Signals+

THE INTERNATIONAL CYTOKINE & INTERFERON SOCIETY NEWSLETTER

OCTOBER 2021 | VOLUME 9 | NO. 2

In This Issue:

A MESSAGE FROM THE OUTGOING PRESIDENT,

Kate Fitzgerald

Dear Colleagues,

It has been an honor and privilege to serve as President of the ICIS. I want to express my gratitude to you all for your membership and the continued success of our conferences.

It has certainly been a unique time to lead the Society over the last two years. It seems in many ways, a seismic shift has occurred in all aspects of our lives, changing the way we live, work, and commune with each other. Yet despite the challenges, we see the progress and effectiveness of COVID-19 testing, vaccines that have been widely administered in the United States, Europe and around the world, and the hope of vaccines for young children and boosters on the horizon. The work of many of you has helped to continue to inform the response and treatments for this insidious virus. With variants continuing to surge, your work remains critically important as we continue to combat this and other emerging viruses in the future.

While I was hoping to see many of you in Cardiff at this year's meeting, we will again be gathering virtually, due to international travel restrictions amidst the ongoing pandemic. While it is disappointing to move the meeting to a virtual format, the virtual platform does facilitate unique opportunities to gather in ways that may not have been possible for many of our colleagues, students, and young investigators. After a successful virtual meeting last year, this year's meeting will again feature cutting edge research and be an opportunity for meaningful discussions and exchanges among international colleagues in the field. Thank you to Simon Jones and his co-organizers for taking on this challenge and for organizing a wonderful program for this year's conference. Thank you to Joan Oefner, Elizabeth Gray and our MCI colleagues as well for helping with the transition to virtual. Cytokines 2022 Hybrid will be hosted by James Turkson and colleagues in Hawaii and we look forward to this exciting meeting and a chance to see many of you in person.

Each year, ICIS recognizes members of the society for their scholarly accomplishments. Huge congrats to all of the awardees this year who will be recognized at the meeting in October. I would like to express my sincere gratitude to Pfizer and Regeneron for their sponsorship of new awards this year. Thanks to Pfizer for supporting both the Junior Investigator Awards for Most Promising Research at Cytokines 2021 and the 2021 ICIS-Pfizer Award for Excellence in Interferon and Cytokine Research. In addition, sincere thanks to Regeneron for sponsoring the New Investigator Awards for Excellence in Cytokine and Interferon Research.

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Future Meetings

Cytokines 2021,
October 17 - 20, 2021
Cardiff, Wales, UK

Cytokines 2022,
September 20 - 23, 2022
Big Island, Hawaii USA

ICIS
International Cytokine & Interferon Society

A MESSAGE FROM THE OUTGOING PRESIDENT,

Kate Fitzgerald

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We are also grateful for the continued support of BioLegend for their sponsorship of the ICIS-BioLegend William E. Paul Award for Excellence in Cytokine Research, the Luminex Corporation for sponsoring the 2021 ICIS-Luminex John R. Kettman Award for Excellence in Interferon & Cytokine Research for a Mid-career researcher. Thank you to the Fleischmann Family for sponsoring the Christina Fleischmann Award to Young Women Investigators, PBL Assay Science for sponsoring the Sidney & Joan Pestka Graduate and Post-Graduate Awards, friends and colleagues of the late Amanda Proudfoot for sponsoring the ICIS Chemokine trainee award. I am grateful to all for this support of our members and young investigators allowing our community to celebrate their accomplishments in our field.

As my term draws to a close a special thank you to Christopher Hunter, President-Elect, and Joan Oefner, Managing Director of the Society for all your efforts over the last 2 years. Thank you also to the ICIS Council, and all of the dedicated individuals who serve on our committees for their ongoing service. A special thank you to David Artis, Chair of our Development Committee, who played a central role in finding support for our awards from new sponsors. It has been an honor to serve with all of these dedicated individuals. The future of the Society is in terrific hands with Chris Hunter as our next President. His leadership will build upon the important work and progress that been made over the last few years and will no doubt do a fantastic job helping the Society to continue to grow.

In closing, thank you for your membership of the ICIS and for your work in the field of cytokines and interferons. The field continues to evolve, and I cannot wait to see what the future holds for our members and bright trainees and young investigators. I look forward to being with you all “virtually” in Cardiff.

Be well and stay safe,

Kate

HENRY KUNKEL SOCIETY

29th Annual
Henry Kunkel Society
Meeting

APRIL 7-9, 2022

METROPOL PALACE HOTEL, BELGRADE, SERBIA

The 29th annual meeting of the Henry Kunkel Society on “Innate Immunity: from basic biology to human disease” will take place on April 7-9, 2022 at the Metropol Palace Hotel in Belgrade, Serbia.

The meeting is chaired by Dusan Bogunovic, the Icahn School of Medicine at Mount Sinai in New York, and Federica Sallusto, from the Institute for Research in Biomedicine in Bellinzona and the ETH Zürich, Switzerland, will deliver the Kunkel Memorial Lecture.

Link to full list of speakers: https://www.henrykunkelsociety.org/registration

Link to registration: https://www.henrykunkelsociety.org/meeting-program

ICIS 2021 Leadership Election Results

OFFICERS – 2 YEAR TERMS

Sarah L. Gaffen, PhD
President-Elect (2021 - 2023)

Dusan Bogunovic, PhD
Treasurer (2021-2023)

COUNCIL MEMBERS – 3 YEAR TERMS

Judith E Allen, FRSE, FRSB, FMedSci
Council (2022-2024)

You-Me Kim, PhD
Council (2022 - 2024)

NOMINATIONS COMMITTEE – 3 YEAR TERMS

Rune Hartmann, PhD
Nominating Committee
(2022 - 2024)

Lydia Lynch, PhD
Nominating Committee
(2022 - 2024)

COUNCIL MEMBER OR FOR INCLUSION AND TRAINING, 1-3 YEAR TERM; 1-2 YEAR TERM

Justina Kulikauskaite
Council member or for Inclusion and Training, (2021 - 2023)

Ruby Dawson, PhD
Council member or for Inclusion and Training, (2021 - 2022)

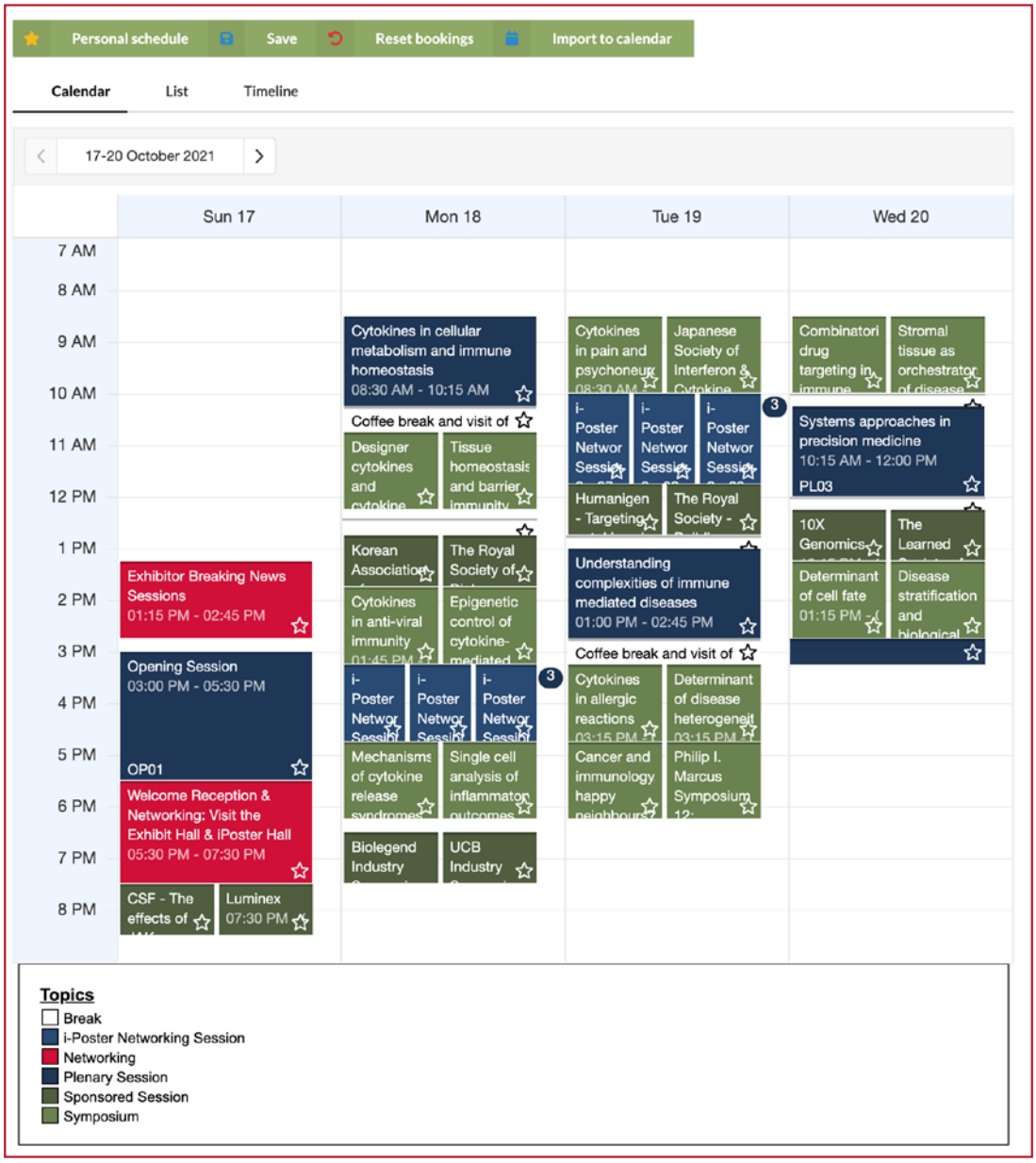
Thanks to all the ICIS members who made nominations and voted in the 2021 election.

ICIS NOMINATING COMMITTEE:

- **Paul Hertzog**
  Australia Chair (2020-2022)
- **Thirumala-Devi Kanneganti**
  USA (2019-2021)
- **Claudia Nold**, Australia
  (2021 – 2023)
- **Leonidas C. Platanias**
  USA (2019 – 2021)
- **Nancy C. Reich Marshall**
  USA (2021 – 2023)
- **Andreas Wack**
  UK (2021 – 2023)

As communicated previously, the ever-changing uncertainties associated with the current pandemic has placed various pressures on the organization of our forthcoming Cytokines2021 meeting. After careful reflection, the ICIS has made the hard decision to transfer the annual meeting to a FULLY VIRTUAL conference. This decision will safeguard the health and wellbeing of our delegates and alleviate the stress related to the uncertainties of travelling and in-person gatherings.

In anticipation of this eventuality, the Local Organizing Committee and ICIS secretariat have worked hard to create a virtual event that will offer exciting opportunities to engage with friends, colleagues, and other members of the scientific community, including industrial partners and supporting academic societies. Building on the success of last year's virtual meeting, we will ensure fruitful exchanges and presentations of original findings.



Click here to access the interactive online program & create a personal schedule

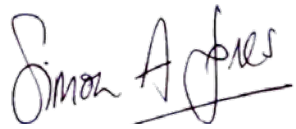
Our industry partners have put so much effort into their interactive virtual exhibit booths and Breaking News presentations to be live streamed from their booths on Sunday before the opening session. There are many breaks in the program for participants to visit the virtual exhibits. Please note the following booths are either promoting Careers or Post-doc Opportunities in their booths and/or their Breaking News:

- Boehringer Ingleheim
- GSK
- Janssen
- ICIS
- KAI
- Pfizer
- Xilio

Cytokines2021 would not be possible without the continued support of the leading companies advancing the most promising cytokine-based therapies and inhibitors, cell analysis, biomarkers, antibodies, reagents, and assay tools working on behalf of ICIS member researchers across the globe. Partnerships between the Society and Industry works to advance cytokine biology impacting all aspects of medicine, leading to new treatments in inflammation, autoimmune diseases, cancer, COVID-19, infectious disease, metabolism, microbiome health and immune-mediated conditions such as rheumatoid arthritis. We are also hugely grateful for the involvement of The Royal Society, The Learned Society of Wales, The Royal Society for Biology, The Korean Immunology Association and the Japanese Society for Cytokine and Interferon Research. Each of these academic societies have supported bespoke sessions within the program that broaden the overall content and flavor of the meeting. We are delighted to have these on board.

We would like to wholeheartedly thank you for your confidence and support in these troubled times and remain optimistic about the success of the 2021 Virtual Meeting, with a Welsh touch of course!
Please visit the Cytokines2021 website https://cardiff.cytokinesociety.org/ to view the updated program. We look forward to seeing you virtually October 17-20 (and on-demand through November 12th).
We very much hope you enjoy the format of the meeting.

Best regards,



Professor Simon A. Jones
Division of Infection & Immunity
Cardiff University
Cardiff, Wales, UK
JonesSA@cardiff.ac.uk

Yr Athro Simon A Jones

Deon Ymchwil Ysgol
Meddygaeth Prifysgol Caerdydd
Yr Isadran Haint ac Imiwnedd
Adeilad Tenovus
Parc y Mynydd Bychan
Caerdydd, Cymru, DU

Local Organizing Committee

From Left to Right:
- Luke O'Neill, Trinity College Dublin, Ireland
- Clare Bryant, University of Cambridge, UK
- Clare M. Lloyd, Imperial College, UK
- Iain McInnes, University of Glasgow, Scotland, UK
- Simon A Jones, (Chair) Cardiff University, Wales, UK

(formerly the Seymour & Vivian Milstein Award from 1988 – 2020)

2021 ICIS-Pfizer Award for Excellence in Interferon and Cytokine Research Winner

JENNY PAN-YUN TING, Ph.D.

William R and Kenan Professor of Genetics, University of North Carolina at Chapel Hill, Chapel Hill, USA and is the Director of the Center for Translational Immunology and the Immunology Program co-leader at the Lineberger Comprehensive Cancer Center at UNC, Chapel Hill, USA

Dr. Ting, combining her knowledge of cytokine regulation and function with state-of-the-art approaches to unravel the immunologic basis for inflammation in infection, inflammatory diseases and cancer, has elevated world-wide research on interferons and cytokines, most notably through her seminal work in NLRs that in many ways started the field of NOD-like receptor proteins.

As an active member of the cytokine community working on various aspects of cytokine biology since 1984, Dr. Ting's focus for the last 25 years has been on understanding how cytokines such as interleukin-1 and type I Interferons are regulated during immune activation and how these cytokines in turn regulate the immune response to a plethora of diseases including inflammatory diseases, autoimmunity, metabolic diseases, neuroinflammation, cancer and infection by bacterial and viral pathogens. Her work has focused on the events that lead to the development of protective immunity as well as to understanding how cytokine dysregulation leads to an array of chronic inflammatory diseases. While most of her early research focused on the regulation of cytokine-induced major histocompatibility complex class II and the function of immune genes in brain glial cells, her pioneering work on pattern recognition receptors, especially the role of the NOD like receptor superfamily as sensors of microbial infection and sterile inflammation is perhaps her most significant and impactful contributions to the field of immunology.

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(formerly the Seymour & Vivian Milstein Award from 1988 – 2020)

JENNY PAN-YUN TING, Ph.D.

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This body of work coupled with her curiosity, generosity, and mentoring skills, has led to other equally path-breaking observations relevant to cytokine biology and human diseases. Her lab was amongst the first to describe the NLR family of proteins. These studies have been extended in many different ways to define NLRs and other novel intracellular sensors that respond to viral and intracellular bacterial infections. Since her early work identifying the CATERPILLER family (NLR family), Dr. Ting has worked steadfastly to identify the molecular mechanisms regulating these proteins and their ability to induce inflammasome formation, regulate interferon and inflammatory cytokines, impact microbiota and alter immunometabolism. Her lab has also shown the relevance of some of the NLRs in adaptive immune cells to alter T effector cells. These efforts have led to a large body of literature from her lab linking NLRs to the regulation of both inflammasome NLRs and non-inflammasome NLRs in a wide range of disorders. This body of work has provided compelling data to suggest that therapeutic targeting of NLRP3 and related inflammasomes could be a viable therapeutic approach for the treatment of a wide range of inflammatory diseases. Indeed, several biotech companies are exploring this issue now.

Jenny Pan-Yun Ting received her B.S. in medical technology from Illinois State University, and her Ph.D. from Northwestern University, USA. She did her postdoctoral training at the University of Southern California and Duke University. She joined the University of North Carolina at Chapel Hill as a faculty in 1984, and is currently the William Rand Kenan Professor of Genetics, with a joint appointment in the Department of Microbiology-Immunology. She is also the Immunology Program Leader at the Lineberger Comprehensive Cancer Center at UNC-CH. She has over 300 publications and is consistently one of the highly cited researchers recognized by Thomson Reuters/Clarivate Analytics. She has served on several councils at the National Institutes of Health and is currently a member of the Burroughs Wellcome Fund Board of Directors. She has taken on numerous leadership roles including serving as the President of the American Association of Immunologists from 2020-2021. She has mentored over 100 post-doctoral and pre-doctoral researchers in her lab.

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(formerly the Seymour & Vivian Milstein Award from 1988 – 2020)

JENNY PAN-YUN TING, Ph.D.

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2021 ICIS-Pfizer Award for Excellence in Interferon and Cytokine Research Presentation

Professor Ting will give her ICIS-Pfizer Award Presentation at Cytokines 2021 Virtual Meeting on Sunday, October 17, 2021 on: ***"The all-encompassing importance of innate immune receptors".***

Sponsored by a generous grant from Pfizer

The Pfizer Award for Excellence in Interferon and Cytokine Research *(formerly the Seymour & Vivian Milstein Award from 1988 – 2020)*, represents the pinnacle of scientific achievement in interferon and cytokine research since 1988, two years after interferon was first approved for the treatment of hairy cell leukemia. Since that time, it has been widely recognized that interferons and the larger class of cytokines play critical roles in the development and progression of many major diseases including **cancer, viral diseases** such as **hepatitis and influenza,** and **autoimmune disorders** like **multiple sclerosis** and **lupus.**

This award (formerly the Milstein Award from 1988 - 2020) is bestowed upon a leading biomedical research scientist who has made outstanding contributions to interferon and cytokine research, either in a basic or applied field. Many laureates have made seminal advancements that have enabled the successful treatment of disease or have the potential to lead to significant health benefits.

2021 THE ICIS-BIOLEGEND WILLIAM E. PAUL AWARD for Excellence in Cytokine Research

BioLegend®
Enabling Legendary Discovery™

K. CHRISTOPHER GARCIA, Ph.D.

Younger Family Professor of Structural Biology, Departments of Molecular and Cellular Physiology, and Structural Biology, Investigator, Howard Hughes Medical Institute, Stanford University, Stanford, USA.

Dr. Garcia has been chosen as the ICIS-BioLegend William E. Paul Award winner in recognition of his enormous contributions to understanding receptor-ligand interactions which is unparalleled in the area of cytokine and interferon research. This award is bestowed on Dr. Garcia for his unwavering commitment to visualizing the fascinating architectures of cytokine-receptor interaction, his pivotal role in all the major advances in understanding the structural basis for how cytokine receptors engage and signal in response to cytokine binding, and for his innovative use of protein engineering to translate this information into the development of new therapeutic strategies and molecules. His application of traditional principles of pharmacology used in small molecule drug discovery to cytokine systems has initiated a new field of cytokine pharmacology.

"I knew Bill Paul well so its a special honor. In fact we did some structural and engineering work around IL-4 working with Bill (LaPorte et al., Cell 2008; Bates et al, Nat Chem Biol 2012). I cant think of anyone who loved cytokines more and we would spend hours at meetings talking about cytokines. This honor really makes me glad I took this path. Much to come still, I feel that we are in the midst of a renaissance in this field now that we are learning how better to use them therapeutically."

Studies from the Garcia lab in the fields of structural biology, protein engineering, cell signaling, immunology, autoimmunity, have now matured to the point where they are the foundation for the development of new classes of drugs for cancer, autoimmune disease, and regenerative medicine. Dr. Garcia's innovative interdisciplinary work is catapulting transformative advances across the realms of science, engineering, and medicine. His group has made seminal contributions toward elucidating the molecular details of protein engagement, with a particular emphasis on cytokine complexes, including all three classes of IFNs, IL-1, IL-2, IL-4, IL-6, IL-10, IL-12, IL-13, IL-15, IL-17, IL-22, IL-23, CNTF, and LIF. The findings from Dr. Garcia's cytokine structure studies have led to new paradigms across disciplines, including neurobiology, immunology, and developmental biology. Empowered by these biophysical discoveries, the Garcia Lab has pioneered a new phase of cytokine research, wherein the lab applies molecular principles to engineer tunable proteins that exhibit biased or targeted behavior.

In summary, Dr. Garcia's contributions to our understanding of cytokines and how they engage their receptors are truly outstanding, opening new fields for investigation with his innovative, and pioneering accomplishments that have advanced multiple fields. Dr, Garcia has made significant contributions that serve as a foundation for a new era of immunotherapy, cytokine biology, regenerative medicine and drug design.

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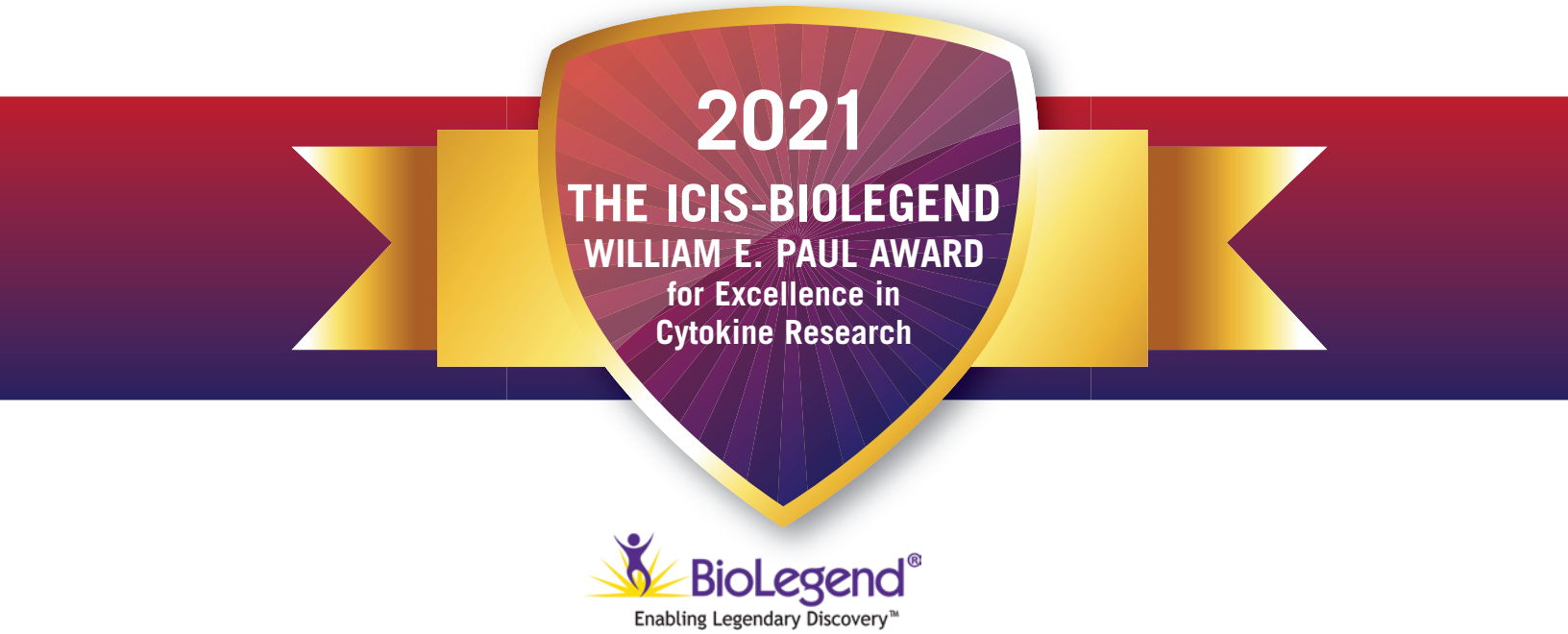

K. CHRISTOPHER GARCIA, Ph.D.

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Christopher Garcia, Ph.D. is a Professor of Molecular and Cellular Physiology, and of Structural Biology at the Stanford University School of Medicine. He received his B.S. in Biochemistry from Tulane University, and his Ph.D. in Biophysics from Johns Hopkins University. After two years of post-doctoral work at Genentech, Inc. under Dr. David Goeddel in the Dept. of Molecular Biology, where he learned the emerging technologies of protein engineering and recombinant protein expression, Dr. Garcia moved to a second post-doctoral fellowship at The Scripps Research Institute in the laboratory of Prof. Ian Wilson, where he succeeded in determining the first crystal structures of the T cell receptor and then its complex with peptide-MHC. In 1999, Dr. Garcia started his lab at Stanford University School of Medicine in 1999 where he also became an Investigator in the Howard Hughes Medical Institute. Dr. Garcia was elected to the National Academy of Sciences in 2012, and the National Academy of Medicine in 2016.

Dr. Garcia's interests reside at the cell surface, and his laboratory is investigating structural and functional aspects of cell surface receptor recognition and activation, in receptor-ligand systems with relevance to human health and disease. Structural information on receptor-ligand complexes is used to engineer variant proteins and/or surrogates to manipulate receptor signaling and cellular function, with an eye towards therapeutic applications. The receptor systems studied derive principally from the immune system (TCR/MHC, cytokines, chemokine GPCR), but additionally encompass several systems that are also important in neurobiology (Neurotrophins, Semaphorins) and development (Notch, Wnt). A focus is on "shared" pleiotropic receptors, to understand the biophysical basis by which different ligands are able to elicit unique intracellular responses and functional outcomes, and to exploit this information to engineer receptor-specific ligands Dr. Garcia has founded or co-founded several biotech companies that are attempting to clinically develop technologies from his lab, including ALXO (SIRP/CD7 antagonist), Synthekine (cytokine engineering), Surrozen (Wnt agonists), 3T (TCR antigen discovery), and Mozart (immune modulation by regulatory T cells).

Dr. Garcia will give a talk on ***"An emerging field of cytokine pharmacology"*** at Cytokines 2021 Virtual 9th Annual Meeting of the International Cytokine & Interferon Society, on Sunday, October 17, 2021.

This award is sponsored by a generous grant from BioLegend.

Past winners of the ICIS BioLegend William E. Paul award are as follows:

- 2020 – **Sarah L. Gaffen, Ph.D**. Gerald P. Rodnan Professor of Rheumatology Director of Basic Rheumatology Research University of Pittsburgh School of Medicine Department of Medicine, Division of Rheumatology and Clinical Immunology Pittsburgh, USA AND
- 2020 – **Vijay K. Kuchroo, DVM, Ph.D.** Samuel L. Wasserstrom Professor of Neurology at Harvard Medical School & Director, Evergrande Center for Immunologic Diseases Harvard Medical School and Brigham and Women's Hospital, Boston, USA
- 2019 – **Chen Dong, Ph.D.**, Professor and Director of the Institute for Immunology and Dean of the School of Medicine, Tsinghua University, Beijing, China
- 2018 – **Giorgio Trinchieri, MD**, NIH, National Cancer Institute, Center for Cancer Research, CHIEF: Laboratory of Integrative Cancer Immunology, NIH DISTINGUISHED INVESTIGATOR, HEAD, CANCER IMMUNOLOGY SECTION

2017 – **Alan Sher, Ph.D.**, Chief, Laboratory of Parasitic Diseases, NIAID, Bethesda, USA

- 2016 – **Richard M. Locksley, MD**, Director of the Sandler Asthma Basic Research Center (SABRE) and a Howard Hughes Medical Institute Investigator, University of California, San Francisco

2021 ICIS-LUMINEX John R. Kettman Award for Excellence in Interferon & Cytokine Research

Luminex

MARION PEPPER, Ph.D.

Associate Professor. Department of Immunology, University of Washington, Seattle, USA

Twitter: @PepperMarion

The 2021 ICIS-Luminex John R. Kettman Award for Excellence in Interferon & Cytokine Research Mid-career recognizes **Marion Pepper, Ph.D.** as being in the very top tier of the current wave of mid-career immunologists who continue to make cytokine research exciting.

While a graduate student at the University of Pennsylvania, Marion pioneered the use of transgenic parasites that expressed model antigens in a series of studies to understand the events that lead to T cell production of IFN-gamma required for resistance to this pathogen. This was followed by studies that were the first to show that plasmacytoid DC (pDC) were activated during non-viral infections and acted as a source of early IL-12 required for resistance to this infection. At the time the predominant dogma was that pDC did not present antigen and her studies, were perhaps one of the first showing that pDC from sites of inflammation could present antigen. It was during this time that she developed an interest in the ability to manipulate pathogens but also to identify the relevant antigenic peptides recognized by T and B cells that mediate long-term adaptive resistance to infection, which remain the core principles of her scientific career.

As a postdoc in Marc Jenkins' laboratory in the Center for Immunology at the University of Minnesota, Dr. Pepper focused on how CD4+ effector populations translate into memory cells. To determine if paradigms about T cell memory largely described for CD8+ T cells, applied to CD4+ T cells she generated reagents and techniques to investigate the longevity of antigen-specific CD4+ T cells initially in response to infection. Using MHC Class II tetramers to track bacterial-specific CD4+ T cells, she demonstrated that unlike CD8+ T cell memory, CD4+ memory slowly waned over time. Dr. Pepper's finding that CD4+ memory T cells can decline because they compete poorly for IL-15 is one of the few insights in the field as to how vaccine immunity could fade over time. These studies also showed that the route of bacterial infection directs the acquisition of specific effector functions (Th1 and Th17 cells) and memory potential within a given epitope-specific population. These were the first studies of an endogenous antigen-specific CD4+ T cell response from the pre-immune repertoire through the memory phase and provided insights into the cytokine pathways critical for these events. This work was followed by studies that focused on elucidating the signals provided by IL-2 that drive the differentiation of two well-defined subsets of CD4+ memory cells, lymph-node homing central memory cells (Tcm) and tissue homing effector memory cells (Tem). Importantly, these studies also defined some of the early differentiaiton cues for Th1 effector and B cell helping T follicular helper (Tfh) cells that leads to the formation of Tem and Tcm, respectively.

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2021 ICIS-LUMINEX John R. Kettman Award for Excellence in Interferon & Cytokine Research

Luminex®

MARION PEPPER, Ph.D.

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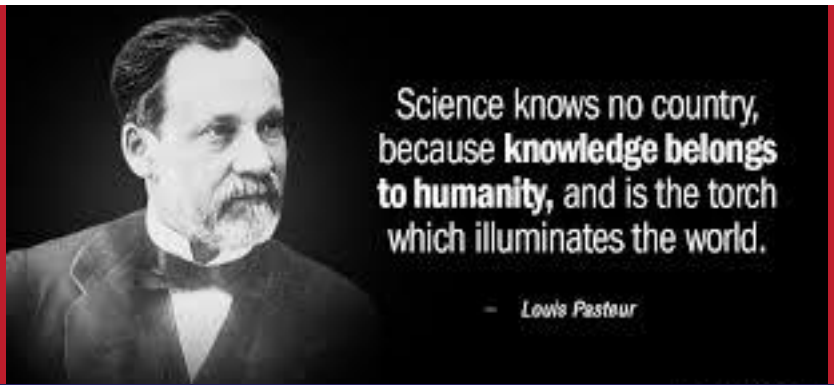
Since establishing her own laboratory in the Department of Immunology at the University of Washington, Dr Pepper continued to address how early cytokine production influenced CD4+ T cell memory formation and showed that IL-2 signaling is required for both Th1 and Th2 tissue resident memory (Trm) formation in the lung.

Her lab has also focused on determining how malaria-associated inflammation influences CD4+ T cell and B cell memory formation and has developed novel tetramers to study human and mouse cells to the same malaria antigen. Understanding key interactions between B and CD4+ T cells, and how this influences the generation of both memory populations is an ongoing focus of her lab. Most recently, she defined the role of B cell priming in the generation of Th1 Tfh/Tcm responses during malaria. Her work on both T and B cell responses provided an important foundation that allowed her to pivot to study the development of long-lasting, functional antigen-specific T and B cell responses to SARS-CoV-2 in patients with mild infections. This independent body of work illustrates Dr. Pepper's capacity to initiate meaningful projects and integrate newer technologies to perform impactful studies to understand how cytokines impact on the generation and maintenance of T (and B) cell responses in diverse biological settings.

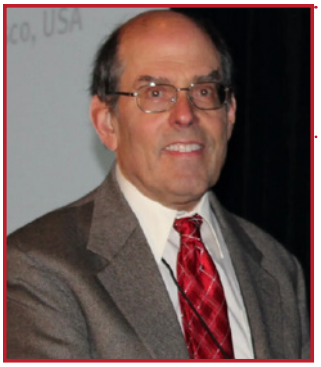
Dr. Pepper will give a talk at Cytokines 2021 Virtual Meeting in the opening session on "It's all about the cytokines", Sunday, October 17, 2021.

This award generously supported by Luminex Corporation recognizes a ***mid-career investigator*** who has made outstanding contributions to the field of interferon or cytokine biology. The awardee will receive a $5,000 cash prize that covers meeting registration, and where applicable travel support to the ICIS annual meeting for presentation of his or her research in an award lecture. The award is named after Dr. John R (Jack) Kettman, an immunologist who was instrumental in the development of Luminex's technologies and the Luminex Corporation.

Twitter: @Luminex



NEW ICIS Mentorship Award



HOWARD A. YOUNG, Ph.D.

Senior Investigator at the Center for Cancer Research, National Cancer Institute, NIH, Bethesda, USA

Dr. Howard Young has been chosen to be the first recipient of the newly established ICIS Mentorship Award in recognition of significant and sustained contributions to the career development of trainees and to the profession through outstanding mentoring over four decades. Howard has trained a number of post-docs and post-bacs who have gone on to establish their own labs around the world and who, in turn, mentored hundreds of additional trainees following the example that Howard set of promoting high-level human and scientific interactions.

Nominating Mentees:

- Professor Ram Savan, who was a post-doctoral fellow in his laboratory from 2005 – 2011 and currently is an Associate Professor of Immunology at the University of Washington in Seattle.
- Professor Elizabeth J. Kovacs, who was his first postdoctoral fellow, joining his lab in 1984. Dr. Kovacs went on to faculty positions at Loyola and is now Professor, Department of Surgery, Division of GI, Trauma & Endocrine Surgery at the University of Colorado Denver / Anschutz Medical Campus.
- Professor Antonio Sica spent 5 years as a postdoc in the Young lab at NCI-Frederick, from 1990 to 1995. He has since become the head of laboratory at the Mario Negri Institute for Pharmacological Research in Milan and later at the Humanitas and Clinical research Center, Rozzano Milan. Since 2009, he is Full Professor of General Pathology at the University of Eastern Piedmont, Novara, Italy, managing the Molecular Immunology laboratory, Humanitas and Clinical research Center, Rozzano, Milan

Dr. Young has received NCI and NIH mentorship awards for his mentorship and his leadership role in establishing the Werner H Kristen High-School Summer internship program. Dr. Werner Kristen, a previous NCI Frederick Director, started an internship program in 1989 (around 30-40 students/ year) that introduces lab science to high school seniors and which has been a tremendous success with over 1000 students having gone through the program. Howard has also significantly invested time and effort in training post-bacs, many of whom have gone onto successful careers in science and medicine.

Dr. Howard Young is a Senior Investigator in the Laboratory of Cancer Immunometabolism, Center for Cancer Research, National Cancer Institute in Frederick, MD. His research focuses on the regulation and characterization of cytokine gene expression with a special emphasis on interferons. His laboratory has developed a mouse model of chronic interferon-gamma expression that results in at least 4 different autoimmune diseases in C57 BL/6 mice, resembling lupus, myocarditis, autoimmune ovarian failure and primary biliary cholangitis with a female bias. He is also investigating therapeutic approaches to monitoring and treating these autoimmune diseases as well as identifying the basis of disease initiation and progression. Furthermore, his laboratory is studying how cancer progresses in the context of an autoimmune host background.

During his career at the NIH, Dr. Young is a 3 time recipient of the NIH outstanding mentor award and is a recipient of the mentorship award from the Center for Cancer Research Women Scientists Association. He has also twice chaired both the NIH Immunology Interest Group and Cytokine Interest Group.

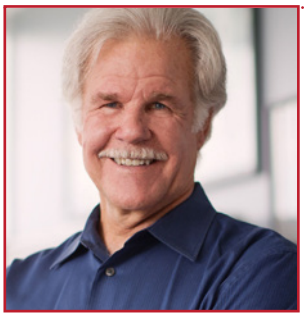
He has served on many ICIS committees, was President of the International Society for Interferon and Cytokine Research and has edited this Signals+ Newsletter (ICIS/ISICR newsletter) since its inception in 1994.

2021 ICIS AWARD WINNER

HONORARY LIFETIME MEMBERSHIP

Honorary Lifetime Membership Award

Nominations are solicited for Honorary Life Memberships in the ICIS. Each year an individual will be awarded Life Membership as a tribute to his/her contributions to the field. Nominees should be individuals who have made substantive contributions to the cytokine/ chemokine/ interferon field over much of their careers, either in basic, clinical or applied research. Honorary members are esteemed members of the Society and provide us with an historical perspective and valued research tradition.



CARL F. WARE, Ph.D.

Director, Infectious and Inflammatory Diseases Center, Professor, Laboratory of Molecular Immunology, Sanford Burnham Prebys Medical Discovery Institute, La Jolla, USA

Dr. Carl Ware is honored with the ICIS Honorary Lifetime Membership award as a tribute to his seminal and original contributions to our understanding of the role of cytokines in immunobiology and active engagement in cytokine research.

Dr. Ware's career studying cytokines began in the early 1970's at a time when the techniques we now take for granted were just being developed, and before the advent of molecular biology through his recent research directed at identifying translational opportunities in infectious, inflammatory diseases, and cancer. He identified the LIGHT-HEVEM pathway as the mechanism underlying an effective vaccine for Herpes Simplex Virus-1/2. Recently he showed that LIGHT levels are increased in COVID-19 patients progressing to pneumonia (Perlin, Safir-Levi et al, 2020) which launched a Phase 2 trial using the neutralized mAb to human LIGHT that he developed. Two other biologics created by the Ware group are for checkpoint inhibitor resistant cancers and follicular lymphoma.

Dr. Ware continues to apply his fundamental understanding of cytokine networks as a source of therapeutics for diseases without effective treatment. This was a time of ferment in the cytokine field as new supernatant biologic activities were being described at a rapid pace. This was a difficult time for many in the field, but Dr. Ware persisted, to the great benefit of the TNF field in particular, and the cytokine field in general. In later studies during a sabbatical at Biogen with Jeff Browning, he described LTβ. This molecule, when complexed with the original LTα, is a crucial contributor to the development of the lymphoid system. He went on to characterize additional members of the family including LIGHT and HVEM and solved problems that might have daunted others less tenacious with regard to the multiple interactions of the ligand receptor pairs in the expanded LT/TNF/LIGHT family. Dr. Ware has made fundamental discoveries concerning the role of the herpes virus entry mediator (HVEM), a member of the TNF receptor family. This has led to his elucidation of immune evasion mechanisms used by the various herpes viruses and provided important insight into the co-evolution of cytokine receptors and viruses. He is the holder of 6 patents and his discoveries have led to the development of novel therapeutics, namely, Baminercept, an LTbR-Fc fusion protein, and an anti-Light antibody.

Dr. Ware continues to be extremely active- as witnessed by the success of his recent grant applications, including a $3 million grant from the National Institutes of Health (NIH) to study how SARS-CoV-19 weakens the immune system–and identify drugs to help infected individuals recover, as well as his steady publication record, including a paper on ILC3 regulation of cDCs to be published this month. His expertise is sought by many institutions, including the Manchot Graduate School at the University of Dusselforf where he serves on the Scientific Advisory Board.

Carl Ware has been an outstanding member of the scientific community in general and the cytokine field in particular. He has been unfailingly generous in sharing reagents and knowledge. Among his several positions, he served with distinction as President of the International Cytokine Society, has served on the scientific advisory board of the International Congress on TNF-related cytokines for many years, and chaired the International Cytokine Society Annual Meeting in 2001 in Maui soon after 9/11 in which Dr. Ware's calm fortitude and concern were remarkable and contributed to the success of the meeting. He has also served on numerous boards and study sections including the editorial board of the Journal of Interferon and Cytokine Research from 1996 to the present. In addition to his many scientific accomplishments and service to the cytokine field, Dr. Ware has an outstanding record of mentorship with numerous successful trainees who have continued to shape the cytokine field all over the world.

2021 ICIS DISTINGUISHED SERVICE AWARD

The ICIS will on occasion bestow this honor on an ICIS member who has made an extraordinary contribution to the Society. The individual will have devoted significant time and energy over a period of years to elevating the goals of the Society in furthering research on interferon, cytokines and chemokines.

NANCY C. REICH MARSHALL, Ph.D.

Professor, Microbiology & Immunology
Stony Brook University
Stony Brook, USA
Fellow of The American Association for the Advancement of Science (AAAS)
Fellow of The American Academy of Microbiology (AAM)

Dr. Nancy Reich is honored with the ICIS Distinguished Service award in recognition of her extraordinary contributions to the cytokine research community. She has been active as a member in the ISICR and ICIS since 1987. Dr. Reich served as a member of the Meetings Committee, Awards Committee, Nominating Committee, International Council, and co-Chaired the Society annual conference in Puerto Rico 2004. Following her election as ICIS President-Elect in 2015, she Chaired a Reorganizing Committee and was responsible for streamlining the management of the organization to better serve the needs of the community. Subsequently as ICIS President, she implemented policies to further enhance the standing of the ICIS internationally, and also to ensure that members engaged in the ICIS. Dr. Reich is respected for her perspective, thoughtful input, and service. Dr. Reich has been and continues to be an invaluable member of the ICIS, engaging in Society activities and contributing in many different areas of decision making. Her research accomplishments were recognized by the Society as a 2005 recipient of the Vivian and Seymour Milstein Award for Outstanding Interferon and Cytokine Research. Dr. Reich is also a dedicated science educator and has personally guided the research training of 20 Ph.D. candidates, seeding the community with highly trained scientists.

Dr. Reich received her Ph.D. from the State University of New York in 1984 for research with the p53 tumor suppressor in the laboratory of Dr. Arnold J. Levine. She pursued postdoctoral training on interferon signaling at The Rockefeller University with Dr. James E. Darnell Jr., and continued studies on the response of cells and organisms to cytokines and interferons at Stony Brook University where she is currently Professor of Microbiology and Immunology. Her studies converged on the activation of two transcription factor families, the interferon regulatory factors (IRFs) and the signal transducers and activators of transcription (STATs). She discovered a novel cellular DNA-binding factor activated in response to dsRNA and capable of inducing interferon-stimulated genes in the absence of interferon (Daly et al. MCB, 1993). This factor was later identified as IRF-3 and plays an essential role in the early responses of cells to viral invasion (Weaver et al. MCB, 1998; Kumar et al. MCB, 2000). During this time Dr. Reich reported the requirement for tyrosine phosphorylation in the activation of interferon stimulated transcription factors later designated STAT1 and STAT2 (Gutch et al. PNAS, 1992), interleukin-4 stimulated STAT6 (Kotanides et al. Science, 1993) and interleukin-5 stimulated STAT5 (Gilmour et al PNAS, 1995). She elucidated mechanisms that regulate STAT1 nuclear trafficking dependent on conformational changes that occur subsequent to tyrosine phosphorylation, and both import and export signals were found to have co-evolved with the DNA binding domain (McBride et al. EMBO J, 2000, 2002). Her work later showed that STAT1 nuclear trafficking was distinct from other STATs. STAT3, STAT5 and STAT6 were shown to traffic in and out of the nucleus continually without phosphorylation (Liu et al. PNAS, 2005). These findings are important to conceptual approaches to enable or disable STAT transcription factors in cancer or infectious disease.

More recently Dr. Reich has contributed to our understanding of the pathology of infections and cancer using murine model systems. STAT3 was shown to be critical in promoting chronic infection and establishment of B cell latency in a model of gammaherpesvirus (Reddy et al. mBio, 2016). Viral latency is a critical medical challenge, and these results provide a potential therapeutic cellular target as well as an understanding of the molecular basis of viral latency. She also defined a fundamental and previously unrecognized function of STAT3 in the maintenance of epithelial cell identity and differentiation in cancer. Loss of STAT3 preferentially associated with the acquisition of mesenchymal-like phenotypes and more aggressive tumor behavior in mutant KRAS-initiated pancreatic cancer (D'Amico et al., G&D 2018). Immune evasion is a hallmark of KRAS-driven cancers, but the underlying causes remain unresolved. Dr. Reich's team used a murine model of pancreatic ductal adenocarcinoma to inactivate mutant KRAS by CRISPR-mediated genome editing and demonstrated that at an advanced tumor stage, dependence on KRAS for tumor growth is reduced and is manifested in the suppression of antitumor immunity (Ischenko et al. Nat Comm 2021). With the development of KRAS inhibitors, the data imply that treatment with inhibitors will require concurrent activation of immune pathways suppressed by the cancer.

2021 ICIS Young Investigator Awards

2021 REGENERON NEW INVESTIGATOR AWARDS FOR EXCELLENCE IN CYTOKINE & INTERFERON RESEARCH

Announcing the Winners of The 2021 Regeneron New Investigator Awards for Excellence in Cytokine & Interferon Research (formerly The Milstein Young Investigator Awards)

REGENERON

Rebecca C. Coll, Ph.D.
Queen's University Belfast, UK

Keke Celeste Fairfax, Ph.D.
University of Utah, Salt Lake City, USA

Fiachra Humphries, Ph.D.
UMASS Medical School, Worcester, USA

Shruti Naik, Ph.D.
NYU School of Medicine, New York, USA

Jakob von Moltke, Ph.D.
University of Washington, Seattle, USA

THE SIDNEY & JOAN PESTKA GRADUATE AWARD

Brigette Duckworth
The Walter and Eliza Hall Institute of Medical Research (WEHI), Parkville, Victoria, Australia

THE SIDNEY & JOAN PESTKA POST-GRADUATE AWARD

Ai Ing Lim, Ph.D.
National Institutes of Health, Bethesda, MD, USA

THE CHRISTINA FLEISCHMANN AWARD TO YOUNG WOMEN INVESTIGATORS

Snehlata Kumari, Ph.D.

Group Leader, Head of Inflammation and Immunity Laboratory, The University of Queensland, The University of Queensland Diamantina Institute, Translational Research Institute (TRI), Australia, UQ Webpage: https://researchers.uq.edu.au/researcher/25389
Twitter: @Sne_K
LinkedIn: https://www.linkedin.com/in/snehlatakumari/

2021 AMANDA PROUDFOOT TRIBUTE AWARD WINNER FOR ADVANCES IN CHEMOKINE BIOLOGY BY A TRAINEE

Douglas Philip Dyer, Ph.D.
Sir Henry Dale Fellow, Wellcome Centre for Cell-Matrix Research,, University of Manchester, UK
Twitter: @tripledougdyer

Full bios and pictures of the 2021 ICIS Young Investigator & Trainee Award Winners will be in the April 2022 issue of Signals and are on the Society's website.

2021 ICIS Young Investigator Awards

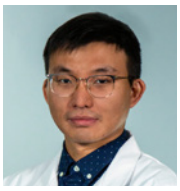
PFIZER JUNIOR INVESTIGATOR AWARD WINNERS FOR MOST PROMISING RESEARCH PRESENTATIONS AT THE CYTOKINES ANNUAL MEETING

The Pfizer Trainee Award Winners will also be invited to participate in a Pfizer symposium (physically at Pfizer Headquarters if possible AND via the ICIS virtual meeting platform on-demand within one year of the Annual Meeting), to showcase their award winning work. The symposium will also feature a networking event to introduce the award winners to associated research groups within Pfizer and expose the trainees to potential collaborations and career opportunities in industry.

These awards are sponsored by Pfizer in recognition of the next generation of cytokine & interferon researchers!

Swarna Beesetti, Ph.D.
Post-Doctoral Research Associate
St Jude Children's Research Hospital, Memphis, USA

Justina Kulikauskaite
fourth year Ph.D.
Francis Crick Institute and University College London, UK



Guanqun 'Leo' Liu, Ph.D.
Postdoc Fellow, Cleveland Clinic Florida Research and Innovation Center
Port St. Lucie, USA

Lucy Sjaastad
University of Minnesota
St Paul, Minnesota, United States

Full bios and pictures of the 2021 ICIS Young Investigator & Trainee Award Winners will be in the April 2022 issue of Signals and are on the Society's website.

"I have not failed. I've successfully discovered 10,000 things that won't work."

— Thomas Edison

NEW ICIS MEMBERS

We welcome these new members to the ICIS and we look forward to their attendance at the annual meeting and involvement in the society. The ICIS Membership Committee and Council especially thanks the Sponsoring Members and Research Advisors noted below. Special thanks to Sarah Gaffen (USA) and You-Me Kim (Korea), for sponsoring FIVE new members each! Christopher Hunter (USA) came in next with FOUR new members. As of September 21, 2021, there are **1,093 ICIS Members**; 604 Academic/Government (including 86 Lifetime Members and 47 Honorary Members); 18 Emeritus Members; 24 Industry Members and 447 Student/Postdoc Members. Over 40 countries are represented. From the USA there are 592 members; from Europe 185; from Australia 85; UK 67; Japan 39; Canada 33; Korea 20; China 14 India and Taiwan 9 each; Israel and Russia 8 each. All ICIS members have access to the online membership directory and can search out colleagues in their country, city, or by name

Reza Ahmadi
Shahrekord Universiy of Medical Sciences
Iran, Islamic Republic of
Sponsoring Member: *Kunihiro Yamaoka*

Jihong Bae
United States
Research Advisor: *You-Me Kim*

Swarna Beesetti
St Jude Children's research Hospital
United States
Research Advisor: *Douglas R Green*

Yehudi Bloch
Belgium
Research Advisor: *Savvas N. Savvides*
Sponsoring Member: *Katarzyna Skladanowska*

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United Kingdom
Research Advisor: *Dennis McGonagle*

Zarina Brune
United States
Research Advisor: *Betsy Barnes*

Tanja Bulat
Austria
Research Advisor: *Mathias Müller*

Nicole Campbell
Hudson Institute of Medical Research
Australia
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Madalina Carter Timofte
Denmark
Research Advisor & Sponsoring Member: *David Olagnier*

Orlando Cervantes
United States
Research Advisor & Sponsoring Member: *Kristina Adams Waldorf*

Ritu Chakravarti
University of Toledo
United States
Sponsoring Member: *Saurabh Chattopadhyay*

Steven Chang
Immunetrics, Inc.
United States

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TWINCORE Centre for Experimental and Clinical Infection Research
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National Institutes of Health
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Cardiff University
United Kingdom

Yeonseok Chung
Seoul National University
Republic of Korea
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Cardiff University
United Kingdom
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Leslie A Crews
University of California, San Diego
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The Francis Cricck Institute
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Chaitanya Dende
UT Southwestern
United States
Research Advisor: *Lora Hooper*

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Oklahoma Medical Research Foundation
United States

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University of Pittsburgh
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Brigette Duckworth
WEHI
Australia
Research Advisor: *Joanna Groom*

NEW ICIS MEMBERS

Continued

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University of Manchester
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Takeshi Noda

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The Francis Crick Institute
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Dominique Bonnet

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Keke Celeste Fairfax
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Katja Finsterbusch
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Ulrich Kalinke

Elizabeth Geerling
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Stephanie Gomez
The George Washington University
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Oklahoma Medical Research Foundation
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Basaksehir, Internal Medicine Department
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Lucy Helen Jackson-Jones
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United States

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Jong Hoon Kim
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Venkatesh Gary Krishnan
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Republic of Korea

Sang-il Lee
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Republic of Korea
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You-Me Kim

Won-Woo Lee
Seoul National University College of Medicine
Republic of Korea
Sponsoring Member:
You-Me Kim

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Su-Hyung Park
Republic of Korea

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Ruhr University Bochum
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Margarida Ribeiro
CIRI INSERM
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Marlene Dreux

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William McEwan

Savvas Savvides
Ghent University
Belgium

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Peter Stäheli

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University
United States

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Michael Walsh
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David Knipe

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Seth Coffelt

Huilin Yang
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Research Advisor:
Jamie Spangler

Xiaobao Yang
United States
Research Advisor:
Dakang Xu

Olha Yaroshko
institute of cell biology and
genetic engineering NAS of
Ukraine
Ukraine
Research Advisor:
Mykola Kuchuk

Ya-Ru Yu
Taiwan
Research Advisor & Sponsoring
Member: *Chien-Kuo Lee*

David Zander
German Cancer Research
Center (DKFZ)
Germany
Research Advisor:
Marco Binder

Lei Zhou
United States
Research Advisor:
Gregory Sonnenberg

New Member MINIBIOs

Tanja Bulat, Ph.D.
Institute of Animal Breeding and Genetics
University of Veterinary Medicine Vienna
Vienna, Austria

Dr. Tanja Bulat is a postdoctoral fellow at the Institute of Animal Breeding and Genetics, Veterinary University of Vienna, Austria, in the group of Univ. Prof. Dr. Mathias Müller. In 2013 she started working in the field of functional proteomics at the Medical University of Vienna and University of Vienna. In July 2017, she defended her Ph.D. and in September joined Prof. Müller's lab as a PostDoc in the highly competitive Infect-ERA project, focusing on the role of STAT1 signalling in myeloid cells during murine cytomegalovirus infection. Recently she was named as co-author of the stand-alone project funded by The Austrian Science Fund. Tanja's primary research focus is STAT1 signalling in splenic macrophages in infection-induced extramedullary haematopoiesis (EMH).

Nicole Campbell, Ph.D.
Postdoctoral Scientist
Centre for Innate Immunity and Infectious Diseases
Hudson Institute of Medical Research
Clayton Australia

Dr. Nicole Campbell completed her Ph.D. in Immunology under the supervision of Dr. Aisling Dunne at Trinity College Dublin (Ireland) in 2018. Her Ph.D. research focused on the anti-inflammatory functions of the enzyme heme oxygenase 1 (HO-1), through which she published one of the first characterisations of human dendritic cell immunometabolism, and identified a novel relationship between metabolic signalling and immunoregulation via HO-1. In January 2019 she commenced a postdoctoral research position with Prof Paul Hertzog at the Hudson Institute of Medical Research in Melbourne, Australia. Her current research is centered on interferon epsilon; a unique type I interferon discovered by Prof Hertzog's lab, which is constitutively expressed under hormonal control in the female reproductive tract. Dr. Campbell leads efforts within Prof Hertzog's lab to characterise the anti-tumour potential of interferon epsilon, and its immunoregulatory role within the peritoneal cavity.

Orlando Cervantes
University of Washington, Seattle, United States

I cultivated an interest in emerging infectious diseases of global health importance while conducting research in my time as an undergraduate. I started my research career in the laboratory of Dr. Rebecca Rico-Hesse at Baylor College of Medicine (BCM) studying the effect viral glycosylation has on the pathogenesis of Zika virus. I continued to diversify my research background in the laboratory of Dr. Job Lopez by developing a senior honors thesis project characterizing operons of Borrelia turicatae. Both of these research experiences led to presentation opportunities at local research symposiums. By the end of my undergraduate studies, I was resolute in my intention to pursue my doctorate degree. Now after my first year of doctoral studies, I have committed to conducting my dissertation research under the mentorship of Dr. Kristina Adams Waldorf, investigating the effects of emerging viruses on maternal-fetal health. Currently, I am working with her to assemble a National Institutes of Health diversity grant supplement that focuses on the innate immune response to pandemic influenza infection at the maternal-fetal interface. As part of that, I expect to make contributions to our understanding of cytokine signaling in the placenta and lungs and how downstream effects of cytokine activation impact the offspring.

New Member MINIBIOs *Continued*

Leslie A. Crews, Ph.D.
Assistant Professor of Medicine
Division of Regenerative Medicine and Moores Cancer Center
University of California, San Diego
La Jolla, USA
http://crewslab.ucsd.edu

Dr. Leslie Crews is an Assistant Professor of Medicine at UC San Diego with a passion for stem cell biology and translational cancer research. She received her bachelor's degree from UCLA and a Ph.D. in Molecular Pathology from UCSD. She recently started her independent laboratory in the Division of Regenerative Medicine, also at UCSD. Dr. Crews's research interests focus on understanding the molecular mechanisms that cause adult stem cells to behave abnormally in age-related and malignant disorders. She has investigated this topic across diverse fields of study, from the brain to the blood, and has co-authored over 65 peer-reviewed research articles in these areas. She has recently identified vital inflammation-responsive and interferon-regulatory genes that drive stem cell pathway activation and malignant regeneration in multiple myeloma, the second most common blood cancer in the world. In 2017, Dr. Crews and her collaborators discovered that the interferon-responsive RNA editing gene ADAR1 is hyper-activated in myeloma and that this molecule coordinates with IL-6 receptor activation and IL-6 signal transduction to promote disease progression and drug resistance. More recently, her laboratory helped identify a lead antisense oligonucleotide-based therapeutic candidate targeting human IRF4 (an interferon-regulatory gene and key B cell transcription factor), which is now in clinical trials for patients with relapsed/refractory multiple myeloma. Her team further demonstrated that selective inhibition of IRF4 blocks malignant regeneration in high-risk models of the disease. Her work has been supported by the International Myeloma Foundation, the Multiple Myeloma Research Foundation, the San Diego Foundation, and the National Cancer Institute. Dr. Crews is also a past recipient of the Lund Stem Cell Center Award for Conceptual Advance in the field of Stem Cell Biology. In addition, she is a long-time member of the Association for Women in Science and is an active supporter and mentor of women and other underrepresented individuals advancing careers in STEM fields. Her ongoing work aims to delve deeper into the role of inflammation-responsive transcriptional regulators of multiple myeloma initiation and progression, with the goal of identifying novel, more selective therapies to treat individuals with this fatal disease.

Brigette Duckworth
Ph.D. Candidate,
Walter and Eliza Hall Institute of Medical Research
Parkville Australia
Twitter: @BrigDoesScience

Brigette is a third year Ph.D. student in the lab of Dr Joanna Groom at the Walter and Eliza Hall Institute of Medical Research (WEHI), Australia. Her research employs cutting-edge light-sheet microscopy to reveal the spatial determinants of T cell fate decisions within lymph nodes. Her recent work has demonstrated that T cell fate is imprinted in distinct lymph node niches following viral infection, directed by the chemokine receptor CXCR3. Specifically, CXCR3 directs effector differentiation in the lymph node periphery, while in the absence of CXCR3, T cells remain confined to the lymph node centre and alternatively differentiate into stem-like memory precursors (Duckworth et al. Nature Immunology 2021). These findings have important implications for understanding the establishment and maintenance of immune memory.

Brigette completed a Bachelor of Biomedicine Degree with Honours at the University of Melbourne, Australia in 2016. During her undergraduate degree, she undertook a research placement at WEHI under the supervision of Professor Gabrielle Belz and Dr Lisa Mielke, studying the transcriptional regulation of T cell differentiation. Brigette continued her Honours-level research with Professor Belz, studying the clonal regulation of memory T cell fate. She worked as a research assistant for two years before commencing her Ph.D. studies in 2019. Brigette's work has been recognized by the David McFarlane Ph.D. Award (2020) and a Rotary Club of Melbourne Victorian Young Achievers Award (2018).

New Member MINIBIOs *Continued*

Douglas Philip Dyer, Ph.D.
Sir Henry Dale Fellow
Wellcome Centre for Cell-Matrix Research, University of Manchester, UK
Twitter: @tripledougdyer

Dr. Dyer undertook his Ph.D. research investigating how an anti-inflammatory protein functions by disrupting the interactions between chemokines and their extracellular matrix glycosaminoglycan binding partners. Supervised by Prof. Anthony Day, Dr. Caroline Milner and Dr. Amanda Proudfoot.

Dr. Dyer then went on to focus on the biological importance of chemokine: GAG interactions in leukocyte migration during his postdoc in the lab of Prof. Tracy Handel. During this time, he and his colleagues demonstrated that chemokines have strikingly different interactions with GAGs according to their oligomerisation potential. A collaboration with Dr. Ralf Richter's group then described how chemokines can re-structure these GAG chains, proposing a new mechanism underlying chemokine function.

During his second postdoc, with Prof. Gerry Graham, Dr. Dyer focused on the biological role of the chemokine receptors CXCR2, CCR1, CCR2, CCR3 and CCR5 and was part of the team that demonstrated their specificity of function during leukocyte recruitment.

Dr. Dyer is now a Wellcome Trust and Royal Society funded Sir Henry Dale fellow leading a group at the University of Manchester exploring the collaboration and biological importance of chemokines and the glycocalyx.

Hector Huerga Encabo, Ph.D.
Post-doctoral Fellow
Haematopoietic Stem Cell Laboratory
The Francis Crick Institute
London, United Kingdom
Twitter: @DrHHEncabo and @TReNDinAfrica

Postdoctoral Fellow at The Francis Crick Institute (London, UK), he received the Kay Kendall Leukemia fellowship to develop his research in the Haematopoietic Stem Cell laboratory led by Dominique Bonnet.

Hector performed his Ph.D. in the Immunology group of Pompeu Fabra University (UPF) located at the PRBB (Barcelona) led by Dr. Cristina López-Rodríguez (2013-2018). During his Ph.D., he obtained a fellowship from the Spanish Ministry of Science to study how innate immune cells work in homeostasis and sense and respond to pathogens. Specifically, he characterised a new mechanism that limits type I interferon (IFN-I) and the antiviral response in innate immune cells. For his Ph.D. thesis, Hector received the Doctoral School Ph.D. Extraordinary Award for the academic year 2018-2019 at UPF.

Dr. Encabo is focused on the development of the FlowAfrica initiative, a collaborative project that he leads within the non-profit organisation TReND (https://trendinafrica.org/flowafrica/). The objective of this project is to bring Flow Cytometry to research institutes in Africa, who struggle to have access to this expensive equipment, by setting new flow cytometry facilities and providing access to online training.

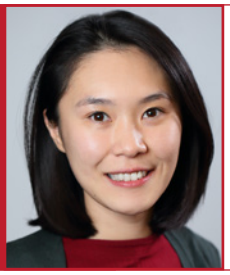
Mehmet Hursitoglu
Basaksehir Cam and Sakura Sehir Hospital
Basaksehir, Internal Medicine Department
Istanbul, Turkey

I am Professor of Internal Medicine at Basaksehir Cam and Sakura Sehir Hospital, University of Health Sciences, Istsnbul, Turkey. I am also member of EASD. I have graduated from Erbil Medical Faculty at Iraq. Thrn, completed my postgraduate study at Istanbul Medicsl Faculty. Now I am in the position of Professor st Internal Medicine at the biggest teaching Hospital of Istanbul. Beside dealing with the teaching of the students and postgraduate students, I am a part and head of a team that conducts basic and clinical studies in different diseases.

New Member MINIBIOs *Continued*

Keke Celeste Fairfax, Ph.D.
Assistant Professor and Director of Diversity, Equity, and Inclusion
Department of Pathology
Division of Microbiology and Immunology
University of Utah
Salt Lake City, USA
Twitter: @LabFairfax
https://medicine.utah.edu/pathology/research/labs/keke-fairfax/

Keke Fairfax received her Ph.D. from Yale in Microbial Pathogenesis in 2009. Her dissertation work focused on identifying novel fatty acid binding proteins in the human hookworm *Ancylostoma ceylanicum*. She completed her post-doctoral training in Schistosoma mansoni immuno-parasitology with Edward Pearce and Gwendalyn Randolph in 2014. Dr. Fairfax began her independent laboratory at Purdue University in 2014 and moved to the University of Utah in 2018. The Fairfax laboratory at the University of Utah broadly focuses on using the helminth parasite *Schistosoma mansoni* as a tool to understand both, the relative contributions of schistosome antigen vs IL-4 in inducing host immuno-modulation, and the complex interplay between lymphoid and stromal cells necessary to develop an optimal T and B cell memory response. Under this umbrella we currently have three main projects: 1) Understanding the immunological implications of maternal schistosomiasis; 2) Dissecting the role of IL-4 in shaping the cellular environment of peripheral lymph nodes during homeostasis and antigenic challenge; 3) Delineating the mechanistic role of antigen driven immunological re-programing in helminth-induced protection from metabolic diseases.



Ai Ing Lim, Ph.D.
Postdoctoral Research Fellow
Metaorganism Immunity Section, Laboratory of Host Immunity and Microbiome
National Institute of Allergy and Infectious Diseases
National Institutes of Health, Bethesda, USA
Twitter: @AiingLim

I view science as an adventure into the unknown. How a single cell divides and differentiates into specialized tissues and organs, constituting a whole organism, is a seminal scientific question that has always fascinated me. Specifically, I have always been intrigued by how a single hematopoietic stem cell can produce diverse immune cells with distinct functions that coordinate to optimally respond to the multitude of infectious and environmental challenges encountered by the host. Despite growing up in Malaysia, where scientific careers were rare for women, I have been determined to pursue my passion to become a scientist and uncover the hidden mysteries of developmental immunology. With the support of several scholarships, I moved to Hong Kong for my bachelor's and master's degrees at The University of Hong Kong. Subsequently, as a European Union Marie Curie Fellow, I joined Prof. James Di Santo at Pasteur Institute (France) for my Ph.D. There, we identified innate lymphocyte precursor from blood of healthy individuals. This precursor can give rise to diverse mature innate lymphocytes within tissues, depending on micro-environmental signals. We defined a cytokines milieu that supports human ILC-poiesis. This finding was pivotal because it challenged the prevailing dogma stating that the fetal liver and adult bone marrow were the sources of this unique precursor. It also sparked my interest in tissue immunity, where I am eager to understand, mechanistically, how immune cells integrate with tissue development, and how tissue micro-environments and resident microbiota reciprocally wire immune function. A critical boost to my scientific career was being recognized as an International Rising Talents by the L'Oreal-UNESCO and the best European Immunology Thesis (Acteria Doctoral Prize) by European Federation of Immunological Societies. These awards together with Human Frontier Science Program fellowship empowered me to join the laboratory of Dr. Yasmine Belkaid at National Institutes of Health (NIH) for my postdoctoral training. The central question that I attempt to address is how do maternal environmental exposures impact on offspring tissue immunity and predisposition to diseases. We recently discovered that a maternally restricted infection can have permanent and tissue-specific impacts on offspring intestinal immunity. This impact was dominantly mediated by a single cytokine, IL-6 acting on epithelial stem cells during fetal development. While this phenomenon can be co-opted by the fetus to develop optimal immune fitness, altered offspring immunity imposed by maternal infection comes at the cost of enhanced susceptibility to mucosal inflammation.

New Member MINIBIOs *Continued*

Michail Lionakis, MD, Sc.D.
Chief, Fungal Pathogenesis Section
Deputy Chief, Laboratory of Clinical Immunology and Microbiology, National Institute of Allergy and Infectious Disease, National Institutes of Health
Twitter: @LionakisLab
https://www.niaid.nih.gov/research/michail-s-lionakis-md-scd

Dr. Lionakis is a physician-scientist and Head of the Fungal Pathogenesis Section in NIAID's Laboratory of Clinical Immunology and Microbiology where he is Deputy Chief. He obtained his MD and Sc.D. degrees from the University of Crete, Greece. He did postdoctoral research training at MD Anderson Cancer Center, Houston, followed by Internal Medicine Residency at Baylor College of Medicine, Houston, and Infectious Disease Fellowship at NIAID/NIH. Following research training at NIAID related to how chemotactic factors regulate the innate immune response in invasive candidiasis, he established his own laboratory in 2012 at NIAID and received tenure in 2017.

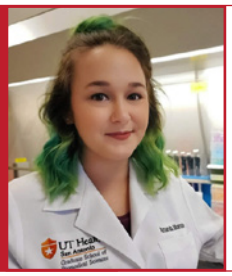
Dr. Lionakis' laboratory research focuses on 1) better understanding the genetic and immune defects that underlie enhanced susceptibility to fungal infections in humans and on 2) cellular and molecular factors that regulate the immune response against mucosal and systemic fungal infections in clinically relevant animal models. Thus far, his work has defined precise genetic, biochemical, immunologic, and cellular disease mechanisms that have led to targeted immunotherapies. He has identified interferonopathy as a critical driver of mucosal candidiasis in patients with APECED and has identified local neutropenia due to impaired microglial-neutrophil crosstalk as a critical driver of central nervous system-targeted candidiasis in patients with CARD9 deficiency. He has delineated novel inherited (CARD9 immunodeficiency, STAT3 haploinsufficiency, and ISG15 deficiency) and acquired (BTK inhibitors) immunodeficiency states that increase invasive mold infection susceptibility.

Dr. Lionakis has published >170 peer-reviewed papers in journals such as Science, *Science Translational Medicine, Science Immunology, Nature Immunology, JCI, JCI Insight, Journal of Experimental Medicine, Cell Host Microbe, Cancer Cell,* and others. He has served in the editorial boards of *JCI Insight, Journal of Infectious Diseases, Antimicrobial Agents & Chemotherapy, Infection & Immunity, F1000*, among others. He is a Member of the American Society for Clinical Investigation, a Fellow of the American Academy of Microbiology, and a Fellow of the Infectious Diseases Society of America. He has received several awards (detailed list below) including the NIH Director's award, the Junior Investigator Award from the Immunocompromised Host Society, the American College of Physicians Walter J. McDonald Award for Early Career Physicians, and the IDSA Investigator Award.

GuanQun 'Leo' Liu, Ph.D.
Postdoc Fellow
Cleveland Clinic Florida Research and Innovation Center
Port St. Lucie, USA
Twitter: @leonardliu88

Dr. GuanQun 'Leo' Liu is a postdoctoral fellow in the laboratory of Prof. Michaela Gack at the Cleveland Clinic Florida Research and Innovation Center. He was trained as a molecular virologist with extensive research experience in innate immune sensing of viral infections and type I interferon-mediated antiviral immunity. During his Ph.D. training at the University of Saskatchewan in Canada, he identified and characterized a series of viral RNA ligands produced from influenza A virus infection that are key to the activation of the innate immune RNA sensor, retinoic acid-inducible gene I (RIG-I). He also identified nuclear-resident RIG-I that senses nuclear-replicating viruses and induces antiviral cytokine responses, which provides the first evidence of a non-self RNA sensing paradigm in the nucleus, a previously unrecognized subcellular milieu for RIG-I-like receptor (RLR) sensing. Leo's postdoctoral training with Dr. Gack has extended his research scope to the regulation of antiviral innate immunity with an emphasis on the post-translational control of RLR activation. He recently identified ISGylation as an essential post-translational modification responsible for the activation of the RNA sensor melanoma differentiation-associated protein 5 (MDA5), and unraveled how SARS coronaviruses, by antagonizing this mechanism, evade the MDA5-mediated antiviral cytokine response. As an enthusiastic and highly motivated researcher driven by scientific unknowns, his long-term research goal is to develop a comprehensive understanding of the mechanistic relationships between cellular compartmentalization and the regulation of innate immune sensing and cytokine responses during viral infections and in autoimmune diseases. Leo's work has been recognized in the 2018 Young Innovators series by the University of Saskatchewan Research Profile and Impact office in partnership with the Saskatoon StarPhoenix.

New Member MINIBIOs *Continued*



Amanda Rae Mannino, MLS(ASCP)^{CM}
Ph.D. Candidate and Graduate Research Assistant
UT Health San Antonio
San Antonio, USA

Amanda Mannino's research focuses on simian immunodeficiency virus, the nonhuman primate (NHP) analog of HIV, and its restriction in baboons. The mechanisms underlying baboon's natural immunity against SIV remain unknown. Understanding the mechanisms behind some individual's ability to control human immunodeficiency virus (HIV) infections without the assistance of antiretroviral therapy could be the key that unlocks a functional cure for this debilitating disease. This select group, known as elite controllers (EC), are a heterogeneous population. An animal model for investigating EC's innate immunity against immunodeficiency virus would be invaluable to the scientific community. Her aim is to characterize baboon as a model organism for innate immunity against SIV and developing baboons as a model for EC. For her dissertation, she has developed a two-pronged approach to investigate this unique host-pathogen interaction, including investigating both host response to viral challenge, as well as viral adaptation to baboon's inherent selective pressures. Additionally, during the height of the COVID-19 pandemic, she investigated the immune responses of different NHP to SARS-CoV-2 infection, and along with her colleagues, published their work characterizing these NHP as animal models for COVID-19 pathology.

Jakob von Moltke, Ph.D.
Assistant Professor
University of Washington
Department of Immunology
Seattle, USA
Twitter: @jakob_moltke

Dr. von Moltke is an Assistant Professor in the Immunology Department at the University of Washington Medical School in Seattle. Dr. von Moltke graduated with a Bachelor's degree in Genetics, Cell and Developmental Biology from Dartmouth College and a Masters of Arts in Biotechnology from Columbia University. For his Ph.D., he studied sensing of bacteria by inflammasomes with Dr. Russell Vance at the University of California, Berkeley. Dr. von Moltke completed his postdoctoral training with Dr. Richard Locksley at the University of California, San Francisco, where he investigated early type 2 immune responses and discovered a role for epithelial tuft cells in initiation of intestinal helminth infection. The Moltke Lab continues to study immune responses to parasitic worms and allergens, with a current focus on the immune sensing and effector functions of tuft cells. Dr. von Moltke was selected as a Searle Scholar and recipient of a Burroughs Wellcome Award for Investigators in Pathogenesis of Infectious Disease.

Olha Yaroshko
Ph.D. Candidate and Graduate Research Assistant
Institute of Cell Biology and Genetic Engineering NAS of Ukraine
Kyiv, Ukraine

Olga Yaroshko is a Ph.D. student in Biotechnology at the Institute of Cell biology and Genetic Engineering, NAS, in Kyiv, Ukraine. The theme of her Ph.D. thesis is "Development of biotechnological approaches to the genus Amaranthus L." She is engaged in genetic engineering of plants and they have chosen amaranth as the subject of the research, due to its usefulness in food, medicine, cosmetics, agriculture. The aim of the work is to develop the conditions for obtaining recombinant proteins of human interferon (INF☙β) in plants of *Amaranthus caudatus* L., which can be used as a "plant-based vaccine". Industrially synthesized interferon is used to treat viral infections and various types of tumors.

Genetic engineering of plants for the purpose of obtaining medicinal substances is a promising direction in science. For example, in Ukraine there are national programs dealing with the development of "plant vaccines".

MEMBERS IN THE NEWS

Two ICIS Lifetime Members, **Warren J. Leonard** and **John J. O'Shea**, awarded the **2021 Harrington Prize for Innovation in Medicine** for their Contributions to the Field of Immunology, from Fundamental Discovery to Therapeutic Impact

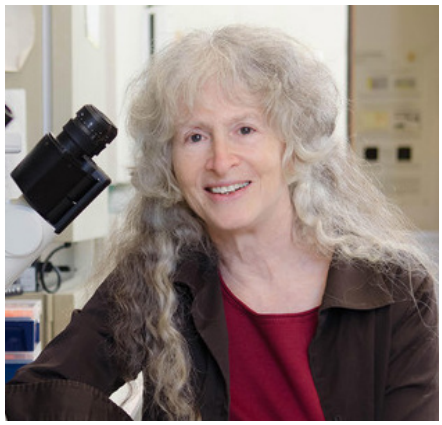
Dr. Warren J. Leonard

Dr. John J. O'Shea

Three ICIS Members elected to the **National Academy of Sciences** for their contributions to epidemiology, innate immunity and immunology – Congratulations!

Ralph S. Baric, William R. Kenan Jr. Distinguished Professor, Department of Epidemiology, and Professor, Department of Microbiology and Immunology, University of North Carolina, Chapel Hill, for his contributions to epidemiology

Katherine A. Fitzgerald, (ICIS President) Professor, Department of Medicine, and Worcester Foundation for Biomedical Research Chair, University of Massachusetts Medical School, Worcester, for her contributions to innate immunity.



Ellen V. Rothenberg, Distinguised Professor, Division of Biology and Biological Engineering, California Institute of Technology, Pasadena, for her contributions to immunology.

Emerging Roles of Type III Interferons in COVID-19, Gut Microbiome, Adaptive Immunity, and Anti-Fungal Immunity

The symposium started with a brief overview of type III IFNs by Sergei Kotenko, Rutgers University. He covered discoveries leading to the identification of this cytokine family and their receptor complex, introduced individual members of the IFN-lambda family, described the basic biology of type III IFNs, and reviewed their known functions. He presented differences between type I and type III IFN-based antiviral systems, emphasizing that type III IFNs are now well recognized for their important and indispensable role in protecting epithelial barriers against diverse viral pathogens. He also accentuated that since their discovery in 2003 and 2013, novel functions of IFN lambdas continue to be discovered, affecting diverse aspects of host immunity and homeostasis in health and disease, including various infections, cancer and autoimmune conditions. He briefly introduced the speakers and their presentation topics covering the role of type III IFNs in the gastrointestinal virus interaction with intestinal microbiota, antifungal immunity, adaptive immunity, tissue inflammation and integrity, and in COVID-19. Following the presentations, all speakers had an engaging Q&A session and answered questions and comments submitted through the chat.

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Guest ICIS Symposium at virtual AAI meeting IMMUNOLOGY2021, May 13, 2021

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The symposium included the following presentations.

Kristin Hogquist, University of Minnesota, "Distinct roles for type I and III interferons in thymic selection".

We understand how the thymus achieves tolerance to tissue-restricted antigens through the action of a critical transcription regulator, AIRE. But how it achieves tolerance to temporal antigens, particularly those displayed during infections, is not understood. Here we showed that the thymus produces both type I and III IFNs at a steady state. These cytokines are produced primarily by medullary epithelial cells, particularly the MHC-ClassII/CD80 expressing "mTEChi" cells, and their expression in mTEChi cells is AIRE dependent. Using Mx1GFP reporter mice, RNAseq, and single-cell RNAseq in mice lacking Ifnar1, Ifnlr, both, or Stat1, we showed that multiple thymic APC types respond to type I and III IFNs, causing changes in antigen processing and presentation in addition to the expressed transcriptome. Thymocytes were sensitive only to type I IFN. B cells, in contrast, depended exclusively on type III IFNs for their activation and class switch properties. Using deep sequencing of expressed TCRS in WT and Ifnar1-/- mice, we showed that IFN profoundly impacts the T cell repertoire, changing approximately 2% of the conventional CD4 T cell repertoire and 10% of the Treg cell repertoire.

Megan Baldridge, Washington University Medical School, "Restriction of intestinal viral cellular tropism by IFN-lambda".

IFN-lambda (IFN-λ) has been shown to mediate powerful antiviral effects in the intestine, playing important roles in controlling multiple enteric RNA viruses which infect intestinal epithelial cells. Persistent murine norovirus (MNoV) is sensitive to exogenous IFN-λ treatment, which acts via the IFN-λ receptor expressed on epithelial cells. Genetic disruption of either the receptor or IFN-λ cytokines permits enhanced viral replication of MNoV, and we have found that IFN-λ substantially restricts the cellular tropism of MNoV within the epithelium, with a 10-fold increase in infected permissive cells when IFN-λ signaling is disrupted, though the specific cell type infected (tuft cells) is unchanged. Importantly, MNoV has evolved mechanisms to evade IFN-λ signaling, specifically via secretion of a non-structural viral protein, which permits it to establish persistent infection in the epithelium. Despite differences in cellular tropism, we have observed similar effects of IFN-λ in regulating chronic murine astrovirus (muAstV) infection. Chronic muAstV infection in immunocompromised mice dramatically upregulates IFN-λ signaling, which in turn is important for limiting both infection by other viruses as well as controlling levels of muAstV itself. Again, while single-cell RNAseq has recently revealed that the general cell type(s) infected remain unchanged (goblet cells and enterocytes) when IFN-λ signaling is disrupted, a dramatic increase in the number of muAstV-infected cells is observed. Thus, in lieu of controlling the amount of virus produced within individual infected cells, IFN-λ serves to limit the number of infected cells in the intestinal epithelium to control multiple chronic enteric viral infections.

Amariliz Rivera, Rutgers-New Jersey Medical School, "Novel insights on IFN-lambda and the activation of innate antifungal immunity".

Our studies have uncovered a novel role for type III IFN as the regulator of the antifungal response of neutrophils. We found that type I and III IFNs are both produced in response to pulmonary infection with the clinically important fungal pathogen *Aspergillus fumigatus* (*Af*). Production of type I IFN is very rapid and transient, while type III IFN is produced with delayed but sustained kinetics. IFN-I is best appreciated as a potent antiviral cytokine and several innate receptors are known to be involved in recognition of viral-derived nucleic acids to trigger its production. In the current study, we set out to examine pathways that may be involved in the production of type I and III IFNs in response to infection with *Af*. We determined that dectin-1-mediated recognition of *Af*-derived b-glucans is involved in the activation of type I and III IFNs. Dectin-$1^{-/-}$ mice had diminished production of both IFNs and succumbed to infection with *Af*-CEA10. Importantly, administration of recombinant type I and III IFNs to dectin-$1^{-/-}$ animals was able to significantly improve antifungal neutrophil responses and global control of infection (1). These findings suggest that dectin-1 promotes effective antifungal immunity at least in part by inducing optimal production of type I and III IFNs. In collaborative studies with Josh Obar's laboratory, we further determined that the MDA5/MAVS pathway is also involved in the optimal production of IFN-I in response to infection with *Af*. Altogether, our studies suggest that IFN production in response to fungal infection is coordinated by early detection of b-glucan by dectin-1 followed by nucleic acid sensing by the MDA5/MAVS pathway. Some of the exciting questions for further study include the mechanism by which fungal RNA becomes accessible to the cytosol as well as what are the relevant cellular sources of IFN-I during infection with *Af*.

Ivan Zanoni, Harvard Medical School, Boston Children's Hospital, "Impact and regulation of type III interferon production in COVID-19".

The SARS-CoV-2 pandemic raised an unprecedented flux of studies aimed at unraveling the molecular mechanisms that determine severe COVID-19 and at identifying new therapies. Among available therapeutic options, the use of clinical-grade type I (IFN-I) or type III (IFN-III) families raised great hope and interest. IFN-III is particularly relevant, as it is notable for inducing an antiviral state while simultaneously limiting inflammation-driven tissue damage. Recombinant IFNs have been used in several COVID-19 clinical trials, leading, though, to somewhat inconclusive results. Our group recently demonstrated that, in a mouse model that mimics a viral infection, prolonged IFN-III production causes tissue damage and decreases the effectiveness of the lung barrier.

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Guest ICIS Symposium at virtual AAI meeting IMMUNOLOGY2021, May 13, 2021

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But are IFNs produced in COVID-19 patients? And are they good or bad? We recently collected new data from over 150 COVID-19 patients stratified by age and viral load. By analyzing gene and protein expression in the lower or upper airways, we revealed a complex picture that suggests IFN-III play opposing roles at distinct anatomical sites. Our data give a potent mandate to take into account the timing and localization of IFN-III production to explain their effectiveness in protecting against SARS-CoV-2.

Ludmila Prokunina-Olsson, National Cancer Institute, "Human genetics analysis identifies type III interferon-related biological mechanisms and treatments for COVID-19 and beyond".

Variable response to SARS-CoV-2 infection suggests that host genetic factors might mediate this response and clinical severity of COVID-19 ranging from mild to fatal disease. Efforts of the COVID-19 Host Genetics Initiative (HGI), which compared infected individuals with the general population, reported 13 genome-wide significant loci harboring genes that might contribute to this differential immune response. Several of these loci include genes potentially involved in interferon signaling. We are performing a detailed genetic analysis of one of these genetic loci, which includes known antiviral genes OAS1 and OAS3 encoded on chromosome 12. In contrast to HGI efforts, our study is limited to patients. Specifically, our initial analysis is based on 1555 patients of European ancestry, including 566 patients with mild and 954 patients with hospitalized COVID-19. We also analyzed the results of a clinical trial for outpatient COVID-19 in relation to genetic variants within the OAS1/OAS3 region. We demonstrated that both COVID-19 severity and the rate of clearance of SARS-COV-2 are dependent on the haplotypes of several OAS1 genetic variants that define the level of expression of OAS1 mRNA and its protection from nonsense-mediated decay (NMD). The rate of viral clearance after treatment with pegIFNλ1 was not associated with OAS1 genetic variants suggesting that early IFN treatment overcomes genetic deficiencies underlying impaired viral clearance. We also explored the association between genetic variants within the IFNL3/IFNL4 region with the same outcomes but did not observe any association. This analysis is now being expanded to include more patients.

ICR is The Institute for Cancer Research and the image shows tertiary lymphoid structures in sarcoma triggering an immune response.

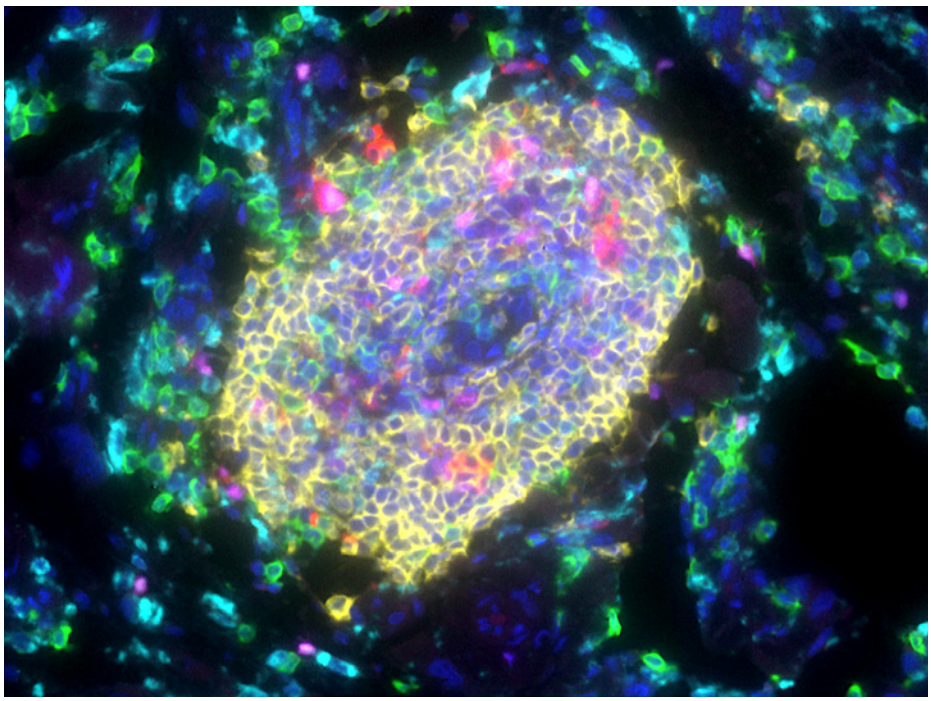
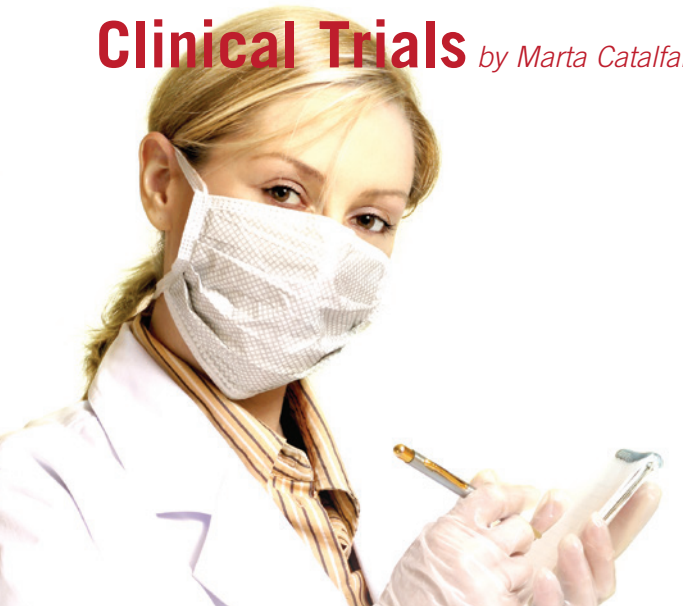


Image by David Mansfield,The Institute of Cancer Research (ICR): Royal Cancer Hospital, a charitable Company Limited by Guarantee, Registered in England under Company No. 534147 with its Registered Office at 123 Old Brompton Road, London SW7 3RP.

Clinical Trials *by Marta Catalfamo*



Rintatolimod and IFN Alpha-2b for the Treatment of COVID-19 in Cancer Patients
Principal Investigators: Brahm H Sega, MD. Roswell Park Cancer Institute. Buffalo, New York, United States, 14263
Contact: Brahm H. Segal, MD, Phone: +1-716-845-5721
ClinicalTrials.gov Identifier: NCT04379518

Peginterferon Lambda-1a for the Prevention and Treatment of SARS-CoV-2 (COVID-19) Infection (PROTECT)
Principal Investigators: Mark Sulkowski, MD. Johns Hopkins Hospital. Baltimore, Maryland, United States, 21287
Contact: Mark Sulkowski, MD., Phone: +1 410-955-7538
ClinicalTrials.gov Identifier: NCT04344600

Early Treatment of Cytokine Storm Syndrome in Covid-19
Principal Investigators: Walter W Chatham, MD. University of Alabama at Birmingham. Birmingham, Alabama, United States, 35294
Contact: Angelia Kendrach, Phone: +1-205-996-5602
ClinicalTrials.gov Identifier: NCT04362111

InterLeukin-7 to Improve Clinical Outcomes in Lymphopenic Patients With COVID-19 Infection (ILIAD-7-US-0) (ILIAD-7-US-0)
Principal Investigators: Marcel van den Brink, MD, PhD and Stephen Pastores, MD. Memorial pSloan Kettering Cancer Center. New York, New York, United States, 10065
Contact: Stephen Pastores, MD., Phone:+1 212-639-6673
ClinicalTrials.gov Identifier: NCT04426201

Study to Evaluate the Role of Siltuximab in Treatment of Cytokine Release Syndrome (CRS) and Immune Effector Cell Associated Neurotoxicity (ICANS) Related to CAR-T Cell Therapy
Principal Investigators: Mayur S Narkhede, MD. University of Alabama at Birmingham. Birmingham, Alabama, United States, 35294
Contact: Mayur Narkhede, Phone: +1-205-934-2248
ClinicalTrials.gov Identifier: NCT04975555

Safety and Efficacy of Interferon-Gamma 1b in Patients With Candidemia
Principal Investigators: Dr. Frank vd Veerdonk. Radboud University. Nijmegen, Gelderland, Netherlands, 6525 GA
Contact: Dr. Frank vd Veerdonk, Phone: 0031243618819
ClinicalTrials.gov Identifier: NCT04979052

Reducing the Residual Reservoir of HIV-1 Infected Cells in Patients Receiving Antiretroviral Therapy (ACTIVATE)
Principal Investigators: Mathias Lichterfeld, MD, PhD. Massachusetts General Hospital CRS (MGH CRS). Boston, Massachusetts, United States, 02114
Contact: Theresa Flynn, R.N., M.S.N., A.N.P, B.S.N, Phone: +1(617) 724-0072
ClinicalTrials.gov Identifier: NCT02471430

Modified Virus VSV-IFNbetaTYRP1 in Treating Patients With Stage III-IV Melanoma
Principal Investigators: Roxana S Dronca, MD. Mayo Clinic in Florida, Jacksonville, Florida, United States, 32224-9980
Contact: Roxana S Dronca, MD, Phone: +1 855-776-0015
ClinicalTrials.gov Identifier: NCT03865212

Virotherapy and Natural History Study of KHSV-Associated Multricentric Castleman s Disease With Correlates of Disease Activity
Principal Investigators: Robert Yarchoan, M.D. ational Cancer Institute. National Institutes of Health Clinical Center, 9000 Rockville Pike, Bethesda, Maryland, United States, 20892
Contact: Irene Ekwede, R.N., Phone: +1(240) 760-6126
ClinicalTrials.gov Identifier: NCT00092222

Recombinant Interleukin-15 in Combination With Checkpoint Inhibitors Nivolumab and Ipilimumab in People With Refractory Cancers
Principal Investigators: Geraldine H O'Sullivan Coyne, M.D. National Cancer Institute. National Institutes of Health Clinical Center. Bethesda, Maryland, United States, 20892
Contact: Ashley B Bruns, Phone: +1 (240) 858-3162
ClinicalTrials.gov Identifier: NCT03388632

Poor Response to Monoclonal Therapy in Asthma (PROCLAIM)
Principal Investigators: Dominick Shaw, MBBS, FRCS, MD., Nottingham Respiratory BRU. Nottingham, United Kingdom, NG51PB.
Contact: Yik L Pang, BMedSci, MBBS, MRCP, Phone: 01158231702
ClinicalTrials.gov Identifier: NCT04114396

Low-dose Interleukin-2 for the Reduction of Vascular Inflammation in Acute Coronary Syndromes - IVORY (IVORY)
Principal Investigators: Joseph Cheriyan, MBChB,FRCP. Hospitals NHS Foundation Trust. Unversity of Cambridge. Cambridge, Cambridgeshire, United Kingdom, CB20QQ
Contact: Heike Templin., Phone: +44(0)1223 250874
ClinicalTrials.gov Identifier: NCT04241601

TNFalpha and Interleukin 2 Coding Oncolytic Adenovirus TILT-123 During TIL Treatment of Advanced Melanoma (TUNINTIL)
Principal Investigators: Inge Marie Svane, MD. National Center for Cancer Immune Therapy Herlev Hospital, Copenhagen University. Copenhagen, Denmark.
Brigitte Dréno, MD. CHU Nantes. Nantes, France
Contact: Herlev Hospital, Phone: +45 38 68 38 68
ClinicalTrials.gov Identifier: NCT04217473

Treatment and Natural History Study of Lymphomatoid Granulomatosis
Principal Investigators: Christopher J Melani, M.D. National Cancer Institute. National Institutes of Health Clinical Center, 9000 Rockville Pike. Bethesda, Maryland, United States, 20892
Contact: NCI Medical Oncology Referral Office, Phone: (240) 760-6050
ClinicalTrials.gov Identifier: NCT00001379

REVIEWS OF INTEREST

Contributed by Zhian Chen and Di Yu

PMID: 34002066
Cytokine release syndrome and associated neurotoxicity in cancer immunotherapy.
Morris EC, Neelapu SS, Giavridis T, Sadelain M.
Nat Rev Immunol. 2021 May 17:1-12. doi: 10.1038/s41577-021-00547-6. Online ahead of print.PMID: 34002066 **Free PMC article**. Review.

PMID: 34155388
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Gocher AM, Workman CJ, Vignali DAA.
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PMID: 34226727
Insights into the biology and therapeutic implications of TNF and regulatory T cells.
Salomon BL.
Nat Rev Rheumatol. 2021 Aug;17(8):487-504. doi: 10.1038/s41584-021-00639-6. Epub 2021 Jul 5.PMID: 34226727 Review.

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Goel RR, Kotenko SV, Kaplan MJ.
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PMID: 34354255
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Attwood MM, Fabbro D, Sokolov AV, Knapp S, Schiöth HB.
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PMID: 34083781
Interleukins in cancer: from biology to therapy.
Briukhovetska D, Dörr J, Endres S, Libby P, Dinarello CA, Kobold S.
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PMID: 33872590
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McElvaney OJ, Curley GF, Rose-John S, McElvaney NG.
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PMID: 33838745
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Ozga AJ, Chow MT, Luster AD.
Immunity. 2021 May 11;54(5):859-874. doi: 10.1016/j.immuni.2021.01.012. Epub 2021 Apr 10.PMID: 33838745 Review.

PMID: 34217595
The 'cytokine storm': molecular mechanisms and therapeutic prospects.
Karki R, Kanneganti TD.
Trends Immunol. 2021 Aug;42(8):681-705. doi: 10.1016/j.it.2021.06.001. Epub 2021 Jul 1.PMID: 34217595 Review.

PMID: 33972167
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Olatunde AC, Hale JS, Lamb TJ.
Trends Immunol. 2021 Jun;42(6):536-550. doi: 10.1016/j.it.2021.04.006. Epub 2021 May 8.PMID: 33972167 Review.

PMID: 34266767
LFA-1 in T cell priming, differentiation, and effector functions.
Gérard A, Cope AP, Kemper C, Alon R, Köchl R.
Trends Immunol. 2021 Aug;42(8):706-722. doi: 10.1016/j.it.2021.06.004. Epub 2021 Jul 12.PMID: 34266767 Review.

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Dev Cell. 2021 Mar 22;56(6):726-746. doi: 10.1016/j.devcel.2021.02.028.PMID: 33756119 Review.

PMID: 33822846
The metabolism-modulating activity of IL-17 signaling in health and disease.
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J Exp Med. 2021 May 3;218(5):e20202191. doi: 10.1084/jem.20202191.PMID: 33822846

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Cytokine "fine tuning" of enthesis tissue homeostasis as a pointer to spondyloarthritis pathogenesis with a focus on relevant TNF and IL-17 targeted therapies.
Russell T, Bridgewood C, Rowe H, Altaie A, Jones E, McGonagle D.
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REVIEWS OF INTEREST

Contributed by Zhian Chen and Di Yu

Continued

PMID: 34021269
Reactivation of latent tuberculosis with TNF inhibitors: critical role of the beta 2 chain of the IL-12 receptor.
Robert M, Miossec P.
Cell Mol Immunol. 2021 Jul;18(7):1644-1651. doi: 10.1038/s41423-021-00694-9. Epub 2021 May 21.PMID: 34021269 Review.

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Cytokine engineering for targeted cancer immunotherapy.
Bonati L, Tang L.
Curr Opin Chem Biol. 2021 Jun;62:43-52. doi: 10.1016/j.cbpa.2021.01.007. Epub 2021 Mar 6.PMID: 33684633 Review.

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Yuan S, Jiang SC, Zhang ZW, Fu YF, Hu J, Li ZL.
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Gubernatorova EO, Namakanova OA, Gorshkova EA, Medvedovskaya AD, Nedospasov SA, Drutskaya MS.
Front Immunol. 2021 May 18;12:601842. doi: 10.3389/fimmu.2021.601842. eCollection 2021.PMID: 34084159 **Free PMC article**. Review.

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Bell M, Gottschalk S.
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PMID: 34299273
Cytokine Release Syndrome Associated with T-Cell-Based Therapies for Hematological Malignancies: Pathophysiology, Clinical Presentation, and Treatment.
Cosenza M, Sacchi S, Pozzi S.
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Cytokine signaling convergence regulates the microglial state transition in Alzheimer's disease.
Lau SF, Fu AKY, Ip NY.
Cell Mol Life Sci. 2021 May;78(10):4703-4712. doi: 10.1007/s00018-021-03810-0. Epub 2021 Apr 13.PMID: 33847763 **Free PMC article**. Review.

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Endosomes as Signaling Platforms for IL-6 Family Cytokine Receptors.
Schmidt-Arras D, Rose-John S.
Front Cell Dev Biol. 2021 Jun 1;9:688314. doi: 10.3389/fcell.2021.688314. eCollection 2021. PMID: 34141712 **Free PMC article**. Review.

COVID-19 SPECIAL COLLECTION

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Is IL-6 a key cytokine target for therapy in COVID-19?
Jones SA, Hunter CA.
Nat Rev Immunol. 2021 Jun;21(6):337-339. doi: 10.1038/s41577-021-00553-8. PMID: 33850327 **Free PMC article**. Review.

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IL-6 modulation for COVID-19: the right patients at the right time?
Ascierto PA, Fu B, Wei H.
J Immunother Cancer. 2021 Apr;9(4):e002285. doi: 10.1136/jitc-2020-002285.PMID: 33837054 **Free PMC article**. Review.

PMID: 33676592
IL-6 blockade for COVID-19: a global scientific call to arms.
Murthy S, Lee TC.
Lancet Respir Med. 2021 May;9(5):438-440. doi: 10.1016/S2213-2600(21)00127-2. Epub 2021 Mar 4.PMID: 33676592 **Free PMC article**. Review. No abstract available.

REVIEWS OF INTEREST

Contributed by Zhian Chen and Di Yu

Continued

PMID: 33837596
Capturing Cytokines with Advanced Materials: A Potential Strategy to Tackle COVID-19 Cytokine Storm.
Meng QF, Tian R, Long H, Wu X, Lai J, Zharkova O, Wang JW, Chen X, Rao L. *Adv Mater.* 2021 May;33(20):e2100012. doi: 10.1002/adma.202100012. Epub 2021 Apr 10.PMID: 33837596 **Free PMC article**. Review.

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Yang L, Xie X, Tu Z, Fu J, Xu D, Zhou Y. *Signal Transduct Target Ther.* 2021 Jul 7;6(1):255. doi: 10.1038/s41392-021-00679-0.PMID: 34234112 **Free PMC article**. Review.

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Croce L, Gangemi D, Ancona G, Liboà F, Bendotti G, Minelli L, Chiovato L. *J Endocrinol Invest.* 2021 May;44(5):891-904. doi: 10.1007/s40618-021-01506-7. Epub 2021 Feb 9.PMID: 33559848 **Free PMC article**. Review.

PMID: 33981314
Interleukin-6, CXCL10 and Infiltrating Macrophages in COVID-19-Related Cytokine Storm: Not One for All But All for One!
Coperchini F, Chiovato L, Rotondi M. *Front Immunol.* 2021 Apr 26;12:668507. doi: 10.3389/fimmu.2021.668507. eCollection 2021.PMID: 33981314 **Free PMC article**. Review.

PMID: 34149697
Cytokine Overproduction and Immune System Dysregulation in alloHSCT and COVID-19 Patients.
Lange A, Lange J, Jaskuła E. *Front Immunol.* 2021 Jun 2;12:658896. doi: 10.3389/fimmu.2021.658896. eCollection 2021.PMID: 34149697 **Free PMC article**. Review.

PMID: 33995341
Cytokine Storm: The Primary Determinant for the Pathophysiological Evolution of COVID-19 Deterioration.
Chen R, Lan Z, Ye J, Pang L, Liu Y, Wu W, Qin X, Guo Y, Zhang P. *Front Immunol.* 2021 Apr 28;12:589095. doi: 10.3389/fimmu.2021.589095. eCollection 2021.PMID: 33995341 **Free PMC article**. Review.

PMID: 34220807
COVID-19 Severity in Obesity: Leptin and Inflammatory Cytokine Interplay in the Link Between High Morbidity and Mortality.
Maurya R, Sebastian P, Namdeo M, Devender M, Gertler A. *Front Immunol.* 2021 Jun 18;12:649359. doi: 10.3389/fimmu.2021.649359. eCollection 2021.PMID: 34220807 **Free PMC article**. Review.

PMID: 33573850
The cytokine storm in COVID-19: Further advances in our understanding the role of specific chemokines involved.
Coperchini F, Chiovato L, Ricci G, Croce L, Magri F, Rotondi M. *Cytokine Growth Factor Rev.* 2021 Apr;58:82-91. doi: 10.1016/j.cytogfr.2020.12.005. Epub 2021 Jan 8.PMID: 33573850 **Free PMC article**. Review.

PMID: 33563543
Interferons and other cytokines, genetics and beyond in COVID-19 and autoimmunity.
Opdenakker G, Van Damme J. *Cytokine Growth Factor Rev.* 2021 Apr;58:134-140. doi: 10.1016/j.cytogfr.2021.01.004. Epub 2021 Jan 29.PMID: 33563543 **Free PMC article**. Review.

PMID: 33071044
Type I IFN-dependent antibody response at the basis of sex dimorphism in the outcome of COVID-19.
Gabriele L, Fragale A, Romagnoli G, Parlato S, Lapenta C, Santini SM, Ozato K, Capone I. *Cytokine Growth Factor Rev.* 2021 Apr;58:66-74. doi: 10.1016/j.cytogfr.2020.10.001. Epub 2020 Oct 8.PMID: 33071044 **Free PMC article**. Review.

PMID: 34183243
The NLRP3 inflammasome and COVID-19: Activation, pathogenesis and therapeutic strategies.
Zhao N, Di B, Xu LL. *Cytokine Growth Factor Rev.* 2021 Jun 18:S1359-6101(21)00054-X. doi: 10.1016/j.cytogfr.2021.06.002. Online ahead of print.PMID: 34183243 **Free PMC article**. Review.

PMID: 33926774
Perspectives on anti-IL-1 inhibitors as potential therapeutic interventions for severe COVID-19.
Geng J, Wang F, Huang Z, Chen X, Wang Y. *Cytokine.* 2021 Jul;143:155544. doi: 10.1016/j.cyto.2021.155544. Epub 2021 Apr 17.PMID: 33926774 **Free PMC article**. Review.

WWW

Contributions from Supreet Agarwal

b2bTools: online predictions for protein biophysical features and their conservation

https://bio2byte.be/b2btools/

B2bTools provide integrated protein sequence-based predictions via https://bio2byte.be/b2btools/. The aim of predictions is to identify the biophysical behaviour or features of proteins that are not readily captured by structural biology and/or molecular dynamics approaches. Upload of a FASTA file or text input of a sequence provides integrated predictions from DynaMine backbone and side-chain dynamics, conformational propensities, and derived EFoldMine early folding, DisoMine disorder, and Agmata beta-sheet aggregation. These predictions, several of which were previously not available online, capture 'emergent' properties of proteins, i.e. the inherent biophysical propensities encoded in their sequence, rather than context-dependent behaviour (e.g. final folded state). Online visualisation is available as interactive plots, with brief explanations and tutorial pages included.

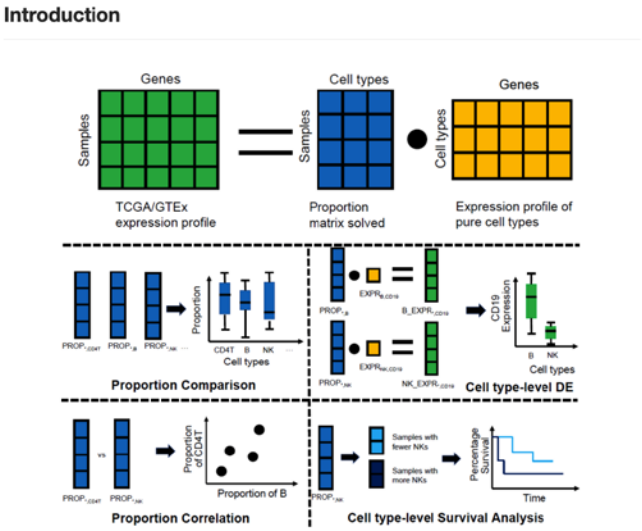
DrugComb update: a more comprehensive drug sensitivity data repository and analysis portal

https://drugcomb.org/

Combinatorial therapies that target multiple pathways have shown great promises for treating complex diseases. DrugComb (https://drugcomb.org/) is a web-based portal for the deposition and analysis of drug combination screening datasets. Since its first release, DrugComb has received continuous updates on the coverage of data resources, as well as on the functionality of the web server to improve the analysis, visualization and interpretation of drug combination screens. Here, we report significant updates of DrugComb, including: (i) manual curation and harmonization of more comprehensive drug combination and monotherapy screening data, not only for cancers but also for other diseases such as malaria and COVID-19; (ii) enhanced algorithms for assessing the sensitivity and synergy of drug combinations; (iii) network modelling tools to visualize the mechanisms of action of drugs or drug combinations for a given cancer sample and (iv) state-of-the-art machine learning models to predict drug combination sensitivity and synergy. These improvements have been provided with more user-friendly graphical interface and faster database infrastructure, which make DrugComb the most comprehensive web-based resources for the study of drug sensitivities for multiple diseases.

GEPIA2021: integrating multiple deconvolution-based analysis into GEPIA

http://gepia2021.cancer-pku.cn/



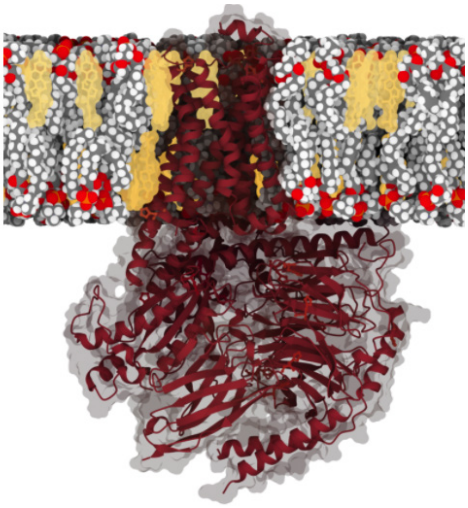
GEPIA (Gene Expression Profiling Interactive Analysis) webserver facilitates the widely used analyses based on the bulk gene expression datasets in the TCGA and the GTEx projects, providing the biologists and clinicians with a handy tool to perform comprehensive and complex data mining tasks. Recently, the deconvolution tools have led to revolutionary trends to resolve bulk RNA datasets at cell type-level resolution, interrogating the characteristics of different cell types in cancer and controlled cohorts became an important strategy to investigate the biological questions. Thus, GEPIA2021, a standalone extension of GEPIA, allowing users to perform multiple interactive analysis based on the deconvolution results, including cell type-level proportion comparison, correlation analysis, differential expression, and survival analysis. With GEPIA2021, experimental biologists could easily explore the large TCGA and GTEx datasets and validate their hypotheses in an enhanced resolution. GEPIA2021 is publicly accessible at http://gepia2021.cancer-pku.cn/.

WWW

Continued

ProLint: a web-based framework for the automated data analysis and visualization of lipid-protein interactions

https://www.prolint.ca/



The functional activity of membrane proteins is carried out in a complex lipid environment. Increasingly, it is becoming clear that lipids are an important player in regulating or generally modulating their activity. A routinely used method to gain insight into this interplay between lipids and proteins are Molecular Dynamics (MD) simulations, since they allow us to study interactions at atomic or near-atomic detail as a function of time. A major bottleneck, however, is analyzing and visualizing lipid-protein interactions, which, in practice, is a time-demanding task. ProLint (www.prolint.ca), is a webserver that completely automates analysis of MD generated files and visualization of lipid-protein interactions. Analysis is modular allowing users to select their preferred method, and visualization is entirely interactive through custom built applications that enable a detailed qualitative and quantitative exploration of lipid-protein interactions. ProLint also includes a database of published MD results that have been processed through the ProLint workflow and can be visualized by anyone regardless of their level of experience with MD. The automated analysis, feature-rich visualization, database integration, and open-source distribution with an easy to install process, will allow ProLint to become a routine workflow in lipid-protein interaction studies.

CNVxplorer: a web tool to assist clinical interpretation of CNVs in rare disease patients

http://cnvxplorer.com

Copy Number Variants (CNVs) are an important cause of rare diseases. Array-based Comparative Genomic Hybridization tests yield a similar to 12% diagnostic rate, with similar to 8% of patients presenting CNVs of unknown significance. CNVs interpretation is particularly challenging on genomic regions outside of those overlapping with previously reported structural variants or disease-associated genes. Recent studies showed that a more comprehensive evaluation of CNV features, leveraging both coding and non-coding impacts, can significantly improve diagnostic rates. However, currently available CNV interpretation tools are mostly gene-centric or provide only non-interactive annotations difficult to assess in the clinical practice. Here, we present CNVxplorer, a web server suited for the functional assessment of CNVs in a clinical diagnostic setting. CNVxplorer mines a comprehensive set of clinical, genomic, and epigenomic features associated with CNVs. It provides sequence constraint metrics, impact on regulatory elements and topologically associating domains, as well as expression patterns. Analyses offered cover (a) agreement with patient phenotypes; (b) visualizations of associations among genes, regulatory elements and transcription factors; (c) enrichment on functional and pathway annotations and (d) co-occurrence of terms across PubMed publications related to the query CNVs. A flexible evaluation workflow allows dynamic re-interrogation in clinical sessions. CNVxplorer is publicly available at http://cnvxplorer.com.

snpXplorer: a web application to explore human SNP-associations and annotate SNP-sets

https://snpxplorer.net

Genetic association studies are frequently used to study the genetic basis of numerous human phenotypes. However, the rapid interrogation of how well a certain genomic region associates across traits as well as the interpretation of genetic associations is often complex and requires the integration of multiple sources of annotation, which involves advanced bioinformatic skills. We developed snpXplorer, an easy-to-use web-server application for exploring Single Nucleotide Polymorphisms (SNP) association statistics and to functionally annotate sets of SNPs. snpXplorer can superimpose association statistics from multiple studies, and displays regional information including SNP associations, structural variations, recombination rates, eQTL, linkage disequilibrium patterns, genes and gene-expressions per tissue. By overlaying multiple GWAS studies, snpXplorer can be used to compare levels of association across different traits, which may help the interpretation of variant consequences. Given a list of SNPs, snpXplorer can also be used to perform variant-to-gene mapping and gene-set enrichment analysis to identify molecular pathways that are overrepresented in the list of input SNPs. snpXplorer is freely available at https://snpxplorer.net. Source code, documentation, example files and tutorial videos are available within the Help section of snpXplorer and at https://github.com/TesiNicco/snpXplorer.

WWW

Continued

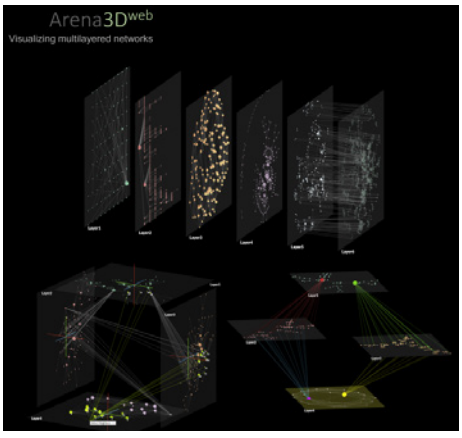
TIMEOR: a web-based tool to uncover temporal regulatory mechanisms from multi-omics data

http://timeor.brown.edu.

Uncovering how transcription factors regulate their targets at DNA, RNA and protein levels over time is critical to define gene regulatory networks (GRNs) and assign mechanisms in normal and diseased states. RNA-seq is a standard method measuring gene regulation using an established set of analysis stages. However, none of the currently available pipeline methods for interpreting ordered genomic data (in time or space) use time-series models to assign cause and effect relationships within GRNs, are adaptive to diverse experimental designs, or enable user interpretation through a web-based platform. Furthermore, methods integrating ordered RNA-seq data with protein-DNA binding data to distinguish direct from indirect interactions are urgently needed. We present TIMEOR (Trajectory Inference and Mechanism Exploration with Omics data in R), the first web-based and adaptive time-series multi-omics pipeline method which infers the relationship between gene regulatory events across time. TIMEOR addresses the critical need for methods to determine causal regulatory mechanism networks by leveraging time-series RNA-seq, motif analysis, protein-DNA binding data, and protein-protein interaction networks. TIMEOR's user-catered approach helps non-coders generate new hypotheses and validate known mechanisms. We used TIMEOR to identify a novel link between insulin stimulation and the circadian rhythm cycle. TIMEOR is available at https://github.com/ashleymaeconard/TIMEOR.git and http://timeor.brown.edu.

Arena3D(web): interactive 3D visualization of multilayered networks

http://bib.fleming.gr/Arena3D



Efficient integration and visualization of heterogeneous biomedical information in a single view is a key challenge. In this study, we present Arena3D(web), the first, fully interactive and dependency-free, web application which allows the visualization of multilayered graphs in 3D space. With Arena3D(web), users can integrate multiple networks in a single view along with their intra- and inter-layer connections. For clearer and more informative views, users can choose between a plethora of layout algorithms and apply them on a set of selected layers either individually or in combination. Users can align networks and highlight node topological features, whereas each layer as well as the whole scene can be translated, rotated and scaled in 3D space. User-selected edge colors can be used to highlight important paths, while node positioning, coloring and resizing can be adjusted on-the-fly. In its current version, Arena3D(web) supports weighted and unweighted undirected graphs and is written in R, Shiny and JavaScript. We demonstrate the functionality of Arena3D(web) using two different use-case scenarios; one regarding drug repurposing for SARS-CoV-2 and one related to GPCR signaling pathways implicated in melanoma. Arena3D(web) is available at http://bib.fleming.gr:3838/Arena3D or http://bib.fleming.gr/Arena3D.

ProteoSign v2: a faster and evolved user-friendly online tool for statistical analyses of differential proteomics

http://bioinformatics.med. uoc.gr/ProteoSign

Bottom-up proteomics analyses have been proved over the last years to be a powerful tool in the characterization of the proteome and are crucial for understanding cellular and organism behaviour. Through differential proteomic analysis researchers can shed light on groups of proteins or individual proteins that play key roles in certain, normal or pathological conditions. However, several tools for the analysis of such complex datasets are powerful, but hard-to-use with steep learning curves. In addition, some other tools are easy to use, but are weak in terms of analytical power. Previously, we have introduced ProteoSign, a powerful, yet user-friendly open-source online platform for protein differential expression/abundance analysis designed with the end-proteomics user in mind. Part of Proteosign's power stems from the utilization of the well-established Linear Models For Microarray Data (LIMMA) methodology. Here, we present a substantial upgrade of this computational resource, called ProteoSign v2, where we introduce major improvements, also based on user feedback. The new version offers more plot options, supports additional experimental designs, analyzes updated input datasets and performs a gene enrichment analysis of the differentially expressed proteins. We also introduce the deployment of the Docker technology and significantly increase the speed of a full analysis. ProteoSign v2 is available at http://bioinformatics.med. uoc.gr/ProteoSign.

New Interferon-beta standard now available from US Pharmacopia

https://store.usp.org/product/1342401 **$425.00**

THIS ITEM REQUIRES SPECIAL COLD CHAIN SHIPMENT. SPECIAL SHIPPING METHODS AND CHARGES MAY APPLY. PLEASE CONTACT USP CUSTOMER SERVICE AT 800-227-8772 OR 301-881-0666 TO SPEAK TO A CUSTOMER SERVICE REPRESENTATIVE FOR ORDER ASSISTANCE.

Interferon Beta-1A (1.0 mL) (INTERNATIONAL COLD CHAIN SHIPMENT REQUIRED)

Catalog No:**1342401**

Net Weight: **1.0 mL**

CAS No: **145258-61-3**

NDC No: N/A

Current Lot Information

- Current Lot: F04390
- CAS No: 145258-61-3
- Harmonized System (HS) Code *: 3002130000
- UN No: N/A
- NDC No: N/A
- Associated Documentary Standard(s): View
- Molecular Formula: C908H1406N246O252S7 (protein moiety)
- Container Type: AMPULE
- Base Control Substance (substance %): N/A

Product Information

SDS: Safety data sheet.pdf

USP Certificates/Product Information Sheets and Valid Use Dates

Lot No	USP Certificate or Product Information Sheet	Valid Use Date (if applicable)	Country of Origin*	Material Origin
F04390 (Current)	1342401 - F04390	Current	United States	Recombinant

Recipes from Wales:

Welsh Cakes

By Good Food team

Pice ar y maen, a Welsh teatime treat passed on through generations and still as popular as ever. Perfect for making with the children.

INGREDIENTS

- 225g plain flour
- 85g caster sugar (Caster, or castor, sugar is a **type of fine granulated sugar** that's widely available in the United Kingdom. It's not quite as common in the United States, though you can find it in some baking aisles under the name "superfine sugar." Its texture is somewhere between regular granulated sugar and confectioners' sugar.)
- ½ tsp mixed spice (f you need a substitute for mixed spice in a recipe and don't want to make your own you can just use **Pumpkin Pie Spice** instead. Both are made up of similar spices.)
- ½ tsp baking powder
- 50g butter, cut into small pieces
- 50g lard, cut into small pieces, plus extra for frying
- 50g currant
- 1 egg, beaten
- splash milk

METHOD

STEP 1

Tip the flour, sugar, mixed spice, baking powder and a pinch of salt into a bowl. Then, with your fingers, rub in the butter and lard until crumbly. Mix in the currants. Work the egg into the mixture until you have soft dough, adding a splash of milk if it seems a little dry – it should be the same consistency as shortcrust pastry.

•

STEP 2

Roll out the dough on a lightly floured work surface to the thickness of your little finger. Cut out rounds using a 6cm cutter, re-rolling any trimmings. Grease a flat griddle pan or heavy frying pan with lard, and place over a medium heat. Cook the Welsh cakes in batches, for about 3 mins each side, until golden brown, crisp and cooked through. Delicious served warm with butter and jam, or simply sprinkled with caster sugar. Cakes will stay fresh in a tin for 1 week.

VILCEK
FOUNDATION

PRESS RELEASE UNDER EMBARGO
UNTIL SEP 7, 2021 | 12:00 PM EDT

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The Vilcek Foundation awards $250,000 in prizes to immigrant scientists

Vishva M. Dixit, Markita del Carpio Landry, Hani Goodarzi, and Harris Wang receive 2022 Vilcek Foundation Prizes in Biomedical Science

NEW YORK, September 7, 2021—The Vilcek Foundation announces the recipients of the 2022 Vilcek Foundation Prizes in Biomedical Science, totaling $250,000. Awarded annually, the prizes honor the contributions of foreign-born scientists to scientific research, discovery, and innovation in the United States.

"Scientists from around the globe have long been drawn to work in the United States due to the opportunities that exist in research science here: Scientists are free to pursue funding for work that they are passionate about, and encouraged to collaborate across institutions in the pursuit of their research goals," said Vilcek Foundation Chairman and CEO Jan Vilcek. "Immigrants are a vital part of the scientific community in the United States; their contributions have helped establish and maintain the United States' primacy in biomedical science and research."

In 2022, the Vilcek Foundation is awarding four prizes in biomedical science. The Vilcek Prize in Biomedical Science includes a cash award of $100,000. Three additional prizes—the Vilcek Prizes for Creative Promise in Biomedical Science—each includes a cash award of $50,000.

The Vilcek Prize in Biomedical Science

The Vilcek Prize in Biomedical Science recognizes an immigrant scientist for outstanding career contributions to biomedical science with a global impact. The recipient of the 2022 Vilcek Prize in Biomedical Science is Vishva M. Dixit, Vice President of Early Discovery Research and Physiological Chemistry at Genentech. Born in Kenya to Indian parents, Dixit studied and trained as a physician in Kenya before pursuing a career in biomedical research and academia in the United States.

"Vishva Dixit is a molecular biologist, physician and pathologist whose scientific publications rank among the most-cited in the world; his work has elucidated molecular mechanisms of inflammation and has become part of standard scientific textbooks," said Vilcek. "As the recipient of the 2022 Vilcek Prize in Biomedical Science, Dixit joins the ranks of other exceptional immigrant scientists whose work has shaped our scientific understanding of biology and human health."

The Vilcek Prizes for Creative Promise in Biomedical Science

The Vilcek Prizes for Creative Promise in Biomedical Science are awarded to young foreign-born scientists living and working in the United States. Prizewinners are selected for the innovative promise of their early-career work: research and discoveries that represent a major step forward in their respective area of study, and advance the landscape of scientific research in the United States. Markita del Carpio Landry, Hani Goodarzi, and Harris Wang are the recipients of the 2022 Vilcek Prizes for Creative Promise in Biomedical Science.

Markita del Carpio Landry receives the Vilcek Prize for Creative Promise in Biomedical Science for the development of probes to visualize neurochemical communication in the brain, and for breakthroughs in gene-editing technologies with applications for agriculture and the development of biologic drugs. She is an assistant professor at the University of California, Berkeley, and an investigator with the Innovative Genomics Institute and with the Chan Zuckerberg Initiative. Born in Canada to a Bolivian mother and French Canadian father, del Carpio Landry is a member of the Society for the Advancement of Chicanos and Native Americans in Science (SACNAS) and the Society of Hispanic Professional Engineers (SHPE).

Hani Goodarzi receives the Vilcek Prize for Creative Promise in Biomedical Science for using disease modeling, computational methods, and experiments on mouse models and clinical samples to uncover the mechanisms of cancer metastasis and reveal therapeutic targets in cancer. He is the principal investigator of the Goodarzi Lab at the University of California, San Francisco, where he is an assistant professor in biochemistry and biophysics. Under his leadership, the Goodarzi Lab discovered that the protein SNRPA1 drives metastasis in breast cancer and that controlling the protein's levels in cancer cells alters their ability to metastasize; most recently, the lab team discovered a novel class of RNA found in cancerous cells—orphan noncoding RNA (oncRNA)—which has led to new modes for detecting and monitoring cancer. Goodarzi was born in Tehran, Iran, and immigrated to the United States in 2006.

Harris Wang receives the Vilcek Prize for Creative Promise in Biomedical Science for the development and application of Multiplex Automated Genome Engineering (MAGE), a new framework for manipulating DNA to produce synthetic or engineered recombinant genetic material, and for his use of CRISPR technology to track and record transient cellular processes in the human gut microbiome. Wang's work has the potential to shape a new area in genomics, modeling, and analysis of complex microbial metabolism and ecosystems. Born in Beijing, China, Wang is an associate professor of systems biology and pathology and cell biology at Columbia University in New York.

The Vilcek Foundation Prizes Program

The 2022 Vilcek Foundation Prizes in Biomedical Science are a part of the Vilcek Foundation Prizes program; the foundation's prizes include the Vilcek Foundation Prizes in Biomedical Science, the Vilcek Foundation Prizes in the Arts and Humanities, and the Vilcek Prize for Excellence.

The recipients of the 2022 Vilcek Foundation Prizes Biomedical Science will be honored in an online ceremony alongside the recipients of the Vilcek Foundation Prizes in Dance and the Vilcek Prize for Excellence in the spring of 2022.

The Vilcek Foundation

The Vilcek Foundation raises awareness of immigrant contributions in the United States and fosters appreciation for the arts and sciences. The foundation was established in 2000 by Jan and Marica Vilcek, immigrants from the former Czechoslovakia. The mission of the foundation was inspired by the couple's respective careers in biomedical science and art history. Since 2000, the foundation has awarded over $6.4 million in prizes to foreign-born individuals and has supported organizations with over $5.5 million in grants.

The Vilcek Foundation is a private operating foundation, a federally tax-exempt nonprofit organization under IRS Section 501(c)(3).

THE ANNUAL INTERNATIONAL MEETING OF KOREAN ASSOCIATION OF IMMUNOLOGISTS (KAI 2021) WAS HELD ON JUNE 2 - 4, 2021 AT THE SWISS GRAND HOTEL IN SEOUL, KOREA.

Despite the continuing global COVID-19 pandemic and a strict social distancing policy in Korea, the on/offline hybrid meeting was highly successful with about 900 participants (181 abstracts) from 21 countries. The scientific program included 4 plenary lectures, 14 Major Symposia, 3 Satellite Symposia, 6 Workshops, 2 Education Sessions, and many Industry Symposia. The plenary lectures were given by Mi-Na Kwon (Korea), Laurence Zitvogel (France), Mark Davis (USA), and Ruslan Medzhitov (USA). More information on KAI 2021 can be found at https://kai2021.org/register/KAI2021/main.html. KAI 2022 is planned to be held on Nov. 3 - 5, 2022 at the Dragon City Hotel in Seoul, Korea.

The Korean Association of Immunologists (KAI) is the national society of immunology researchers that includes basic immunologists and clinicians. KAI started in1974 with 48 inaugural members and has grown to have more than 3,000 current members. This year KAI is sponsoring one scientific session at Cytokines 2021 on Cytokines and Bystander T Cell Activation.

THE DELTA TRICK OF COVID-19

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Since the first report of SARS-CoV-2 from Wuhan, back in December 2019, the pandemic has ravaged the world with ever-evolving different variants- with changing dominance patterns. Different variant of concerns (alpha, beta, gamma, delta and kappa) with corresponding spike mutations, rendering evasion of the immune system and making them varyingly resistant to different vaccines (1). Presently, the delta variant (B.1.617.2) has outcompeted the other variants of concern and is globally the most intimidatingly dominant one.

The furin cleavage of polybasic motif, 681PRRAR685/S imparts high infectivity and transmissibility to SARS-CoV-2 with the deletion of the motif showing attenuated pathogenesis in humanised ACE2 mice and hamster models (2). Interestingly, P681H/R mutation in the motif was found only in the highly transmissible variants of concern (B.1.1.7, B.1.617 and it's allied siblings). The 681residue substitution to arginine (R in delta variant) from proline (R), makes it more basic and similar to classic furin cleavage sites, than to histidine (H in alpha variant). The ensuing increased basicity makes it more recognisable for furin to cleave the S protein.

The increased S protein cleavage in delta variants in comparison to alpha variants (and other variants), is known to account for enhanced viral replication and fusogenicity, which could contribute to heightened transmissibility and infectious nature of the variant (3,4). The side chain of R682 and R685 residues of spike protein (in infected pneumocytes) getting exposed on the surface, facilitates furin cleavage and further known to activate the scramblase TMEM16F, leading to cell fusion/syncytia formation and T cell exhaustion (5). In conjunction, TMEM16F promotes cell death by enabling phosphatidylserine (PS) exposure on outer leaflet of cells, which is used as a scaffold for coagulation factors, helping in thrombin generation for blood clotting phenomena (6).With GSDM-N terminal fragment known to have propensity for binding phospholipids (like PS) - to enhance it's pore forming capacity (7), TMEM16F activation could lead to heightened cell death by GSDM-N involvement. The flipping of PS residue to outer leaflet of plasma membrane can activate the alternate complement system (8)- which can further be responsible for the hypercoagulability phenotype in COVID-19. Indeed, complement system has been shown to be activated in the disease too (9).

It is noteworthy to say - the apocalyptic surge in India observed during April/May in which a large population of patients reported of sudden lowered oxygenation status coupled with higher mortality, could be an aftermath of aberrant blood clottings, thrombus formations and cell death (ensuing in impaired alveolar gaseous exchange) due to enhanced furin cleavage (P681R) by B.1.617 variant. The sudden huge demand of oxygen cylinders and oxygen concentrators in the country made people direly helpless and clueless. The B.1.617 variant, first identified in India caused a mayhem with 4,00,000 new infections and 4,000 deaths per day in the month of April/May in India (2nd wave) reflecting a near partial collapse of health infrastructure system. The numbers might be under-represented too, with many childrens becoming orphans and many aging parents losing their children. The funeral pyres kept burning incessantly with corpses out-numbering the near and dear ones who come to bid adieu. People unable to find places for burning corpses made their own pyres or even let it go to the Ganges river. Yes indeed, the country was in total shambles, with the second wave targeting the young and middle aged population, in comparison to the aged population – who were vulnerable during the first wave. But what went wrong? The virus mutated to a more virulent strain and we underestimated it and dropped down our guards to allow large populated gatherings- Assembly elections, Kumbh Mela and unrestricted personal convocations. The outcome was dreadful with vaccine roll out not started in full swing with primarily the aged population receiving their doses- leaving the young and middle aged population vulnerable.

The delta variant is also much less potent to antibody neutralization in comparison to other variants, making it a more infectious candidate (10). Hence, enhanced furin cleavage by P681R mutation in delta variant could lead culmination of events like: enhanced viral replication, syncytia formation, cell death, blood coagulations coupled with evading neutralizing antibodies - making it the most transmissible variant. Equally, these events can well be responsible for the Indian catastrophic second wave, attributed to P681R mutation harbouring B.1.617 variant.

Declarations:

– Ethical Approval and Consent to participate- Not applicable
– Consent for publication-Yes
– Availability of supporting data-Literature survey.
– Competing interests-I don't have any competing interests
– Funding- The study hasn't received any funding as yet
– Authors' contributions- Rahul conceptualized the study and wrote the manuscript.
– Acknowledgement: Rahul is very grateful to Dr Katherine Fitzgerald and Dr Douglas Golenbock (UMass Chan Medical School) for the initial insightful discussions.

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Journal of Interferon and Cytokine Research

CALL FOR PAPERS

Basic and Clinical Aspects of Cytokine Storms in Infectious Diseases

Deadline for Manuscript Submission: November 15, 2021

GUEST EDITORS:

Joaquín Zúñiga and Jose Alberto Choreño-Parra

Laboratory of Immunobiology and Genetics

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Mexico City, Mexico

Cytokine storms are characterized by the excessive release of pro-inflammatory soluble mediators (hypercytokinemia) resulting from an overdriven immune response to noxious insults, including infectious agents. The focus of this special issue is to highlight this recent progress in understanding the basic biology and therapeutic control of hypercytokinemia in the context of different types of infection. Original studies, systematic reviews, narrative reviews, commentaries, and case reports on the following topics will be considered for peer review and publication:

- The genetic bases that determine risk for cytokine storm and severe illness during infection
- The underlying biochemical and immunological mechanisms that drive hypercytokinemia
- Analysis of the immunological characteristics of patients with infection-associated cytokine storm syndromes
- Comparisons of the immune signatures and cytokine production patterns of patients with COVID-19, seasonal influenza, and pandemic influenza A(H1N1)
- The diagnostic and prognostic value of hypercytokinemia during infection
- Impact of vaccination on the course of hypercytokinemia
- Impact of co-existing autoimmune diseases on the course of cytokine storms during infection
- Impact of co-existing infections on the course of hypercytokinemia during COVID-19
- Cytokine storm against infection in the context of metabolic comorbidities
- Impact of hypercytokinemia on multiorgan function during infection
- Animal models for studying hypercytokinemia
- The effectiveness of therapeutic agents aimed at calming hyperinflammation during infection
- Case reports offering novel diagnostic and therapeutic perspectives of hypercytokinemia

Editorial Questions? Please Contact: **Karen Cloud-Hansen**

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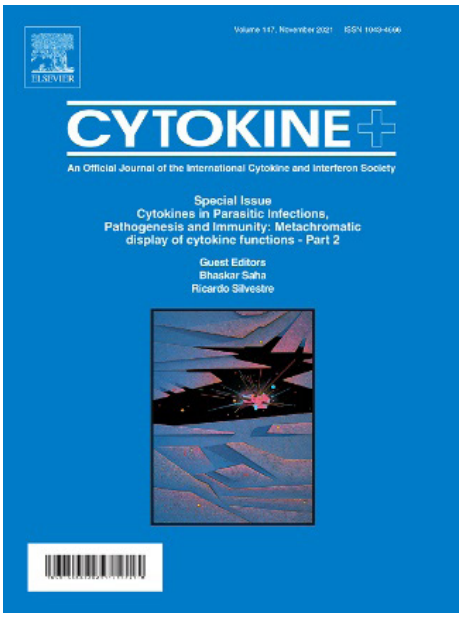

Editor-in-Chief: Dhan V. Kalvakolanu

Most members of the International Cytokine and Interferon Society (ICIS) are familiar with CYTOKINE, an official journal of the society, which is now in the 32nd year of publication. The journal has grown in its size, scope, and editorial board since 2014. Last year, we have reached a new height in the life of CYTOKINE with a record 1260+ submissions. We currently have a collaborative team of 10 Associate editors distributed across the globe which represents gender, ethnic and national diversity. CYTOKINE has an impact factor of 3.86, and a Cite score of 5.6. Our first decision comes in 3.9 weeks, with a total review and publication times of 8.6 is 2.2 weeks, respectively. Between 2014-2021, we have published 23 different special issues on various aspects of cytokine biology.

In 2016 we celebrated the 25th year of CYTOKINE by producing a special issue. Here are some of our recent special issues:

- **Cytokines in Parasitic Infections, Pathogenesis, and Immunity: Metachromatic display of cytokine functions** (2 volumes). Editors: Bhaskar Saha & Ricardo Silvestre
- **IL-6 family cytokines: an updated perspective on their broad pathophysiology.** Editor: Brendan J. Jenkins
- **Type I Interferon in Human Disease.** Editors: Timothy Niewold & Dhan Kalvakolanu

Aims and Scope: CYTOKINE will publish studies that report on the molecular biology, signal transduction, genetics, biochemistry, immunology, genome-wide association, pathobiology, diagnostic, clinical, and therapeutic applications of all known and emerging cytokines, cytotoxins, interferons, chemokines, adipokines, matrikines, hematopoietic factors, and growth factors. Studies reporting all signaling molecules from the pathogens and host-endogenous sources, metabolic products/adducts that mediate inflammation and immunity, either influence and/or operate under this broad class of "biological response modifiers" as they relate to host-defenses and immune responses will be considered for publication. Details can be found here: https://www.journals.elsevier.com/cytokine

We have also opened collaborative channels with a manuscript transfer arrangement between our sister journals Cytokine and Growth Factor Reviews, The Lancet Rheumatology, and International immunopharmacology. This arrangement allows an easy transfer of articles that completed a review but not within the scope of priority of the participating journals, with the author's consent. This will expedite the publication of interesting data in the recipient journal with little lag. An extension of our efforts to provide rapid access to published data is CYTOKINE-X, the online-only open access mirror journal which has the same aims and scope and the peer-review process.

CYTOKINE-X offers authors with high-quality research who want to publish in a gold open access journal the opportunity to make their work immediately, permanently, and freely accessible. CYTOKINE-X authors will pay an article publishing charge (APC), have a choice of license options, and retain copyright. This journal is indexed in Scopus. Please check details at: www.elsevier.com/journals/cytokine-x/2590-1532/open-access-journal

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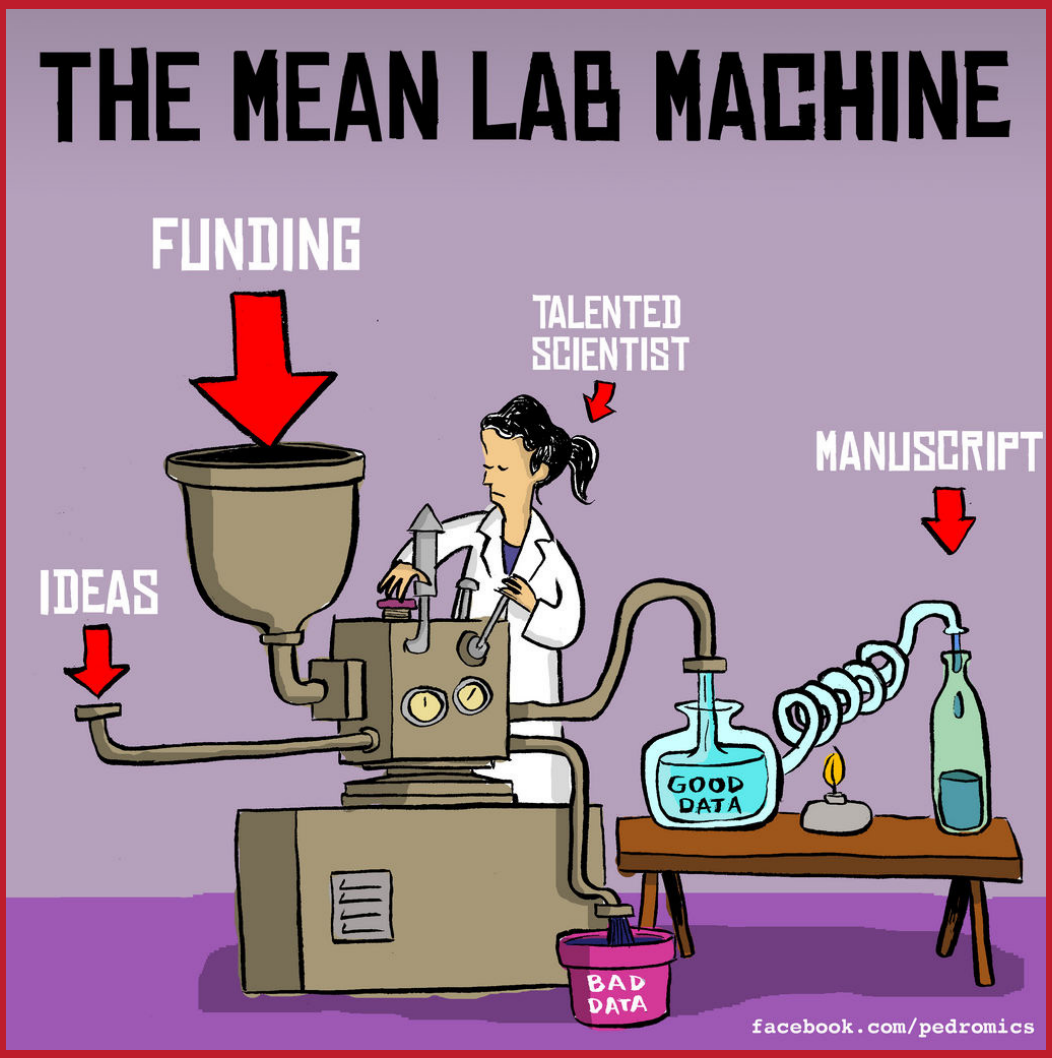

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