

National Institute of Allergy and Infectious Diseases

NASEM Committee for the Assessment of NIH Research on
Autoimmune Diseases

Autoimmunity Research in the Division of Intramural Research

Thursday, March 4 1:30 to 5:30 p.m.

NIAID



National Institute of
Allergy and
Infectious Diseases

Karyl S. Barron, M.D.
Deputy Director
Division of Intramural Research

NIAID's Complex Mandate

- Support and promote basic science
- Enable and foster clinical research
- Provide outstanding patient care to support both
- Respond to emerging threats and diseases

Intramural Program

- Relatively stable resources
- Long-term complex and high impact problems
- Rapid response to public health emergencies
- Retrospective review by BSC, unlike extramural grants

DIR Research: Facts and Figures

- 7.5% of NIAID budget
- 20 Labs/branches
- 133 Principal Investigators
- **44 Research projects related to autoimmunity**

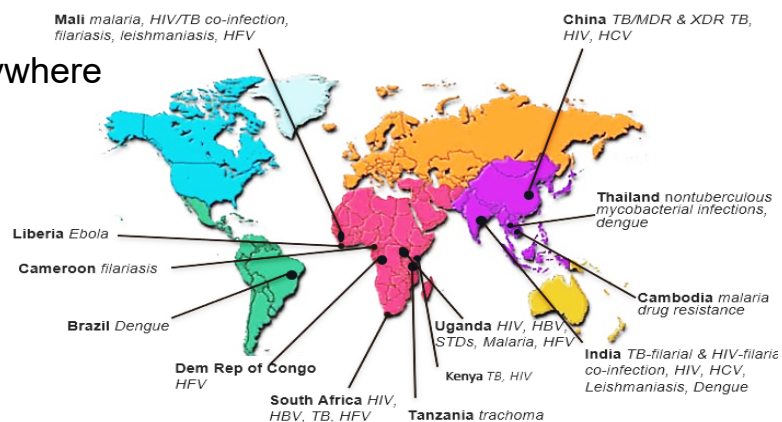
Bethesda/Rockville



RML



Everywhere
else



DIR's Research Programs in Autoimmunity

Long-standing Investment

1973: Revolutionary treatment for anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis (Fauci)

13/15 had total remission – prior to new treatment, 90% fatality w/in 2 years

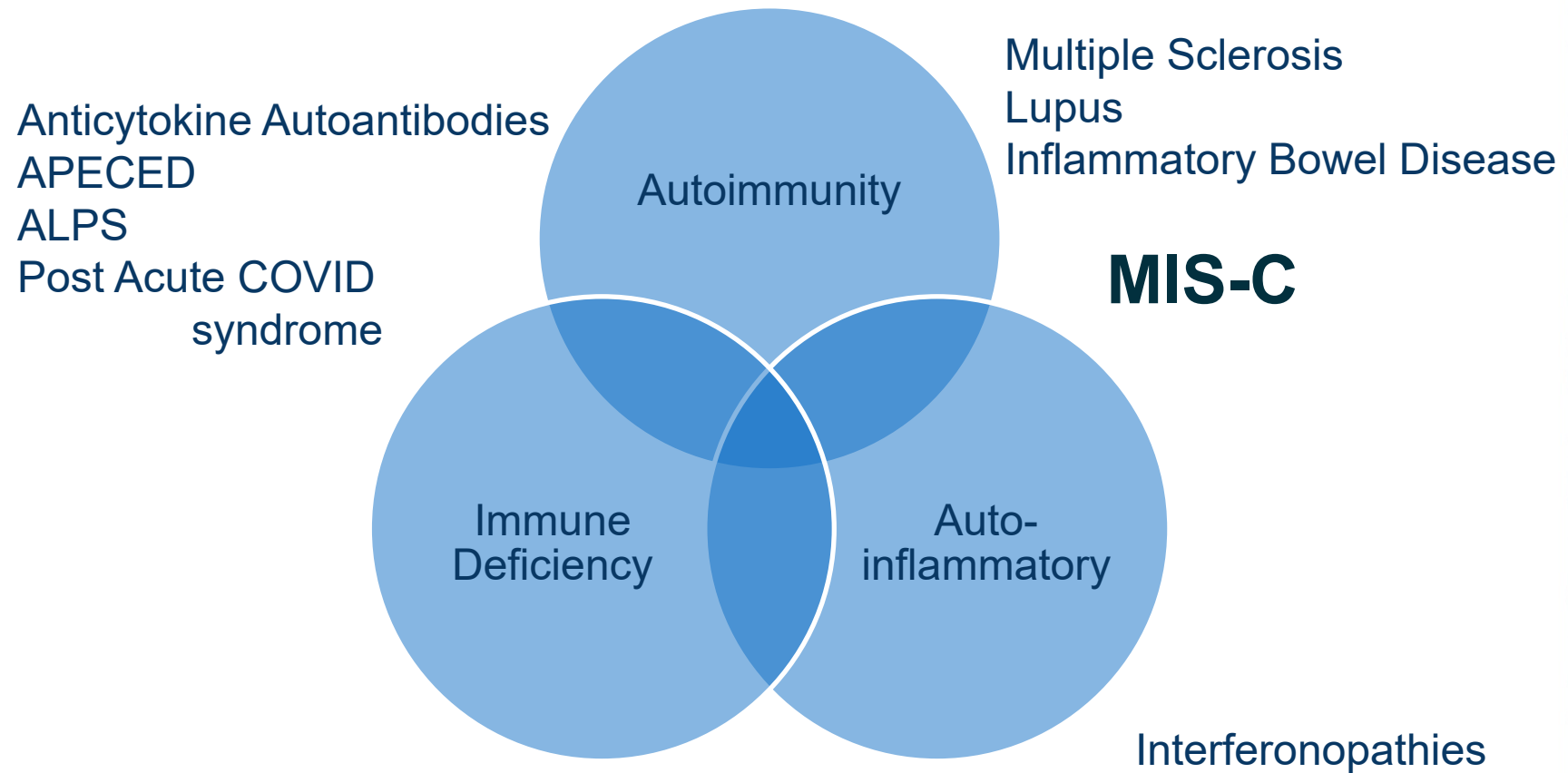
1982: Discovery of IL-4 (Paul)

Master regulator of inflammation underpins all current models of immunity

1995: Identified autoimmune lymphoproliferative syndrome (ALPS) as the first genetic disease of apoptosis (Lenardo)

2012: Linkage of anti-interferon autoantibodies with adult-onset immunodeficiency and opportunistic infections in Thailand (Holland)

DIR Autoimmunity Portfolio Overview



DIR Program Highlights

Clinical and Translational Research

Primary immunodeficiency w/ autoimmunity

- Immunodeficiency can co-present with hyperactive immune disorders (autoimmunity, lymphoproliferation, or atopy)
- NIAID Primary Immune Deficiency Clinic (PID)
- Blood and Immune Deficiency – Cellular Therapy Program (BID-CTP) (NIAID/NCI/NHLBI), established 2019

IMMUNODEFICIENCY

Immune dysregulation in human subjects with heterozygous germline mutations in *CTLA4*

Hye Sun Kuehn,^{1,4} Weiming Ouyang,^{2,4} Bernice Lo,^{5,4,6} Elissa K. Deenick,^{5,6} Julie E. Niemelä,¹ Danielle T. Avery,⁴ Jean-Nicolas Schickel,⁷ Dat Q. Tran,⁸ Jennifer Stoddard,¹ Yu Zhang,^{4,9} David M. Frucht,² Bogdan Dumitriu,¹⁰ Phillip Scheinberg,¹⁰ Les R. Folio,¹¹ Cathleen A. Frein,¹² Susan Price,^{1,4} Christopher Koh,¹² Theo Heller,¹³ Christine M. Serogy,¹⁴ Anna Huttenlocher,¹⁵ V. Koneti Rao,¹⁶ Helen C. Su,^{4,9} David Kleiner,¹⁷ Luigi D. Notarangelo,¹⁸ Yajesh Rampertap,¹⁹ Kenneth N. Olivier,²⁰ Joshua McElwee,²¹ Jason Hughes,²² Stefania Pittaluga,²³ Jose B. Oliveira,²⁴ Eric Meffre,⁷ Thomas A. Fleisher,^{1,1} Steven M. Holland,^{4,18} Michael J. Lenardo,^{2,4,1} Stuart G. Tangye,^{4,6} Gulbu Uzel^{18,1}

Science

AUTOIMMUNE DISEASE

Patients with LRBA deficiency show CTLA4 loss and immune dysregulation responsive to abatacept therapy

Bernice Lo,^{1,18} Kejian Zhang,^{2,4} Wei Lu,^{1,3} Lixin Zheng,^{1,3} Qian Zhang,^{2,4} Chrysi Kanelloupolou,^{1,3} Yu Zhang,^{2,4} Zhiduo Liu,³ Jill M. Fritz,^{3,2} Rebecca Marsh,⁶ Ammar Husami,² Diane Kissell,² Shannon Nortman,² Vijaya Chaturvedi,⁶ Hillary Hadjes,⁷ Lisa R. Young,² Jun Mo,² Alexandra H. Filipovich,⁴ Jack J. Bleesing,⁶ Peter Mustillo,¹⁰ Michael Stephens,¹⁰ Cesar M. Rueda,¹⁰ Claire A. Chongnet,¹⁰ Kasper Hoebe,¹² Joshua McElwee,²¹ Jason D. Hughes,²² Elif Karakoc-Aydiner,¹⁴ Helen F. Matthews,^{1,3} Susan Price,^{1,3} Helen C. Su,^{2,4} V. Koneti Rao,^{1,3} Michael J. Lenardo,^{1,3,2} Michael B. Jordan^{6,13,1}

THE NEW ENGLAND JOURNAL OF MEDICINE

ORIGINAL ARTICLE

CD55 Deficiency, Early-Onset Protein-Losing Enteropathy, and Thrombosis

Ahmet Ozen, M.D., William A. Comrie, Ph.D., Rico C. Ardy, M.Res., Cecilia Dominguez Corde, M.Sc., Buket Dalgiç, M.D., Ömer F. Beser, M.D., Aaron R. Morawski, M.S., Elif Karakoc-Aydiner, M.D., Engin Tutar, M.D., Safa Baris, M.D., Figen Ozcay, M.D., Nina K. Serwas, Ph.D., Yu Zhang, Ph.D., Helen F. Matthews, B.S.N., Stefania Pittaluga, M.D., Ph.D., Les R. Folio, D.O., M.P.H., Ayse Unluoglu Aksoy, M.D., Joshua J. McElwee, Ph.D., Ana Krolig, M.Sc., Ayca Kiykim, M.D., Zeren Baris, M.D., Mehmet Gulisan, M.D., Ismail Ogulur, Ph.D., Scott B. Snapper, M.D., Ph.D., Rodrick H.J. Houwen, M.D., Ph.D., Helen L. Lewis, M.D., Ph.D., Deniz Ertem, M.D., Renate Kain, M.D., Simon Sar, M.D., Talay Erkan, M.D., Helen C. Su, M.D., Ph.D., Kaan Bostug, M.D., and Michael J. Lenardo, M.D.

blood

Early-onset lymphoproliferation and autoimmunity caused by germline *STAT3* gain-of-function mutations

Joshua D. Milner,¹ Tiphonie P. Vogel,^{2,3} Lisa Forbes,^{4,5} Chi A. Ma,¹ Asbjørn Stray-Pedersen,^{4,7} Julie E. Niemela,⁸ Jonathan J. Lyons,⁹ Karin R. Engelhardt,⁹ Yu Zhang,¹⁰ Nermina Topcagic,¹¹ Elshah D. O. Robinson,^{1,11} Helen Matthews,¹² James W. Verbsky,^{13,14} Trivikram Dasu,^{15,16} Alexander Vargas-Hernandez,¹⁷ Nidhi Varghese,¹⁸ Kenneth L. McClain,¹⁹ Lina B. Karam,¹⁶ Karen Nahmod,^{4,5} George Makedonas,^{4,5} Emily M. Mace,^{4,5} Hanne S. Sorte,¹ Gari Pemmion,¹⁷ V. Koneti Rao,¹² Michael P. O'Connell,¹ Susan Price,¹² Helen C. Su,¹⁰ Morgan Butrick,¹² Joshua McElwee,¹⁸ Jason D. Hughes,¹⁹ Joseph Wille,¹ David Swan,¹ Yaboo Xu,¹ Mauro Santibanez-Kovacs,¹⁹ Voryek Slowik,¹⁹ Darrell L. Dinwiddie,^{21,22} Christina E. Clapote,^{21,23} Carol J. Saunders,^{21,24,25} Beth Sepler,²⁶ Stephen F. Kingsmore,^{21,24,25} Andrew J. White,² Andrew J. Cant,^{3,26} Sophie Hamblin,^{3,26} and Megan A. Cooper²⁷



Journal of Allergy and Clinical Immunology

Volume 141, Issue 1, January 2018, Pages 365-371

X-linked carriers of chronic granulomatous disease: Illness, lyonization, and stability

Beatriz E. Marciano, MD,¹ Christa S. Zerbe, MD,² E. Liara Falcone, MD, PhD,³ Li Ding, MD,⁴ Suk See DeRavin, MD, PhD,⁵ Janine Daub, CRNP,⁶ Samantha Kreuzburg, RN,⁴ Lynne Yockey, RN,⁴ Sally Hunsberger, PhD,⁷ Ladan Forouh, CRNP,⁸ Lisa A. Barnhart, RN,⁴ Kabir Matharu, MD,⁹ Victoria Anderson, CRNP,⁴ Dirk N. Darnell, RN,⁴ Cathleen Frein, CRNP,⁴ Danielle L. Fink, MS,⁴ Karen P. Lau, MS,⁴ Debra A. Long Priel, MS,⁴ John I. Gallin, MD,⁴ Harry L. Malech, MD,⁴ Gulbu Uzel, MD,⁴ Alexandra F. Freeman, MD,⁴ Douglas B. Kuhns, PhD,⁴ Sergio D. Rosenzweig, MD, PhD,⁴ and Steven M. Holland, MD⁴

Bethesda and Frederick, Md

JCI The Journal of Clinical Investigation

Complete Absence of CD3 γ Protein Expression Is Responsible for Combined Immunodeficiency with Autoimmunity Rather than SCID

Ottavia M. Delmonte,¹ Jared H. Rowe,² Adam K. Dobbs,¹ Boaz Palterer,³ Riccardo Castagnoli,⁴ Luigi D. Notarangelo¹

Science

IMMUNODEFICIENCIES

HEM1 deficiency disrupts mTORC2 and F-actin control in inherited immunodysregulatory disease

Sarah A. Cook,¹ William A. Comrie,^{2,3} M. Cecilia Poli,^{2,4,5} Morgan Similia,⁶ Andrew J. Oler,⁷ Aliman J. Faruqi,⁸ Douglas B. Kuhns,⁹ Sheng Yang,⁹ Alexander Vargas-Hernandez,¹⁰ Alexandre F. Carlsley,¹¹ Benjamin Fournier,^{12,13} D. Eric Anderson,¹⁴ Susan Price,¹⁵ Margery Smolkinsky,¹⁶ Wafiq Abou Chakla,¹⁷ Lisa R. Forbes,¹⁸ Emily M. Mace,¹⁹ Tram N. Cao,²⁰ Zeynep H. Coban-Akdemir,^{21,22} Shalini N. Jhangiani,^{23,24} Donna M. Muzny,^{25,26} Richard A. Gibbs,^{27,28,29} James R. Lupski,^{27,28,29} Jordan S. Orange,³⁰ Geoffrey D. E. Cuvelier,³⁰ Moza Al Hassan,³¹ Nawal Al Kaabi,³² Zain Al Yafei,³³ Soma Jyonouchi,³⁴ Nikita Raju,³⁵ Jason W. Caldwell,³⁶ Yanning Huang,^{37,38} Jenik K. Burkhardt,³⁷ Sylvain Latour,^{39,40} Baoyu Chen,⁴¹ Gehad Elchazar,⁴² V. Koneti Rao,⁴³ Ivan K. Chinn,⁴⁴ Michael J. Lenardo¹

Inflammatory Bowel Disease

Broad spectrum of basic and clinical studies on the immune system governing the mucosal surface

Patient Recruitment

An Open-Label, Phase I/II Pilot Study to Assess the Safety and Tolerability of Vorinostat for the Treatment of Moderate-to-Severe Crohn's Disease

Do you have uncontrolled Crohn's disease?

JCI The Journal of Clinical Investigation

Loss-of-function CARD8 mutation causes NLRP3 inflammasome activation and Crohn's disease

Liming Mao,¹ Atsushi Kitani,¹ Morgan Similuk,² Andrew J. Oler,³ Lindsey Albenberg,⁴ Judith Kelsen,⁴ Atiye Aktay,⁵ Martha Quezada,⁶ Michael Yao,^{1,7} Kim Montgomery-Recht,⁸ Ivan J. Fuss,¹ and Warren Strober¹

JCI The Journal of Clinical Investigation

Bruton tyrosine kinase deficiency augments NLRP3 inflammasome activation and causes IL-1 β -mediated colitis

Liming Mao, ... , Adrian Wiestner, Warren Strober

J Clin Invest. 2020;130(4):1793-1807. <https://doi.org/10.1172/JCI128322>.

Journal of Clinical Immunology (2019) 39:653–667
<https://doi.org/10.1007/s10875-019-00659-8>

ORIGINAL ARTICLE



Chronic Granulomatous Disease-Associated IBD Resolves and Does Not Adversely Impact Survival Following Allogeneic HCT

Rebecca A. Marsh¹ · Jennifer W. Leiding² · Brent R. Logan³ · Linda M. Griffith⁴ · Danielle E. Arnold⁵ · Elie Haddad⁶ · E. Liana Falcone⁷ · Ziyun Yin⁸ · Kadam Patel³ · Erin Arbuckle⁸ · Jack J. Bleesing¹ · Kathleen E. Sullivan⁹ · Jennifer Heimall⁵ · Lauri M. Burroughs⁹ · Suzanne Skoda-Smith¹⁰ · Shanmuganathan Chandrakasan¹¹ · Lolie C. Yu¹² · Benjamin R. Oshrine¹³ · Geoffrey D. E. Cuvelier¹⁴ · Monica S. Thakar¹⁵ · Karin Chen¹⁶ · Pierre Teira¹⁷ · Shalini Shenoy¹⁸ · Rachel Phelan¹⁹ · Lisa R. Forbes²⁰ · Deepak Chellapandian²¹ · Blachy J. Dávila Saldaña²² · Ami J. Shah²³ · Katja G. Weinacht²⁴ · Avni Joshi²⁵ · Farid Boulad²⁶ · Troy C. Quigg²⁷ · Christopher C. Dvorak²⁸ · Debi Grossman²⁹ · Troy Torgerson³⁰ · Pamela Graham²⁹ · Vinod Prasad³¹ · Alan Knutsen³² · Hey Chong³³ · Holly Miller³⁴ · M. Teresa de la Morena³⁵ · Kenneth DeSantes³⁶ · Morton J. Cowan²⁸ · Luigi D. Notarangelo³⁷ · Donald B. Kohn³⁸ · Elizabeth Stenger³⁹ · Sung-Yun Pai⁴⁰ · John M. Routes⁴¹ · Jennifer M. Puck²⁸ · Neena Kapoor⁴² · Michael A. Pulsipher⁴² · Harry L. Malech²⁹ · Suhag Parikh⁴³ · Elizabeth M. Kang²⁹ · submitted on behalf of the Primary Immune Deficiency Treatment Consortium

Autoimmune Lymphoproliferative Syndrome (ALPS)

- **Lymphoproliferation**
 - Lymph nodes, liver, spleen
- **Autoimmune sequelae**
 - Hemolytic anemia
 - Thrombocytopenia
- **25 year long ongoing study of ALPS patients**



Natural history of autoimmune lymphoproliferative syndrome associated with *FAS* gene mutations

Susan Price,¹ Pamela A. Shaw,² Amy Seitz,³ Gyan Joshi,⁴ Joie Davis,¹ Julie E. Niemela,⁵ Katie Perkins,⁶ Ronald L. Hornung,⁵ Les Folio,⁷ Philip S. Rosenberg,⁸ Jennifer M. Puck,⁹ Amy P. Hsu,³ Bernice Lo,¹ Stefania Pittaluga,¹⁰ Elaine S. Jaffe,¹⁰ Thomas A. Fleisher,⁵ V. Koneti Rao,¹ and Michael J. Lenardo¹



Paradoxical CD4 Lymphopenia in Autoimmune Lymphoproliferative Syndrome (ALPS)

Andrea Lisco^{1*}, Chun-Shu Wong¹, Susan Price², Peiyang Ye¹, Julie Niemela³, Megan Anderson¹, Elizabeth Richards¹, Maura Manion¹, Harry Mystakelis¹, Morgan Similuk⁴, Bernice Lo⁵, Jennifer Stoddard³, Sergio Rosenzweig³, Christophe Vanpouille⁶, Adam Rupert⁷, Irina Maric⁸, Ainhoa Perez-Diez¹, David Parenti⁹, Peter D. Burbelo¹⁰, V. Koneti Rao² and Irini Sereti^{1*}

Autoimmune polyendocrinopathy-candidiasis-ectodermal dystrophy (APECED)

- Monogenic disorder caused by *AIRE* mutations resulting in:
 - chronic yeast infections
 - **autoimmunity** to organs (endocrine system, lungs, etc.)
- Largest single center cohort of patients in the world

SCIENCE TRANSLATIONAL MEDICINE | RESEARCH ARTICLE

AUTOIMMUNITY

Lymphocyte-driven regional immunopathology in pneumonitis caused by impaired central immune tolerance

Elise M. N. Ferré¹, Timothy J. Break^{1*}, Peter D. Burbelo^{2*}, Michael Allgäuer^{3,4}, David E. Kleiner³, Dakai Jin⁵, Ziyue Xu⁵, Les R. Folio⁵, Daniel J. Mollura⁵, Muthulekha Swamydas¹, Wenjuan Gu⁶, Sally Hunsberger⁶, Chyi-Chia R. Lee³, Anamaria Bondici¹, Kevin W. Hoffman⁷, Jean K. Lim⁷, Kerry Dobbs⁸, Julie E. Niemela⁹, Thomas A. Fleisher⁹, Amy P. Hsu¹⁰, Laquita N. Snow¹, Dirk N. Darnell¹, Samar Ojaimi^{11,12}, Megan A. Cooper¹³, Martin Bozzola¹⁴, Gary I. Kleiner¹⁵, Juan C. Martinez¹⁶, Robin R. Deterding¹⁷, Douglas B. Kuhns¹⁸, Theo Heller¹⁹, Karen K. Winer²⁰, Arun Rajan²¹, Steven M. Holland¹⁰, Luigi D. Notarangelo⁸, Kevin P. Fennelly²², Kenneth N. Olivier²², Michail S. Lionakis^{1†}

Science ^{MAAAS}

Aberrant type 1 immunity drives susceptibility to mucosal fungal infections

Timothy J. Break^{*}, Vasileios Oikonomou^{*}, Nicolas Dutzan, Jigar V. Desai, Marc Swidergall, Tilo Freiwald, Daniel Chauss, Oliver J. Harrison, Julie Alejo, Drake W. Williams, Stefania Pittaluga, Chyi-Chia R. Lee, Nicolas Bouladoux, Muthulekha Swamydas, Kevin W. Hoffman, Teresa Greenwell-Wild, Vincent M. Bruno, Lindsey B. Rosen, Wint Lwin, Andy Renteria, Sergio M. Pontejo, John P. Shannon, Ian A. Myles, Peter Olbrich, Elise M. N. Ferré, Monica Schmitt, Daniel Martin, Genomics and Computational Biology Core, Daniel L. Barber, Norma V. Solis, Luigi D. Notarangelo, David V. Serreze, Mitsuru Matsumoto, Heather D. Hickman, Philip M. Murphy, Mark S. Anderson, Jean K. Lim, Steven M. Holland, Scott G. Filler, Behdad Afzali, Yasmine Belkaid, Niki M. Moutsopoulos, Michail S. Lionakis[†]

Autoinflammatory Diseases

- Clinical and translational studies in children with autoinflammatory diseases
 - NOMID/CAPS
 - DIRA
 - CANDLE
 - SAVI
 - NLRC4-MAS
 - Still's-like diseases
 - Undifferentiated
- Identifying novel diseases and treatments

JCI

The Journal of Clinical Investigation

JAK1/2 inhibition with baricitinib in the treatment of autoinflammatory interferonopathies

Gina A. Montealegre Sanchez, ... , William L. Macias, Raphaela Goldbach-Mansky

J Clin Invest. 2018;128(7):3041-3052. <https://doi.org/10.1172/JCI98814>.

Multiple Sclerosis (MS)

Data-driven machine learning approaches in the diagnosis and treatment of MS

Targeting Residual Activity By Precision, Biomarker-Guided Combination Therapies of MS (TRAP-MS) trial (NCT03109288)



Smartphone Level Test Measures Disability in Several Neurological Domains for Patients With Multiple Sclerosis

Alexandra K. Boukhvalova^{1†}, Olivia Fan^{1†}, Ann Marie Weideman^{1†}, Thomas Harris¹, Emily Kowalczyk^{1,2}, Linh Pham¹, Peter Kosa¹ and Bibiana Bielekova^{1*}

Annals of human genetics

Genetic model of MS severity predicts future accumulation of disability

Kayla C. Jackson¹ | Katherine Sun¹ | Christopher Barbour^{1,2} | Dena Hernandez³ | Peter Kosa¹ | Makoto Tanigawa¹ | Ann Marie Weideman¹ | Bibiana Bielekova¹ 

Lupus

- Using newest advances to generate individualized predictions of disease risk and intervention efficacy
- Model for SLE in mice
 - Manipulates model to understand cellular mechanisms that induce pathology,
 - Identify new genes as therapeutic targets

nature medicine

Broad immune activation underlies shared set point signatures for vaccine responsiveness in healthy individuals and disease activity in patients with lupus

Yuri Kotliarov^{1,7,12}, Rachel Sparks^{2,12}, Andrew J. Martins², Matthew P. Mulè^{2,3}, Yong Lu², Meghali Goswami^{2,8}, Lela Kardava⁴, Romain Banchereau^{5,9}, Virginia Pascual^{5,10}, Angélique Biancotto^{1,11}, Jinguo Chen¹, Pamela L. Schwartzberg^{1,6}, Neha Bansal², Candace C. Liu², Foo Cheung¹, Susan Moir⁴ and John S. Tsang^{1,2} 



Antiviral Adaptor MAVS Promotes Murine Lupus With a B Cell Autonomous Role

Wenxiang Sun[†], Hongsheng Wang[†], Chen-Feng Qi, Juan Wu, Bethany Scott and Silvia Bolland*

Fundamental Studies of Immunity

- NIAID DIR Centers provide support for research:
- Center for Human Immunology, Autoimmunity, and Inflammation (CHI)
- Center for Advanced Tissue Imaging (CAT-I)
- NIAID Microbiome Program

ARTICLES

<https://doi.org/10.1038/s41590-018-0280-2>

nature
immunology

Regulatory T cells mediate specific suppression by depleting peptide-MHC class II from dendritic cells

Billur Akkaya^{1,8*}, Yoshihiro Oya^{1,2,8}, Munir Akkaya³, Jafar Al Souz¹, Amanda H. Holstein^{1,6}, Olena Kamenyeva⁴, Juraj Kabat⁴, Ryutaro Matsumura², David W. Dorward⁵, Deborah D. Glass^{1,7} and Ethan M. Shevach^{1*}

PNAS

Proceedings of the
National Academy of Sciences
of the United States of America

Immunity to commensal skin fungi promotes psoriasiform skin inflammation

Charlotte Hurabielle^{a,b,c,1}, Verena M. Link^{a,1}, Nicolas Bouladoux^{a,d}, Seong-Ji Han^a, Eric Dean Merrill^{a,e}, Yaima L. Lightfoot^{f,g}, Nickie Seto^f, Christopher K. E. Bleck^h, Margery Smelkinsonⁱ, Oliver J. Harrison^{a,j}, Jonathan L. Linehan^{a,k}, Samira Tamoutounour^{a,2}, Michail S. Lionakis^l, Mariana J. Kaplan^f, Saeko Nakajima^{a,m,3} and Yasmine Belkaid^{a,d,3}

The Oncoprotein and Transcriptional Regulator Bcl-3 Governs Plasticity and Pathogenicity of Autoimmune T Cells

Wanhu Tang¹, Hongshan Wang¹, Estefania Claudio¹, Ilaria Tassi¹, Hye-lin Ha¹, Sun Saret¹ and Ulrich Siebenlist^{1*}

¹Laboratory of Molecular Immunology, National Institute of Allergy and Infectious Diseases, NIH, Bethesda, MD 20892, USA

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DIR Program Highlights

COVID-19 Research

Anticytokine Autoantibodies in COVID-19

- ~1000 patients with life-threatening COVID-19 pneumonia
- >10% of severe COVID patients have autoantibodies to cytokines
- Predominantly in men

Science 

RESEARCH ARTICLE

CORONAVIRUS

Autoantibodies against type I IFNs in patients with life-threatening COVID-19

Paul Bastard^{1,2,3,*}, Lindsey B. Rosen⁴, Qian Zhang³, Eleftherios Michailidis⁵, Hans-Heinrich Hoffmann⁵, Yu Zhang⁴, Karim Dorgham⁶, Quentin Philippot^{1,2}, Jérémie Rosain^{1,2}, Vivien Béziat^{1,2,3}, Jérémy Manry^{1,2}, Elana Shaw⁴, Liis Haljasmägi⁷, Pärt Peterson⁷, Lazaro Lorenzo^{1,2}, Lucy Bizien^{1,2}, Sophie Trouillet-Assant^{8,9}, Kerry Dobbs⁴, Adriana Almeida de Jesus⁴, Alexandre Belot^{10,11,12}, Anne Kallaste¹³, Emilie Catherinot¹⁴, Yacine Tandjaoui-Lambiotte¹⁵, Jeremie Le Pen⁵, Gaspard Kerner^{1,2}, Benedetta Bigio³, Yoann Seeleuthner^{1,2}, Rui Yang³, Alexandre Bolze¹⁶, Andrés N. Spaan^{3,17}, Ottavia M. Delmonte⁴, Michael S. Abers⁴, Alessandro Aiuti¹⁸, Giorgio Casari¹⁸, Vito Lampasona¹⁸, Lorenzo Piemonti¹⁸, Fabio Ciceri¹⁸, Kaya Bilguvar¹⁹, Richard P. Lifton^{19,20,21}, Marc Vasse²², David M. Smadja²³, Mélanie Migaud^{1,2}, Jérôme Hadjadj²⁴, Benjamin Terrier²⁵, Darragh Duffy²⁶, Luis Quintana-Murci^{27,28}, Diederik van de Beek²⁹, Lucie Roussel^{30,31}, Donald C. Vinh^{30,31}, Stuart G. Tangye^{32,33}, Filomeen Haerynck³⁴, David Dalmau³⁵, Javier Martinez-Picado^{36,37,38}, Petter Brodin^{39,40}, Michel C. Nussenzweig^{41,42}, Stéphanie Boisson-Dupuis^{1,2,3}, Carlos Rodríguez-Gallego^{43,44}, Guillaume Vogt⁴⁵, Trine H. Mogensen^{46,47}, Andrew J. Oler⁴⁸, Jingwen Gu⁴⁸, Peter D. Burbelo⁴⁹, Jeffrey I. Cohen⁵⁰, Andrea Biondi⁵¹, Laura Rachele Bettini⁵¹, Mariella D'Angio⁵¹, Paolo Bonfanti⁵², Patrick Rossignol⁵³, Julien Mayaux⁵⁴, Frédéric Rieux-Laucat²⁴, Eystein S. Husebye^{55,56,57}, Francesca Fusco⁵⁸, Matilde Valeria Ursini⁵⁸, Luisa Imberti⁵⁹, Alessandra Sottini⁵⁹, Simone Paghera⁵⁹, Eugenia Quiros-Roldan⁶⁰, Camillo Rossi⁶¹, Riccardo Castagnoli⁶², Daniela Montagna^{63,64}, Amelia Licari⁶², Gian Luigi Marseglia⁶², Xavier Duval^{65,66,67,68,69}, Jade Ghosn^{68,69}, HGID Lab§, NIAID-USUHS Immune Response to COVID Group§, COVID Clinicians§, COVID-STORM Clinicians§, Imagine COVID Group§, French COVID Cohort Study Group§, The Milieu Intérieur Consortium§, CoV-Contact Cohort§, Amsterdam UMC Covid-19 Biobank§, COVID Human Genetic Effort§, John S. Tsang^{70,71}, Raphaela Goldbach-Mansky⁴, Kai Kisand⁷, Michail S. Lionakis⁴, Anne Pueh^{1,2,3}, Shen-Ying Zhang^{1,2,3}, Steven M. Holland⁴, Guy Gorochov^{6,72}, Emmanuelle Jouanguy^{1,2,3}, Charles M. Rice⁵, Aurélie Cobat^{1,2,3}, Luigi D. Notarangelo⁴, Laurent Abel^{1,2,3}, Helen C. Su⁴, Jean-Laurent Casanova^{1,2,3,4,72,73,*}

Multisystem Inflammatory Syndrome in Children (MIS-C)

Trans-NIH effort

Ongoing clinical studies

- Longitudinal observational study of neutralizing antibodies, biomarkers, and transcriptional signatures in MIS-C
- Mechanisms of immune dysregulation that trigger MIS-C
- Characterization of mucosal oropharyngeal immune responses to SARS-CoV-2 in children
- Immunological characteristics of MIS-C patients from Italy, Chile, Israel, and US
- Assessment of autoantibody presence and function

Post-Acute COVID Syndrome

- Longitudinal study of COVID-19 sequelae and immunity in adults at NIH Clinical Center ([NCT04411147](https://clinicaltrials.gov/ct2/show/study/NCT04411147))
- Longitudinal Study of COVID-19 sequelae and immunity in Italian patient cohorts
- Longitudinal COVID-19 studies in children
 - Will soon launch clinical study of 1000 children recovering from COVID-19 ranging from asymptomatic disease to MIS-C

Pre-existing Autoimmune Diseases

- SARS-CoV-2 nationwide serosurvey in people living with rare diseases who are part of the Rare Disease Clinical Research Network (NIAID, NCI, NCATS, NIBIB)
- Longitudinal study of COVID-19 sequelae and immunity in Italy would capture changes in disease state of patients with ITP and other diseases

DIR Autoimmunity Research Gaps:

Immediate need: COVID-19

- Vaccination efficacy in individuals with immune dysregulation
- Study of allergic responses to vaccination

Long-term needs:

- Recruitment and retention
- Augment pre-clinical research program
- Increased access to genetic, computational biology and machine learning approaches