells.
Schneider S. Helping Cellta Clause to find the naughty B cells.
Bel imam M. Biomarkers for monitoring EoE disease activity.
Küçükkase O. The effect of ketone bodies on intestinal epithelial cells.
Ögülür I. A dangerous journey of gut barrier integrity.
Allergy Team. Allergy: Olympic Champions.

Winner of the SIAF Sciene Day 2021: Pattraporn Satitsuksanoa

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) – Scientific Boardr
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 Guideline member
Member of Scientific Board of Sean Parker Allergy Center, Stanford
Member of Scientific Board of Leo Foundation Skin Immunology Research Center
Workpakcage Member of EU project CURE
Allergy, Editorial Board Member
Journal of Allergy and Clinical Immunology, Reviewer Board Member
SNF project reviewer
PAI, Reviewer Board Member
Science Foundation Ireland, Reviewer Board member
World Immune Regulation Meeting, Member of the scientific committee

Baerenfaller K.

Interim co-leader of the Center for Precision Proteomics at the Medical Campus Davos
Member of the SIB Board of Directors
Jury member for the SIB Best Graduate Paper Award
Group leader of the SIB
Board member of the EAACI WG Genomics&Proteomics
Member of the EAACI ROC Diagnostics group
Abstract Reviewer for the EAACI Congresses
Member of EAACI
Editor of a Frontiers in Immunology Research Topic
Part of the editorial board of the Frontiers in Allergy Allergens Section
Reviewer for a variety of journals
Grant reviewer for a variety of science foundations
Board member of Science City Davos
Member of LS2
Vice-President of the LS2 Bioinformatics intersection
World Immune Regulation Meeting, Member of the scientific committee

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 organizing committee

Sokolowska M.

Principal Investigator-The Microbiology and Immunology PhD program, UZH-ETH
EAACI Immunology Section, Secretary
EAACI TF on Public Otreach, Secretary
EAACI TF on Eicosanoids, Secretary
EAACI TF on Immune Metabolism, Chair
EAACI Research and Outreach Committee (ROC) Member
Allergy, Editorial Board Member
Clinical and Molecular Allergy, Editorial Board member
Frontiers in Pharmacology, Reviewer Board Member
Frontiers in Allergy, Reviewer Board member
World Immune Regulation Meeting, Member of the scientific committee

van de Veen W.

Allergy, Editorial Board Member
Frontiers in Allergy, Reviewer Board Member
Journal of Allergy and Clinical Immunology (JACI), Reviewer Board Member
European Science Foundation (ESF), Member College of Expert Reviewers
The Microbiology and Immunology (MIM) PhD Program, UZH-ETH, Principal Investigator
COST action entitled: "The Core Outcome Measures for Food Allergy (COMFA)", management committee member and deputy lead Immmunological outcomes
The Graduate School Graubünden, Programme committee member
World Immune Regulation Meeting, Member of the scientific committee

2021

National and international collaborations

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

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

Allergy & Pulmonology Depart., Warsaw (PL), Prof. M. Pirozynski

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

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, I-Ting Chow

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

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

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. Alba Querencias

Consejo Superior de Investigaciones Cientificas (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

Dutch Asthma Center Davos, Dr. L H M Rijssenbeek-Nouwens; Dr. MT. Drijver-Messelink

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. Jörg Stelling
-Departement Pharmazie, Prof. G. Folkers
-Department of Biotechnology, Prof. C. Lacroix; Dr. B. Pugin
- Department of Biosystems Science and Engineering, Roqueiro D.

Forschungszentrum Borstel (DE), Prof. U. Jappe, Prof. H. Fehrenbach, Prof. Dr. O. Holst

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, Dr. G. Tan

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

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

Hochgebirgsklinik Davos Wolfgang (CH), Prof. H.W. Duchna, Dr. M. Möhrenschlager, Dr. A. Kalweit, Dr. C. Steiner, Dr. A. Kirsch, Dr. G. Menz

Immunologie et Neurogénétique Expérimentales et Moléculaires (INEM) UMR7355, Department of Molecular Immunology, Orleans (FR), Prof. B. Ryffel, 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

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

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

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

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

Medical University of Lodz (PL), Prof. J. Makowska

Medical University of Vienna (AT)
- Department of Pediatrics, Vienna (AT), Prof. Z. Scephaluzi
- Department of Dermatology, Brunner PM.

Nederlands Astmacentrum, Dr. D. Prins, Dr. M. Drijver

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

Office for Nature and Environment of the Grisons

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

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

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

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-Hoffmann

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

Tokyo University, Dept of Pediatrics (JP), Dr. H. Morita, Prof. K. Matsumoto, Prof. H. Saito

Tottori University, Faculty of Medicine, Yonago (JP), Division of Dermatology, Department of Medicine of Sensory and Motor Organs, Dr. K. Sugita

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, Dr. M.M. Escribese, Dr. A. Villaseñor

Universität Bern
- Dept. Clinical Vet. Medicine (CH), 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

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, COPD & Asthma Researchgroup (CARG), Abtl. für Pneumologie, Freiburg (DE), 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
- 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

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 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 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

University of Würzburg (DE)
- Department of Animal Ecology and Tropical Biology, Prof. Jochen Krauss
- Department of Pharmaceutical Biology, Prof. Martin J. Müller

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 2021

(inklusive Drittmittel)

	31.12.2021	31.12.2020
	CHF	CHF
AKTIVEN		
Flüssige Mittel	1’540’605.87	1’650’477.13
Forderungen	111’115.14	285’434.77
Aktive Rechnungsabgrenzungen	293’039.90	250’850.18
	1’944’760.91	2’186’762.08
PASSIVEN		
Verbindlichkeiten	94’036.79	107’380.19
Bankverbindlichkeiten	0	14.20
Kontokorrent SFI Stiftung	38’721.45	36’919.05
Passive Rechnungsabgrenzungen	1’313’409.13	1’364’673.88
Rückstellungen	278’437.73	457’618.95
Eigenkapital	220’155.81	220’155.81
	1’944’760.91	2’186’762.08

Schweizerisches Institut für Allergie- und Asthmaforschung

Betriebsrechnung 2021

(inklusive Drittmittel)

	Rechnung 2021	Budget 2021	Rechnung 2020
	CHF	CHF	CHF
ERTRAG			
Beitrag Bund Forschungsgesetz Art. 15	1'290'600.00	1'290'600.00	835'200.00
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	382'258.60	369'688.00	366'870.95
Beitrag Stiftung SFI	98'381.40	187'221.00	0
Beitrag Stiftung vormals Bündner Heilstätte Arosa	57'546.00	57'546.00	56'108.50
Beitrag Stiftungen/Drittmittel	158'261.85	0	75'608.80
Overheadbeiträge	0	0	55'458.00
Übriger Ertrag	3'759.20	3'000.00	22'576.34
Finanzertrag	257.10	0	0
Ausserordentlicher Ertrag	3'787.65	30'000.00	23'687.69
Auflösung von Rückstellungen	202'640.87	0	73'567.49
WIRM-Kongress	106'173.85	120'000.00	131'459.01
Drittmittel	2'066'611.90	2'529'208.00	2'112'277.41
	5'414'838.42	5'631'823.00	4'797'374.19
AUFWAND			
Personalaufwand	2'954'847.60	3'007'195.00	2'420'977.20
Verbrauchsmaterial	1'015'551.92	1'368'781.00	991'107.41
Raumaufwand	349'681.44	320'000.00	325'973.77
Unterhalt/Reparaturen/Ersatz	241'010.60	347'663.00	113'766.72
Investitionen	296'613.51	124'484.00	397'189.30
Sachversicherungen/Abgaben	9'935.75	10'000.00	8'626.65
Energie- und Entsorgungsaufwand	132'575.24	120'000.00	139'350.36
Verwaltungsaufwand	92'050.85	99'500.00	89'225.61
Werbeaufwand	5'982.15	0	6'743.60
Reisespesen	38'004.43	50'000.00	41'595.35
WIRM-Kongress	119'297.20	66'000.00	133'813.35
Übriger Betriebsaufwand	1'935.79	11'000.00	6'654.09
Abschreibungen	105'200.00	105'200.00	105'200.00
Finanzaufwand	9'518.60	1'000.00	16'091.53
Bildung von Rückstellungen	23'459.65	0	0
Ausserordentlicher Aufwand	19'173.69	1'000.00	1'059.25
	5'414'838.42	5'631'823.00	4'797'374.19
Ergebnis	0	0	0
	5'414'838.42	5'631'823.00	4'797'374.19

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

ClimatePartner Climate neutral printed on FSC-certified paper