Signals+

THE INTERNATIONAL CYTOKINE & INTERFERON SOCIETY NEWSLETTER

APRIL 2021 | VOLUME 9 | NO. 1

IN THIS ISSUE:

A NOTE FROM THE ICIS PRESIDENT

Kate Fitzgerald

Dear Colleagues,

Greetings from the International Cytokine and Interferon Society! I hope you and your family are staying safe during these still challenging times. Thankfully 2020 is behind us now. We have lived through the COVID-19 pandemic, an event that will continue to impact our lives for some time and likely alter how we live in the future.

Despite the obvious difficulties of this past year, I can't help but marvel at the scientific advances that have been made. With everything from COVID-19 testing, to treatments and especially to the rapid pace of vaccine development, we are so better off today than even a few months back. The approval of remarkably effective COVID-19 vaccines now rolling out in the US, Israel, UK, Europe and across the globe, brings light at the end of the tunnel. The work of many of you has helped shape our understanding of the host response to Sars-CoV2 and the ability of this virus to limit antiviral immunity while simultaneously driving a cytokine driven hyperinflammatory response leading to deadly consequences for patients. The knowledge gained from all of your efforts has been put to good use to stem the threat of this deadly virus. Cytokines and interferons are somewhat mainstream terminology now, which can only be a good thing for the future of our society.

It is an honor to serve as the President of the ICIS. While an unusual time to be president, I am nonetheless excited about the future of this wonderful society. I especially want to thank Christopher Hunter, President-Elect and Joan Oefner, managing director of the society. We are a team in all that we do. I want to thank the ICIS Council and all who serve on our committees for their ongoing service. I see the impact of your work on the society and appreciate your time and commitment to our efforts.

As ICIS embraces the concept of diversity, equity and inclusion (DEI), we are making important progress toward the vision of a forward-looking and inclusive organization. We realize that we are just at the beginning of the journey, and the Council have set the goal to focus on improving DEI among our members in the coming years. As a starting point our meeting organizers, scientific programs and society committees are now more balanced in terms of gender and geographical diversity. Improving representation by those underrepresented in science and medicine is a major goal. To that end, we have amended our bylaws to add two Council members for Inclusion and Training elected in alternating 2-year terms. We encourage interested members to reach out to learn more about this initiative. I also encourage any members interested in participating on one of our committees and serving the society to reach out to me or Joan.

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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 NOTE FROM THE ICIS PRESIDENT

Kate Fitzgerald

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In November 2020, the Society hosted the virtual meeting Cytokines 2020 in Seattle which was a great success and brought a large number of new members to the society, especially increasing student/postdoc memberships. I encourage all our members to stay engaged, maximize the benefits of the society and support the ICIS by renewing your membership for 2021 if you have not already done so. Plans are well underway for our annual meeting in Cardiff. I am very much looking forward to this and hope many of us can be there in person. Simon Jones and colleagues are working hard and have created a spectacular program which you will hear about later in this newsletter. We hope that many of you will join us in-person in Cardiff, but understand this may not be possible depending where different countries are in terms of vaccinations. A hybrid virtual platform is planned to ensure participation is possible regardless. Luke O'Neill's band, The Metabollix, will be playing live at the Cytokines 2021 Networking and the event will be live streamed to our virtual audience as well. Further, plans are well underway for future meetings in Hawaii (2022), Greece (2023), Korea (2024) and Seattle (2025). I want to thank Brendan Jenkins for guiding all of these meeting planning efforts. I encourage members to step-up and reach out to Brendan to discuss organizing future meetings. The Society remains committed to providing a family friendly environment at these annual meetings. We will be providing complimentary childcare support to allow our fellow scientists with young children the opportunity to attend our meetings and social events.

I also want to provide an update on ICIS awards. As many of you know the Milstein family have supported our society for more than 30 years with the Milstein Awards. We are incredibly grateful for their support for the last 32 years. Support for travel awards was carried over from last year and will finish after the Cardiff meeting. We have been working very hard to identify alternate donors who can support both the Senior ICIS annual award, Young Investigator Awards and the travel awards. P Pfizer, a long-time major sponsor of the ICIS, has entered into a grant agreement with the Society to fund the ICIS-Pfizer Award for Excellence in Interferon and Cytokine Research (formerly the Seymour & Vivian Milstein Award from 1988 – 2020). In addition to funding this senior researcher award representing the pinnacle of scientific achievement in interferon and cytokine research since 1988, Pfizer will also sponsor four trainee awards for promising research presentations at the Cytokines Annual Meetings.

We have also reached an agreement for New Investigator Awards for Excellence in Cytokine & Interferon Research, (formerly the Milstein Young Investigator Awards). More details about the sponsor and award amounts will be announced soon. I am also pleased to announce a new ICIS mentoring award. The newly established ICIS Mentorship Award recognizes ICIS members who have made significant and sustained contributions to the career development of trainees and to the profession through outstanding mentoring. This award is based on the training experiences and success of the nominee's mentees, not the mentor's personal career achievements. For the purpose of this award, mentoring is defined as the process of guiding, supporting, and promoting the training and career development of others. A minimum of three mentees will write a supporting letter on how this person has impacted their development, career and lives. Please nominate your mentors now as this award is actively recruiting candidates for consideration.

In closing, I want to thank you for being a member of the ICIS and supporting our field. As a society, we have a lot to do. We will continue to voice your concerns, advocate for scientific research, advance the training of students and post-doctoral fellows, and sustain the progress of our field in this era of breathtaking opportunity.

I look forward to seeing you all in Cardiff.

Stay safe and be well.

Kate

2020 MILSTEIN YOUNG INVESTIGATOR AWARD WINNERS

Every year three-five awards are granted to individuals who have made notable contributions to either basic or clinical research. This award is provided by a generous gift of the Milstein Family and all ICIS members who will attend the upcoming annual conference and who have received a Ph.D or M.D. within the previous 10 years are eligible, but may be extended by 1 year due to parental leave.

2020 AWARD WINNERS

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AARON M RING, MD, Ph.D.

Assistant Professor of Immunobiology
Yale University School of Medicine
New Haven, United States

Aaron Ring received his undergraduate training at Yale University and entered the Stanford Medical Scientist Training Program for his MD and PhD degrees. At Stanford, he worked in the laboratories of Christopher Garcia and Irving Weissman to use structure-based protein engineering to develop new cytokine and immune checkpoint therapies for cancer, including therapies in the CD47 and IL-2 pathways that are now in clinical development. Aaron joined the faculty of the Yale Department of Immunobiology in 2016 as the Robert T. McCluskey Yale Scholar. The focus of his research is to understand and manipulate the activity of immune receptors using precision immunopharmacology and systems immunology. He has been recognized with numerous awards and honors, including a Pew-Stewart Scholar award from the Pew Charitable Trusts, and the NIH Director's Early Independence Award (DP5).

Oral Presentation: **An engineered Interleukin-18 variant expands intratumoral stem-like CD8 T cells and prevents TOX- mediated T cell exhaustion**

@aaronmring
https://medicine.yale.edu/profile/aaron_ring/
Ring Lab

ELIA TAIT WOJNO, Ph.D.

Assistant Professor
Department of Immunology,
University of Washington
Seattle, USA

Dr. Elia Tait Wojno pursues a life-long passion for immunology research as an Assistant Professor in the University of Washington Department of Immunology. Elia received her PhD from the University of Pennsylvania, working with Dr. Christopher Hunter in the School of Veterinary Medicine to examine how cytokines regulate immunity to the protozoan parasite Toxoplasma gondii. She went on complete a postdoctoral fellowship with Dr. David Artis in the University of Pennsylvania Perelman School of Medicine and Weill Cornell Medical College, focusing on cytokine and prostaglandin responses during helminth infection and allergic disease. As an Assistant Professor, first at Cornell University and now at UW, she continues her work in dissecting innate and adaptive immune responses following helminth parasite infection and during allergy, with a special emphasis on cytokines and prostaglandins. Her work aims to inform efforts to develop new therapies to combat infectious diseases, particularly diseases caused by parasite infection, and to limit allergic inflammation.

Oral Presentation: **The prostaglandin D2 receptor CRTH2 suppresses epithelial responses during intestinal helminth infection**

@eliataitwojno
University of Washington
Tait Wojno on PubMed

2020 MILSTEIN YOUNG INVESTIGATOR AWARD WINNER

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ZHENYU ZHONG, Ph.D.

Assistant Professor
Department of Immunology,
University of Texas Southwestern Medical Center
Dallas, USA

Dr. Zhenyu Zhong is an Assistant Professor in the Department of Immunology at UT Southwestern Medical Center, who is working in the area of innate immunity.

He obtained his Ph.D. degree from Loyola University Chicago in late 2013 and was recruited to UT Southwestern Medical Center in the fall of 2018 following his postdoctoral training at University of California, San Diego. During his PhD and postdoctoral training, Dr. Zhong has made several fundamental discoveries that contribute to establishing mitochondria as the command center for innate immunity. While at UT Southwestern, Dr. Zhong has built an outstanding research program centered on understanding how mitochondria in myeloid cells sense tissue damage, initiate inflammatory response, and orchestrate tissue repair/regeneration to restore tissue homeostasis. Additionally. Dr. Zhong's group is also interested in understanding how dysregulation of inflammation promotes the development of chronic liver disorders and neurodegenerative diseases.

Oral Presentation: **Cytosolic DNTP catabolism prevents NLRP3 inflammasome overactivation**

@ZhenyuZhonglab
UT Southwestern
Google Scholar
The Zhong lab

2020 CHRISTINA FLEISCHMANN AWARD TO YOUNG WOMEN INVESTIGATORS

This award is made possible through the generosity of the Fleischmann Family and is dedicated to the memory of ISICR member and outstanding interferon research scientist Christina Fleischmann.

CARRIE L LUCAS, Ph.D.

Yale University
Department of Immunobiology
New Haven, United States

Dr. Carrie Lucas leads a laboratory devoted to discovering new and translationally relevant principles of immunology by defining and studying novel monogenic human immune disorders.

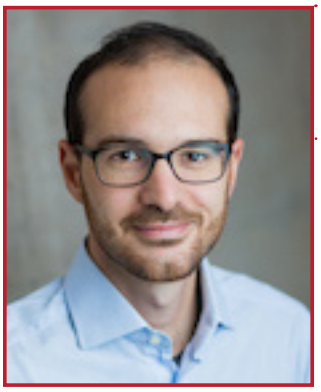
Combining human genomics, *in vitro* studies using primary patient cells, and *in vivo* mouse modeling approaches, her team seeks to gain incisive basic and translational insights starting with patients. Dr. Lucas is an Assistant Professor of Immunobiology at Yale University School of Medicine. She received her PhD from Harvard University, where she investigated T cell tolerance in mouse models, and her postdoctoral training at NIAID/NIH, where she focused on human immunology in monogenic diseases caused by PI3K gene variants.

Oral Presentation: **Cytosolic DNTP catabolism prevents NLRP3 inflammasome overactivation**

@lucasite_lab
Yale School of Medicine
Carrie Lucas Lab

2020 AMANDA PROUDFOOT TRIBUTE GRADUATE STUDENT/POSTDOC AWARD WINNER

This is the Inaugural Amanda Proudfoot Tribute Graduate Student/Postdoc Award for Advances in Chemokine Biology.



MATTEO MASSARA, Ph.D.

Postdoctoral researcher
Prof. Johanna Joyce's Lab
University of Lausanne | Ludwig Institute for Cancer Research
AGORA Cancer Center
Lausanne, Switzerland

Matteo Massara received his Master's degree in Veterinary Biotechnologies with honors in 2014 at the University of Milan.

He started his scientific training at the Experimental Immunopathology Lab supervised by Prof. Cecilia Garlanda studying the role of the negative regulator of inflammation IL-1R8/TIR8 in lymphoma and breast cancer development. Then, he got in 2018 the Ph.D. in Experimental Medicine and Medical Biotechnologies at the University of Milan attending the Laboratory of Leukocytes Biology at Humanitas Clinical and Research Center (Italy) under the supervision of Prof. Raffaella Bonecchi and Prof. Massimo Locati. As PhD student, Dr. Massara contributes to characterize the role of the atypical chemokine receptor ACKR2/D6 in lung metastasis. Dr. Massara is currently a postdoctoral researcher at the Tumor Microenvironment Lab leaded by Prof. Johanna Joyce at University of Lausanne (Switzerland). His scientific activity is focused on fundamental mechanisms of leukocyte recruitment, activation and communication in brain metastasis.

Oral Presentation: **ACKR2 in hematopoietic precursors as a checkpoint of neutrophil release and anti-metastatic activity**

@massara_matteo

2020 SIDNEY AND JOAN PESTKA POST-GRADUATE AWARD WINNER

This Award is generously sponsored by PBL Assay Science, targeted to post-doctoral fellows who have begun to make an impact in interferon and cytokine research.

AUTUMN YORK, Ph.D.

Hanna H. Gray Postdoctoral Fellow
Howard Hughes Medical Institute
Laboratory of Richard Flavell
Department of Immunobiology
Yale University
New Haven, United States

Dr. Autumn York is an HHMI Hanna Gray Fellow in Dr. Richard Flavell's lab in the Department of Immunobiology at Yale University. Her postdoctoral research investigates how the immune system interacts with the body's metabolic pathways to control inflammation and maintain tissue homeostasis.

Autumn received her PhD from University of California, Los Angeles under the supervision of Steven Bensinger, VDM, PhD, where she was a pre-doctoral fellow of the California HIV/AIDS Research Program. During her graduate studies, Autumn delineated a metabolic-inflammatory circuit that linked perturbations in cholesterol biosynthesis with activation of innate immunity via STING/type I interferon signaling. Autumn completed her undergraduate studies with Dr. Dylan Taatjes at University of Colorado- Boulder, where she graduated magna cum laude from the Department of Chemistry and Biochemistry.

Oral Presentation: **Decoding the immunological lipidome**

Yale School of Medicine
@AutumnYork

2020 SIDNEY AND JOAN PESTKA GRADUATE AWARD WINNER

This Award is generously sponsored by PBL Assay Science, targeted to graduate students who have begun to make an impact in interferon and cytokine research.

JACK MAJOR

PhD Student (4th and final year), Francis Crick Institute.
Present Immunoregulation laboratory (student at Imperial College London)
Primary PhD supervisor: Dr Andreas Wack.

Jack is currently a fourth and final year PhD student in the lab of Dr Andreas Wack at the Francis Crick Institute, London.

His graduate research looks at how host antiviral immune responses can be harmful during respiratory viral infection. Specifically, Jack and his co-authors found that type I and III interferons interfere with lung repair during recovery from influenza virus infection, by blocking respiratory epithelial cell proliferation and differentiation. In his infection model, he found that interferon treatment late during the course of infection exacerbates lung damage, which may have implications for ongoing clinical trials testing the efficacy of interferons in treating patients with COVID-19.
Before moving to the Crick institute, Jack completed his undergraduate degree in Immunology at the University of Glasgow, in 2015. He then remained in Glasgow for a year, working as a research technician at the Wellcome Trust Centre for Molecular Parasitology, studying the biology of the apicomplexan parasite Toxoplasma gondii.

Oral Presentation: **Type I and III interferons disrupt lung epithelial repair during recovery from viral infection**

2021 ICIS Awards

ICIS Prestigious Awards for Mid-Career & Senior Researchers

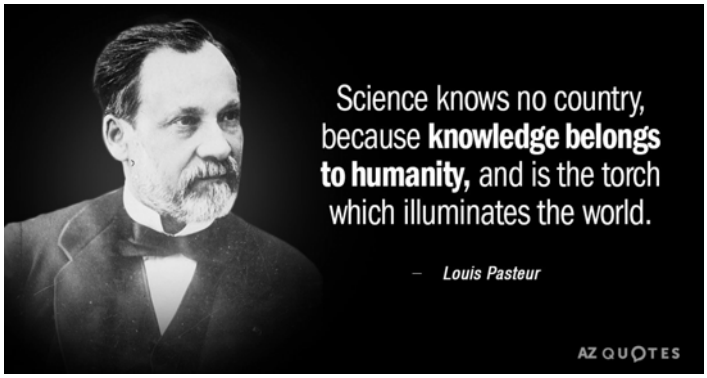
Nomination Submission Form

Nomination Submission Deadline: 20 April, 2021

The ICIS-Pfizer Award for Excellence in Interferon and Cytokine Research (formerly the Seymour & Vivian Milstein Award)

The ICIS-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. This award 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. Sponsored by a generous grant from Pfizer as of 2021.

For more information about the ICIS Award, please **click here**.



ICIS – BIOLEGEND William E. Paul Award for Excellence in Cytokine Research

Sponsored by a generous grant from BioLegend

ICIS-BioLegend William E. Paul Award Winners from 2016 – 2020

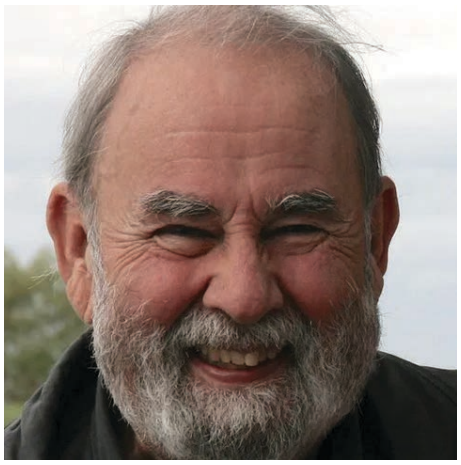
Wiliam E. Paul, MD, (1936–2015)

The ICIS-Biolegend William E. Paul Award for Excellence in Cytokine Research is dedicated to William E. Paul, M.D., who died on September 18, 2015 at age 79. Dr. Paul's extraordinary contributions to the field of cytokine research are best summarized by this paper published in the Journal of Immunology on December 15, 2015. This award was established in 2016 and is given to an investigator that has made significant contributions to cytokine and interferon research throughout their career through the generosity of BioLegend. The award consists of $2,500 and a crystal block with the 3 D structure of IL-4, the cytokine most associated with Dr. Paul's research, as well as up to $2,500 in travel expense reimbursement and complimentary registration to attend and present at the Annual Meeting.

The ICIS-BioLegend William E. Paul Award is bestowed upon a leading biomedical research scientist who has made outstanding contributions to cytokine research, either in a basic or applied field as demonstrated by publications, oral presentations and consistent scientific advancements in cytokine biology throughout their career, through the generosity of BioLegend.

2021 ICIS Awards

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



Luminex®
complexity simplified.

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 to include meeting registration and 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.

2020 Inaugural ICIS-LUMINEX Award Winner

A nominee must be an ICIS member in good standing** who is within 15 years from their terminal degree (Ph.D., M.D., or equivalent). A nominee must be an independent research scientist (PI); postdoctoral fellows are not eligible. Eligibility of the nominee will be checked at time of nomination and before presentation of award.

- Letters of nomination should be sent to the ICIS President via the Submission Form. The nomination package should include a full CV of the nominee and a letter of nomination detailing the accomplishments of the nominee and reasons for the nomination. A candidate may be nominated by more than one ICIS member.

It should be noted that the awardees will be judged based on the following criteria which should be included in the nomination letter:

- outstanding publications and ground-breaking discoveries in the field
- collective contributions to the field of cytokine biology

*This award is intended for a mid-career researcher with a maximum of 15 years post-degree. It is, however, recognized that there may have been family-related, personal, or other circumstances resulting in extended time out of the laboratory. Exceptions to the 15-year limit will be considered based on a description of any special circumstances. Please email with inquiries.

** Member dues paid through the end of 2021.

2021 ICIS Awards

NEW ICIS Mentorship Award

The newly established ICIS Mentorship Award recognizes ICIS members who have made significant and sustained contributions to the career development of trainees and to the profession through outstanding mentoring.

This award is based on the training experiences and success of the nominee's mentees, not the mentor's personal career achievements. For the purpose of this award, mentoring is defined as the process of guiding, supporting, and promoting the training and career development of others. A minimum of three mentees will write a supporting letter on how this person has impacted their development, career and lives, to be submitted together by one of the mentees (an ICIS member). The key roles of a mentor include, but are not limited to, providing:

- Intellectual growth and development
- Career development
- Professional guidance
- Advocacy
- Positive role modeling

Eligibility Criteria:

- To be eligible, the person needs a minimum of three mentees who are willing to write a supporting letter (one page, single spaced) on how this person has impacted their development, career and lives.
- Both the nominee and the corresponding nominator must be ICIS members (not a member, apply today)
- Nominees may include academic, government or industry members
- Nominees should have a sustained record of mentoring over time
- Self-nominations and posthumous nominations will not be accepted.
- Candidates that were nominated in the preceding year but did not win the award are automatically reconsidered as eligible in the ensuing year.
- The nomination must be made by a Regular, Industry or Student/Postdoc Member of the Society and include a minimum of two additional letters of nomination. The winner of this award will be announced at the annual meeting. Awardee will receive an ICIS Crystal and travel costs to attend the Society's Annual Meeting up to $1500, and complimentary meeting registration for the year of the award. Mentees are invited to present the Award to their Mentor at the Annual Awards Ceremony.

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2021 ICIS Awards

ICIS 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. Honorary Life Members are accorded all rights and privileges of active members, are exempted from Society dues and are listed in the dedicated Honorary Life Members section of the Society web site. The winner(s) is elected by vote of the ICIS Council and will be an invited speaker(s) at the next ICIS meeting.

2020 ICIS Honorary Lifetime Membership Awardee
2019 ICIS Honorary Lifetime Membership Awardee

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. Nominations should be communicated to the Awards Committee of the ICIS.

2020 ICIS Distinguished Service Awardee
2019 ICIS Distinguished Service Awardee

2020 AWARD WINNERS

In Memorium

Joseph A. Sonnabend
1933-2021

Pioneering interferon researcher turned AIDS activist

Robert M. Friedman[1] and Jan Vilcek[2]

Front row, from left to right: Robert Friedman, Sam Baron and Joseph Sonnabend in 1964 attending the First International Symposium on Interferon in Smolenice, Czechoslovak

Joseph Sonnabend, a physician, virologist, and multi-talented individual, who participated in pioneering studies on virus replication and on the mechanism of action of interferon died in London on January 24, 2021. He will, however, be best remembered for his activism and contributions to research during the early stages of the AIDS epidemic. His career in general was certainly anything but conventional.

Joseph was born in South Africa but growing up in what is now Zimbabwe, where his Russian-born mother was a practicing physician. His father, a sociologist, was an active Zionist. Joseph lived in a highly cultured atmosphere that endowed him with a love for art and classical music. Throughout his life he played the piano and the organ. He studied medicine at the University of Witwatersrand in Johannesburg, South Africa, and was trained in infectious diseases at The Royal College of Physicians in Edinburgh. He became attracted to virology and interferon research and, in 1961, joined the laboratory group of Alick Isaacs, co-author with Jean Lindenmann of the first description of interferon (1), at the National Institute for Medical Research in London. While working at the NIMR, Joseph contributed to early research on the mechanism of interferon action, establishing that cellular protein synthesis was necessary to its antiviral effect (ref 2, 3). At the time, this was an important finding suggesting that interferon's antiviral action was mediated by newly induced cellular proteins, a fact amply documented in subsequent studies. He also contributed to early research on the mechanism of interferon's inhibition of the replication of arboviruses and poxviruses (4,5).

At the time that Isaacs suffered a severe cerebral hemorrhage in 1964, Joseph contributed significantly to his attempts to keep up his research. Upon Isaacs' death in 1967, Joseph decided to move to the US to assume a position in the Medicine Department of SUNY Downstate Medical School in Brooklyn, NY. He later transferred to the Microbiology Department of the Mt. Sinai Medical School in New York City, where he participated in research on the purification of interferons.

Upon moving to New York, Joseph's original aim was to continue to focus on interferon research. Yet, he was drawn to his original medical specialty of infectious diseases, and in 1977 he established a medical practice in the Greenwich Village neighborhood of New York City. Many of his patients suffered from infectious diseases, especially sexually transmitted infections. These turned out to be among some of the earliest AIDS patients in the US. Among this group, Joseph was highly appreciated for his efforts to treat their multiple clinical problems, including Kaposi's sarcoma and Pneumocystis pneumonia. Once AIDS had been recognized as a major health problem in the early 1980s, Joseph became fully focused on treating patients with AIDS and understanding its etiology and pathogenesis. (This was in the days when AIDS was still referred to as "gay-related immunodeficiency" or GRID. It was not known until 1983 that AIDS is caused by the retrovirus, HIV, nor was it clear at the time that it is a contagious, infectious disease.) Joseph was devoted to his patients, often not billing them for office visits or house calls. He is credited with saving many lives of AIDS patients by treating their Pneumocystis pneumonia with widely available sulfa drugs. Joseph contributed significantly to our understanding of the nature of AIDS. With Stuart Schlossman he found that seriously ill AIDS patients have a marked reversal of their CD4/CD8 ratio and that the loss of CD4 helper T cells accounts for the profound immunodeficiency suffered by these patients (6). Interestingly, Joseph was slow to accept the notion that AIDS is caused by HIV, persisting for some time in his belief that there are multiple factors contributing to its etiology.

Joseph also came up with the idea to look for the presence of interferon in the blood of AIDS patients. He collected blood samples from his patients and invited the co-authors of this obituary to determine if they contained interferon activity. This collaboration led to the discovery that most AIDS patients have in their blood demonstrable levels of an acid-labile form of interferon-alpha (7), a finding corroborated by many subsequent studies. Curiously, the original rationale to look for the presence of interferon in the blood of AIDS patients was not that AIDS is a virus-caused disease—a fact that was not yet known at the time. Rather, it was hypothesized in those days that the underlying cause of AIDS may be some kind of an immune disturbance, and earlier studies showed that the blood of patients with autoimmune diseases, such as systemic lupus erythematosus, contained interferon-alpha (8).

continued on pg 15

[1]Department of Pathology, Uniformed Services University of the Health Sciences, Bethesda, MD 20814 robert.friedman@usuhs.edu

[2]Depoartment of Microbiology, NYU Grossman School of Medicine, New York, NY 10016 jan.vilcek@nyulangone.org

In Memorium

Joseph A. Sonnabend
1933-2021

Pioneering interferon researcher turned AIDS activist

Robert M. Friedman[1] and Jan Vilcek[2]

Front row, from left to right: Robert Friedman, Sam Baron and Joseph Sonnabend in 1964 attending the First International Symposium on Interferon in Smolenice, Czechoslovak

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Inspired by his clinical and research experience with AIDS, Joseph became an outspoken advocate for safe sex for gay men. Together with Mathilde Krim he helped to establish the Foundation for AIDS Research, AmFAR, a leading organization devoted to research and treatment of AIDS.

Joseph spent the last fifteen years of life in London, devoting some of his creative energy to the composition of computer music. One of his compositions was recently performed on the BBC3 music channel.

Acknowledgment. This obituary is also appearing in the Journal of Interferon and Cytokine Research.

References

1. Isaacs, A, and Lindenmann, J, Virus interference. I. The interferon. Proc. Roy. Soc. B 147, 258-267, 1957.
2. Friedman, RM and Sonnabend, JA, Inhibition of interferon action by p-fluorophenylalanine, Nature 203:366-7, 1964.
3. Friedman, RM and Sonnabend, JA, Inhibition of interferon action by puromycin, J Immunol. 95, 696-703, 1965.
4. Friedman, RM and Sonnabend, JA, Inhibition by interferon of production of double-stranded Semliki forest virus ribonucleic acid. Nature 206, 532, 1965.
5. Friedman, RM, Sonnabend, JA, and McDevitt, H, Interferon inhibition of cytoplasmic DNA accumulation in vaccinia virus infection. A radioautographic study. Proc. Soc. Exp. Biol. Med. 119, 551-553, 1965.
6. Wallace JI, Coral FS, Rimm IJ, Lane H, Levine H, Reinherz EL, Schlossman SF, and Sonnabend J, T- cell ratios in homosexuals. (Letter) Lancet, Vol. I, p. 908, 1982.
7. DeStefano E, Friedman RM, Friedman-Kien AE, Goedert JJ, Henriksen D, Preble OT, Sonnabend JA, and Vilcek J, Acid-labile human leukocyte interferon in homosexual men with Kaposi's sarcoma and lymphadenopathy. J Infect Dis 146, 451-9, 1982
8. Preble OT, Black RJ, Friedman RM, Klippel JH, and Vilcek J, Systemic lupus erythematosus: presence in human serum of an unusual acid-labile leukocyte interferon. Science 216, 429-31, 1982.

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. As of April 12, 2021, there are **1,009** ICIS Members as follows: Academic/Government Life Membership (83); Academic/Government Member (381); Emeritus Member (17); Honorary Life Member (46); Industry Member (17); Student PostDoc Three Year Membership (465).

Kristina Adams Waldorf, MD
University of Washington
United States
Sponsoring Member: Michael Gale Jr.
**Academic/Government Life Membership*

Sophie-Marie Aicher, PhD
Infectious Diseases
Institute Pasteur
France
Research Advisor: Nolwenn Jouvenet

Sara Alehashemi, MD, MPH
NIH
United States
Research Advisor: Raphaela Goldbach-Mansky

Jennifer Alexander-Brett, MD, PhD
Washington University
United States

Judith Allen, PhD
University of Manchester
United Kingdom
Sponsoring Member: Christopher Hunter

Milena Andzelm, MD, PhD
Harvard Medical School
United States
Research Advisor: Steven McCarroll, Kevin Eggan

Moshe Arditi, MD
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Ralph S. Baric, PhD
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Catherine Blish, PhD
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Rytis Boreika, MSc
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Fernando Botelho, PhD
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AFRRI
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Theresa Theresa Chang, PhD
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Wei Chen
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Hachung Chung, PhD
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Sara Danielli, DPhil
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Research Advisor & Sponsoring Member: Jelena Bezbradica Mirkovic

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Luxembourg

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Marlène Dreux, PhD
INSERM CIRI immunovirology
France

Julie Eggenberger
University of Washington
United States
Research Advisor & Sponsoring Member: Michael Gale, Jr.

NEW ICIS MEMBERS

Continued

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Daniel R. Fox, PhD
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Research Advisor & Sponsoring Member: Si Ming Man

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Elisha Johnston
High School Student!!!
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Diamantina Institute
Australia

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Steven Ziegler

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Heather Clark

Dan Lazar, PhD
Promega Corporation
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Professor Kingston Mills

Ailing Lu, PhD
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Research Advisor: Kevin Urdahl
Sponsoring Member:
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Jack Major
Imperial College London
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Sponsoring Member:
Andreas Wack

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Lisa Miorin, PhD
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Maryam Mukhamedova, PhD
NIH
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Howard Young

Masato Okada, MD
Immuno-Rheumatology Center, St. Luke's International Hospital,
Japan
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University of GA
United States
Research Advisor:
Kim Klonowski

NEW ICIS MEMBERS

Continued

Andrew Olive, PhD
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United States

R Rex Parris,
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United States

Venuprasad Poojary, PhD
UT Southwestern
United States

Rebecca Amelia Ruth Porritt, PhD
Cedars Sinai Medical Center
United States

Jennifer A Rathe, MD PhD
Seattle Children's Hospital / University of Washington
United States
Sponsoring Member: Michael Gale Jr.

Clifford Rostomily
Institute for Systems Biology
United States
Research Advisor: Naeha Subramanian

Gregory Seumois, PhD
La Jolla Institute for Immunology
United States

Hao Shi, PhD
St. Jude
United States
Sponsoring Member: Xingrong Du

Tomasz Skirecki, MD, PhD
Centre of Postgraduate Medical Education
Poland

Jamie Berta Spangler, PhD
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James Steinhardt, PhD
AstraZeneca
United States

Caleb Stokes, MD, PhD
University of Washington
United States
Sponsoring Member: Michael Gale Jr.

Hiromichi Tamaki, MD
St. Luke's International Hospital
Japan
Sponsoring Member: Masato Okada
*Academic/Government Life Membership

Niamh Troy, PhD
Telethon Kids Institute
Australia
Research Advisor: Anthony Bosco

Samantha Truex
Quench Bio
United States

James Turkson, PhD
Cedars-Sinai Medical Center
United States
*Academic/Government Life Membership
Cytokines 2021 Program Chair

Rachel Van Gelder, PhD
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Research Advisor & Sponsoring Member: Ram Savan

Antonia Wallrapp,
Harvard Medical School and Brigham and Women's Hospital
United States
Research Advisor: Prof. Dr. Vijay K. Kuchroo

Elizabeth White, PhD
University of Pennsylvania
United States

Gregory D. Wiens, PhD
USDA/ARS
United States

Autumn York, PhD
Yale University
United States
Sponsoring Member: Richard Flavell

Melody Zeng, PhD
Weill Cornell Medicine
United States

New Member MINIBIOs

James Turkson, PhD
(Chair of Cytokines 2022 in Hawaii)
Professor, Department of Medicine, Division of Medical Oncology
Associate Director of Strategic Partnerships
Cedars-Sinai Medical Center, Los Angeles, CA USA

Dr. James Turkson joined Cedars-Sinai Medical Center in Los Angeles, CA, in July 2019 as a Professor in the Department of Medicine, Division of Medical Oncology, and he currently also holds the position of Associate Director of Strategic Partnerships at the Cedars-Sinai Cancer Center. He earned his honors BS degree in Biochemistry with Chemistry at the University of Ghana, Legon, Ghana, and PhD in Pharmacology at the University of Alberta in Edmonton, Alberta, Canada, and he completed postdoctoral fellowship training in Molecular Oncology/Drug Discovery at the H. Lee Moffitt Cancer Center and Research Institute, an NCI-designated Comprehensive Cancer Center in Tampa, FL in 2000. Dr. Turkson accepted his first faculty position as an Assistant Professor in Molecular Oncology/Drug Discovery at the Moffitt Cancer Center from 2000-2005, and then joined the Burnett School of Biomedical Sciences in the new College of Medicine at the University of Central Florida, Orlando, FL, as an Associate Professor from 2005-2011. He was subsequently recruited as a Full Professor with tenure to the University of Hawaii Cancer Center, an NCI-designated Cancer Center in Honolulu, Hawaii from 2011-2019, where he held various leadership positions as the Cancer Biology Program Director, Director of the Natural Products Program, Director of Technology Development, Chief Academic Lead, and Basic Science Senior Leader. An internationally recognized leader in STAT signaling and cancer, Dr. Turkson played a leading role in establishing the causal relationship between aberrantly-active STAT3 and oncogenesis. He is credited for the early validation of STAT3 as a novel anticancer target, and he led the research to discover the first small-molecule/peptide inhibitors of STAT3 in the early 2000's, and thereby establishing the proof-of-concept for STAT3 inhibitors as potential anticancer agents. The Turkson laboratory maintains a vibrant research program on STAT3 inhibitor discovery and development, with a strong team of medicinal chemists, cancer cell biologists, structural biologists, computational chemists, and experts in drug discovery research. Short term focus of his current laboratory is on the advanced STAT3 inhibitor lead optimization and the selection of clinical candidate(s) for advancement into clinical trials. In the longer term, the program continues to intensify medicinal chemistry efforts on other lead compounds. Other robust research programs in the lab focus on the optimization of natural product inhibitors of STAT3 as potential new treatments for breast and brain tumors, and on the application of small molecules and natural products as chemical probes to interrogate cancer pathways for novel mechanistic insights. He is currently also leading all drug discovery/development efforts at Cedars-Sinai Cancer Center.

Moshe Arditi, M.D.
Executive Vice-Chair, Department of Pediatrics for Research
Professor of Pediatrics, Cedars Sinai Medical Center and UCLA School of Medicine
Director, Division of Pediatric Infectious Diseases and Immunology,
Director, Infectious and Immunologic Diseases Research Center (IIDRC), Department of Biomedical Science, Cedars Sinai Medical Center, Los Angeles, CA, USA

Moshe Arditi, MD, is the executive vice-chair of the Department of Pediatrics for Research and the director of the Pediatric Infectious Diseases and Immunology Division at Cedars-Sinai. He is also director of the Infectious and Immunological Diseases Research Center in the Department of the Biomedical Sciences and a member of the Cedars-Sinai Smidt Heart Institute. The Arditi Laboratory has received National Institutes of Health (NIH) funding continuously for the past 24 years. The broad focus of the group is on innate immunity and host-pathogen interactions as they relate to acute and chronic inflammatory diseases. A major research focus of Arditi and his team is the discovery of the immunopathologic mechanisms that drive the development of cardiovascular lesions in Kawasaki disease vasculitis. The group uses a well-established and accepted experimental mouse model of Kawasaki disease vasculitis that recapitulates the coronary arteritis, abdominal aorta dilation, aneurysms, and myocarditis observed in human patients. Arditi was the first to discover that the intracellular signaling molecules in LPS-TLR4 signaling in endothelial cells are the same molecules that are used by IL-1b, including MyD88 (JBC, 1999). He discovered the role of TLR4 in atherosclerosis (PNAS, 2004), and made the seminal discovery that mitochondrial oxidative DNA damage plays a key role in the induction of NLRP3 inflammasome and secretion of IL-1beta (Immunity, 2012). Arditi's seminal findings using this experimental mouse model demonstrated the key role of IL-1 beta in the cardiac manifestations of Kawasaki disease and led to ongoing phase II clinical trials using anti-IL-1 therapies in children with Kawasaki disease who are unresponsive to IVIG therapy. The Arditi lab also investigates the innate and adaptive immune mechanisms that contribute to atherosclerosis, including infection-mediated acceleration of atherosclerosis, the role of mitochondrial oxidative DNA damage, activation of the NLRP3 inflammasome, and the IL-1beta pathway. A recent discovery made by his laboratory includes the role of mitochondrial oxidative DNA binding and activating NLRP3 inflammasome for IL-1beta release. He is also pursuing the mechanisms for gender differences in inflammatory diseases, such as Kawasaki Disease vasculitis and atherosclerosis, as well as responses to therapy that may be gender-dependent. He and his collaborators at the University of Pittsburgh discovered the SARS-CoV2 Superantigen-like motif at the furin cleavage site of the spike protein that may bind TCR and MHCII to induce cytokine storm and may play a role in post-acute COVID-19 hyperinflammatory syndromes, such as MIS-C and MIS-A. Dr. Arditi has authored and co-authored more than 166 original articles in peer-reviewed publications. He is the recipient of the 2019 Pioneer of Medicine Award at Cedars-Sinai Medical Center.

New Member MINIBIOs *Continued*

Rebecca Porritt, PhD
Research Scientist I, Department of Pediatrics and Biomedical Sciences
Assistant Professor of Pediatrics, UCLA School of Medicine
Cedars-Sinai Medical Center, Los Angeles, CA, USA

Dr. Porritt is a faculty research scientist in the Departments of Pediatrics and Biomedical Sciences at Cedars Sinai Medical Center, Los Angeles. Dr. Porritt's research focuses on understanding the immunopathogenesis of vasculitis diseases including Kawasaki Disease vasculitis and more recently Multisystem Inflammatory Syndrome in Children (MIS-C), which has emerged with the COVID-19 pandemic. Dr. Porritt received her doctorate at the Hudson Institute of Medical Research, Australia, under the mentorship of Prof. Paul Hertzog and joined the Department of Pediatrics at Cedars Sinai Medical Center in 2016 as a postdoctoral researcher under the mentorship of Prof. Moshe Arditi. Dr. Porritt takes a translational approach to understand Kawasaki Disease vasculitis, drawing hypothesis from human data and applying these to murine models to identify targeted therapeutics to prevent cardiovascular lesion development. Recently, Rebecca's work has focused on immune-stromal interactions driving KD cardiovascular lesion development and sex differences in disease. Dr. Porritt's work on MIS-C has identified a unique HLA class I associated TCR signature in the severe form of the disease and is currently working to understand how these T cell responses may mediate disease pathogenesis.

De'Broski R. Herbert Ph.D.
Associate Professor of Immunology
University of Pennsylvania, PennVet
Philadelphia, PA USA

The Herbert laboratory explores the cellular and molecular regulatory networks controlling the inflammation that drives host protective immunity and tissue repair in humans and rodents infected with parasites. This research program is particularly focused on parasitic helminths, which are a major cause of morbidity in human populations and agricultural animals across the globe. The body of literature generated by this program has provided foundational insight(s) into the host-parasite interaction regarding the development of M2 macrophages, eosinophil effector functions, Type 2 innate lymphocytes (ILC2), and conventional T helper 2 cells (TH2). In recent years, we have turned our focus to the major gaps in understanding Trefoil factor (TFF) biology. TFFs (TFF1-3) are a family of small (6-14kDa) tissue reparative cytokines known to drive tissue repair through regulation of mucus viscosity, epithelial cell adhesion molecule expression, and cell survival. The biology that we are uncovering behind this discovery stands to impact the fields of parasite immunology, mucosal immunology, and regenerative medicine. The Herbert laboratory has active ongoing projects focused on human helminth infection, dendritic cells as unconventional cellular sources of IL-33, Wnt pathway signaling and transgenesis in parasitic nematodes to study the basic tenets of antigen-specific CD4+ T cell biology. Overall, this research program is focused on the cellular and molecular mechanisms operating at the mucosal interface in health and disease.

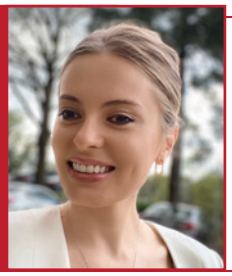
Kristina Adams Waldorf, MD
Professor, Obstetrics & Gynecology and Global Health
UW Medicine, Seattle, WA USA

Dr. Kristina Adams Waldorf is a Professor in the Departments of Obstetrics & Gynecology and Global Health at the University of Washington and an Affiliate Professor at the University of Gothenburg. She has studied bacterial and viral infections in pregnancy, maternal-fetal immunity, and therapeutics to prevent preterm birth and fetal injury for nearly 20 years. She is funded by the National Institutes of Health, the Canadian Institute for Health Research, and the Australian National Health Medical Research Council. She is a core scientist at the Washington National Primate Research Center and a member of the University of Washington Center or Innate Immunity and Immune Diseases. She is a member of the National Institutes of Child Health and Human Development Obstetrics & Maternal-Fetal Biology Study Section.

New Member MINIBIOs *Continued*

Wei Chen, PhD
Postdoctoral Fellow
NIH/NCI
1649 E Jefferson St
Rockville, MD USA

Dr. Chen received his B.A and the veterinary medicine degree from Jilin University (JLU) in China. He trained in microbiology from the Institut Pasteur of Shanghai, Chinese Academy of Sciences (IPS-CAS) and got his Ph.D degree here. He then started a tumor immunotherapy fellowship in Dr. Thomas A. Waldmann's lab at the National Cancer Institute (NCI). Dr. Chen conducts basic research and pre-clinical research to develop IL-15 and anti-CD40 augment mAb therapies for prostate cancer with intratumorally administration.



Maryam Mukhamedova, PhD
Post-Doctoral Fellow
Vaccine Research Center, NIAID, NIH, USA

Maryam Mukhamedova is a post-doctoral fellow at the Vaccine Research Center, NIAID, NIH, USA in Dr. John Mascola's Virology laboratory. She defended her thesis entitled "Genetic Characterization of Antibody Responses After Vaccination with a Prefusion-Stabilized Respiratory Syncytial Virus (RSV) Fusion (F) Protein Vaccine (DS-Cav1)" from the Johns Hopkins University partnership program with NIH in 2021. Maryam enjoys the outdoors, making graphical designs, and spending time with her family.

Elisha Daniel Johnston
Education: Joseph Lister High School for Biomedical Sciences and Technology (Class of 2021)

Elisha Johnston passionately researches solutions for reducing chronic pain, especially osteoarthritis. As a high school student, his focus is at the molecular and cellular biology level. His career goal is to become a physician-scientist, helping people through both clinical practice and clinical research. His research on regenerative medicine has appeared, or is forthcoming, in several peer-reviewed journals. Elisha enjoys volunteering for the Arthritis Foundation and was a 2020 Rookie Champion for his community service, presented by the Los Angeles Team of the Arthritis Foundation. He has already won 24 scientific achievement awards sine 2014, including his most recent awards:

HONORS AND AWARDS

- 2020 Regeneron Science Talent Search (STS) Scholar
- 2020 International Science & Engineering Fair (Regeneron ISEF), Cell and Molecular Biology, Finalist
- 2020 International BioGENEius Challenge, Finalist
- 2020 Arthritis Foundation, Rookie Champion Award (Presented Feb 9, 2020 by Los Angeles Team)
- 2020 Southern California BioGENEius Challenge, 1st Place
- 2020 Los Angeles County Science Fair, Pharmacology, 1st Place

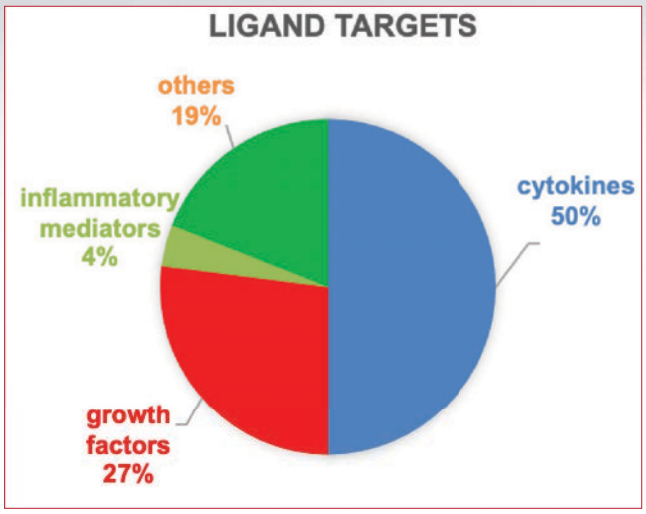
A selection of some of Elisha's scientific accomplishments so far:

- **Peer-Reviewed Articles**
  - Johnston ED, Emani C, Kochan A, Ghebrehawariat,K, Tyburski J; Johnston, M; Rabago D (2020) Prolotherapy Agent P2G Is Associated with Upregulation of Fibroblast Growth Factor-2 Genetic Expression In Vitro; Journal of Experimental Orthopaedics 7: 97.
    https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7719583/
  - Johnston ED, Andrali SS, Kochan A, Johnston M, Lovick J (2017) Prolotherapy-Induced Cartilage Regeneration: Investigating Cellular-Level Mechanisms of Action with Mouse Preosteoblast Cells. JSM Biochem Mol Biol 4(3): 1032.
    https://www.jscimedcentral.com/Biochemistry/biochemistry-4-1032.pdf
  - Johnston ED, Taw L, Lovick JK, Johnston M, Burns P, Prelip M. (2016) Suggestive Evidence Indicates Organic Chicken has a Greater Amount of Protein with the Full Range of Essential Amino Acids. J Hum Nutr Food Sci 4(3): 1091.
    https://www.jscimedcentral.com/Nutrition/nutrition-4-1091.pdf
- **Conference Paper**
  - Johnston ED Western Users of SAS Software, Sept 4-6, 2019 (Seattle WA): "Polynomial Regression for Modeling Curvilinear Data: A Biological Example"
    https://proceedings.wuss.org/2019/207_Final_Paper_PDF.pdf
- **Abstracts**
  - Johnston ED and Tyburski J. (2020) Improving Translatability of an in vitro Model for Studying Hypertonic Dextrose Induced Cartilage Regeneration. In Vitro Cellular and Developmental Biology
    https://doi.org/10.1007/s11626-020-00474-1
  - Johnston ED and Emani C. (2020) Prolotherapy upregulates Fibroblast Growth Factor-2 (FGF-2) and Insulin-like Growth Factor-1 (IGF-1) mRNA which may Increase Chondrocyte Proliferation and Mediates Osteoarthritic Inflammation. The FASEB Journal (Published Abstract from the 2020 Experimental Biology Conference)
    https://doi.org/10.1096/fasebj.2020.34.s1.09039
  - Johnston ED and Tyburski J (2020) Hypertonic Dextrose Stimulates Chondrocyte Proliferation and Collagen Deposition in vitro. Molecular Biology of the Cell (Published Abstract from the 2020 American Society for Cell Biology Conference)
    https://doi.org/10.1091/mbc.E20-10-0665

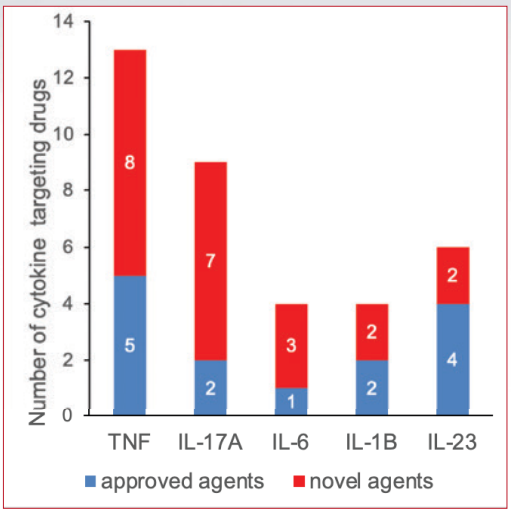
SPOTLIGHT

INDUSTRY NEWS

by Supreet Agarwal



Cytokines represent the major class of all the soluble ligands targeted by FDA-approved drugs



Major cytokines' (interferons, interleukins and chemokines) targeted therapies

Figures adapted from:

Attwood, M.M., Jonsson, J., Rask-Andersen, M. et al. Soluble ligands as drug targets. Nat Rev Drug Discov 19, 695–710 (2020). https://doi.org/10.1038/s41573-020-0078-4

Cytokines based therapies approved in 2020

Two new treatments for patients with a condition called, **deficiency of interleukin-1 receptor antagonist**, a very rare genetic inflammatory condition resembling an infection throughout the body or a bone infection that happens in newborns during the first days of life.

Arcalyst (rilonacept), [see also, Kineret, below], injection, originally approved in 2008 to treat patients with different forms of cryopyrin-associated periodic syndrome, which is a rare hereditary inflammatory disorder with symptoms that can include HIV-1-like rash, fatigue, headache, fever, pain and swelling in joints, and red eyes. In 2020, this drug was also approved for the treatment of patients with **deficiency of interleukin-1 receptor antagonist**, a very rare genetic inflammatory condition resembling an infection throughout the body or a bone infection that happens in newborns during the first days of life.

Kineret (anakinra) [see also, Arcalyst, above], injection, first approved by CDER in 2001 to treat certain patients with active rheumatoid arthritis. It was approved in 2020, for the treatment of patients with **deficiency of interleukin-1 receptor antagonist**, a very rare genetic inflammatory condition resembling an infection throughout the body or a bone infection that happens in newborns during the first days of life.

Source: https://www.fda.gov/drugs/new-drugs-fda-cders-new-molecular-entities-and-new-therapeutic-biological-products/new-drug-therapy-approvals-2020

Other links for cytokine-based therapies – approved to date and in trial https://go.drugbank.com/categories/DBCAT000079

34th Annual Conference: Macrophages and dendritic cells in infection and inflammation, Virtual Meeting June 24-25

EMDS 2021

Due to the Covid-19 pandemic preventing us to meet in person, the 34th EMDS conference has been converted into an online meeting.

The Abstract submission portal is open. Deadline for submission of abstract: **30 April 2021**.

Deadline for registration: 31 May 2021.
Click here for more Information.

Simon A Jones
(Chair) Cardiff University
Wales, UK

A Hybrid Experience: In-person and Online Presentations & Sessions

Our annual gatherings of investigators from academia, government, and industry offer exciting opportunities for you to discuss the latest breakthroughs in cytokine and interferons biology. Accommodating scientists from diverse biomedical backgrounds, the conference has an established tradition of showcasing major scientific discoveries affecting societal health and wellbeing. We very much look forward to continuing this strong tradition in Cardiff this coming October.

The global pandemic continues to impact us all. During these challenging times, our society is actively striving we maintain strong links with the research community. For those unable to travel, the virtual meeting platform offers delegates excellent opportunities to engage with the meeting format and attendees. Providing an outstanding forum for investigations in basic science and clinical research, we have invited an impressive collection of speakers presenting exciting findings affecting cytokine involvements in infection, cancer, allergy, autoimmunity, and the wider aspects of immune-mediated disease. We are also encouraging updates on novel therapeutic interventions in the field and working with other societies to pioneer collaborations with industrial partners and international participants.

The hybrid format for Cytokines2021 will blend the physical experience at the Cardiff City Hall in the Centre of Cardiff, with a custom designed LabRoots Virtual Meeting platform. Facilitating a unique experience for in-person delegates and the virtual community, Webcast video presentations will be intertwined with in-person presentations and live sessions. These will include virtual interactions, live commentaries, online chat & video chat discussions, and a photo booth for those impromptu social interactions and memories. Whether your attendance is in person or virtual, we very much hope you will continue to submit your latest research for discussion. The Cytokines 2020 Virtual Meeting exceeded our expectations, and we are confident that the Hybrid Meeting format will continue to form part of the planning of all future meetings. Thus, ensuring our ability to disseminate the latest research advancements in cytokine biology around the world, and keeping us all connected.

We very much hope to see you all in Cardiff later this year, and I hope you and your families remain healthy and safe in these challenging times.

Local Organizing Committee

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

International Scientific Advisory Committee

- **Evangelos Andreakos**, Laboratory of Immunobiology, Biomedical Research Foundation, Academy of Athens, Greece
- **Yvonne Bordon**, Nature Reviews Immunology, UK
- **Andrew Bowie**, Trinity College Dublin, Ireland
- **Ernest Choy**, Cardiff University, Wales, UK
- **Marcus Feige**, TUM, Germany
- **Kate Fitzgerald**, University of Massachusetts, USA
- **Trude Flow**, Norwegian University of Science and Technology, Norway
- **Brian Fritz**, 10x Genomics, USA
- **Sarah Gaffen**, University of Pittsburgh, USA
- **Christian Holm,** Aarhus University, Denmark
- **Christopher Hunter**, University of Pennsylvania, USA
- **Brendan Jenkins,** Hudson Institute of Medical Research, Australia
- **Gareth W. Jones**, University of Bristol, UK
- **You-Me Kim**, Korea Advanced Institute of Science and Technology, South Korea
- **Carolina López**, Washington University in Saint Louis, USA
- **Ignacio Moraga Gonzalez**, University of Dundee, Scotland, UK
- **Sandra Nicholson**, Walter and Eliza Hall Institute of Medical Research, Australia
- **Anne O'Garra**, Crick Institute, UK
- **Stefan Rose-John**, University of Kiel, Germany
- **Ram Savan**, University of Washington, USA
- **James Turkson**, Cedars-Sinai Samuel Oschin Comprehensive Cancer Institute, USA
- **Irina Udalova**, University of Oxford, UK
- **Hiroki Yoshida**, Saga University, Japan

Preliminary List of Session Topics

- Cytokines in cellular metabolism and immune homeostasis
- Designer cytokines and cytokine immunotherapy
- Tissue homeostasis and barrier immunity
- Cytokines in anti-viral immunity
- Epigenetic control of cytokine responses
- Mechanisms of cytokine release syndromes
- Single cell analysis of inflammatory outcomes
- Understanding multimorbidity in chronic disease
- Cancer inflammation
- Mechanisms of interferonopathies
- Determinants of disease heterogeneity
- Cytokines in allergic reactions
- Cytokines in psychoneuroimmunology and pain
- Stromal tissue as orchestrators of disease outcome
- Determinants of cell fate
- Repurposing of biological therapies
- Advances in precision medicine
- Systems approaches in precision medicine

Cardiff City Hall, within short walking distance of the City centre and hotels, offering superb shopping and located adjacent to Cardiff Castle and Cardiff University

Cardiff's City Hall stands in what has been acclaimed as one of the finest civic centres in Europe – located in the heart of the city of Cardiff, 4-minute walk to hotels, between Cardiff University and Cardiff Castle, the magnificent Edwardian City Hall, built in the English Renaissance style, was opened in 1906, a year after Cardiff was granted its city status. Within the magnificent exterior carved from Portland stone can be found elegant rooms to meet the expectations of conference, function and event organisers. This majestic building offers a spacious venue for large-scale events yet smaller rooms are also available for more intimate gatherings and syndicate sessions. However, behind its magnificent facade and glorious interiors you will find that City Hall can accommodate state of the art conferencing and hi-tech communications systems.

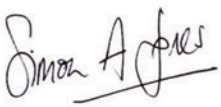
Tabletop Exhibits will be set up in the Marble Hall between all the meeting rooms. Virtual and Live exhibit booth engagement will be available through the LabRoots Virtual Meeting platform.

Historic Coal Exchange Hotel on Cardiff Bay, Tuesday evening Networking Event venue.

Luke O'Neill's band, the Metabollix with special guests, will be playing live at the Cytokines2021 Networking event and will be live streamed from the historic Coal Exchange Hotel to our virtual audience through our virtual networking lounge pictured above.

Please visit the website to view the updated program and confirmed speakers, plan to submit abstracts and award applications by **June 1** and encourage your colleagues to join us. I very much hope to see you all in Cardiff next year, and I hope you and your families are healthy and safe in these challenging times.

Best regards,



Professor Simon A Jones
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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

IMMUNOTHERAPY

Engineering cytokines and cytokine circuits

Learning to speak the secret language of immune cells could improve immunotherapies

By **Aileen W. Li**[1,2] *and* **Wendell A. Lim**[1,2,3]

Cytokines have far-reaching effects on the behavior of immune cells. Given their powerful roles, there has been a long history of trying to harness cytokines as therapeutic drugs for cancer and other diseases. However, there are several problems that severely limit the therapeutic use of cytokines, including their pleiotropic actions and systemic toxicity. Overcoming these issues to create the next generation of cytokine-based therapies will require sophisticated control over their spatial-temporal function. New approaches in protein and cell engineering are emerging that allow distinct and multiple levels at which to program cytokine regulation—from engineering individual cytokines, to cytokine-receptor pairs, and ultimately, more complex cytokine-sensing, -secreting, and -consuming cell circuits. These technologies may confer the ability to precisely sculpt the local cytokine environment, and by doing so, improve the potency of cytokine drugs and deepen our understanding of the language of cytokine communication.

The biological function of cytokines is broad, encompassing immune cell proliferation, death, activation, and inhibition. The effects of these secreted signaling molecules depends on their local concentration, which is driven by the rates of cytokine production, diffusion, and consumption. Cytokine-mediated cell-cell communication can be autocrine, paracrine, or endocrine. Together, these core features of cytokine communication are thought to shape the ecosystem of specific tissues or tumors. Perhaps most notable is how this set of secreted factors can achieve such diverse yet highly spatially coordinated physiological outcomes within the complex environment of the body.

Interleukins and interferons are cytokines that have clinical relevance in cancer. Direct infusion of cytokines into a tissue can have potent therapeutic effects—killing transformed cells in a tumor or stimulating the expansion and cytotoxic activities of host or adoptively transferred immune cells. So far, two cytokine drugs [interferon-α (IFN-α) and interleukin-2 (IL-2)] have been approved by the U.S. Food and Drug Administration (FDA) for the treatment of hairy cell leukemia, melanoma, and other cancers.

Nonetheless, there are fundamental problems that severely limit the therapeutic use of natural cytokines: short circulation half-life, off-target effects, and inherent pleiotropic functions. Clinically, repeated systemic administration of IL-2 at high doses is typically needed to achieve therapeutic response as a result of its short circulation half-life (the serum half-life of IL-2 is ~90 min). Most seriously, cytokines act as a double-edged sword—they target many cell types. Thus, for example, high dosing regimens of IL-2 elicit severe systemic toxicity because the cytokine accumulates not only in the disease tissue, but also in healthy bystander organs, where IL-2 induces severe adverse effects including vascular leak syndrome and pulmonary edema (*1*). IL-2 causes many changes in immune cells, some that may be desired and some that are therapeutically detrimental. IL-2 acts on multiple immune cells—it drives proliferation of effector T cells, but also stimulates T regulatory cells (T_{reg}) that cause suppressive outcomes. T_{reg} stimulation can promote tumor growth by serving as an IL-2 cytokine sink to deplete the growth factor necessary for effector T cell–mediated antitumor activity, and by directly disarming effector T cells.

Much of the existing efforts to engineer improved cytokines have focused on IL-2 because of its long history as a cancer therapeutic target. A more-conventional chemical strategy is to attach IL-2 to moieties such as polyethylene glycol (PEG) to extend its serum half-life. PEGylating IL-2 creates an IL-2 prodrug that mitigates rapid systemic activation upon administration by hindering receptor binding. Once the PEG is slowly released from the prodrug, the active free IL-2 becomes bioavailable over time (*2*). This modified IL-2 showed significantly longer serum half-life and was well tolerated in recent phase 1 trials in patients with advanced solid tumors (NCT02983045). Similarly, a PEGylated form of IFN-α showed longer half-life, and was approved by the FDA for the treatment of melanoma. Nonetheless, current evidence suggests that these approaches do not sufficiently address the major challenges of systemic toxicity and pleiotropic action.

Creating the next generation of cytokine-based therapies that address pleiotropic toxicity will require far greater control over cytokine function. Advances in protein and cell engineering are emerging that provide multiple new levels at which to program the time and space of cytokine-driven immune responses (see the figure). Protein engineering and screening have allowed investigators to more rationally engineer synthetic cytokines with selective bias toward a desired function. Pioneering studies using phage display screens created a human growth hormone (hGH) mutant that bound ~400 fold more tightly to its receptor than the wild-type form (*3*). Following this example, most cytokine engineering strategies use a combination of directed mutagenesis and library-based screens. For instance, an IL-2 mutant (BAY 50-4798) with reduced affinity for IL-2 receptor-β (IL-2Rβ) showed preferential activation for T cells over natural killer (NK) cells (which can cause toxicity) 3000-fold higher than the wild-type IL-2 (*4*). Even though this mutant was shown to be less toxic when tested in preclinical models, phase 1 trials in patients with metastatic melanoma or renal cancer failed to show significant benefit or reduction in side effects over IL-2 (*5*), likely because multiple IL-2–responsive populations can contribute to toxicity.

In a different approach, a superagonist form of IL-2, called "Super2," was engineered to have increased binding affinity for IL-2Rβ, rationalizing that it would preferentially trigger naïve T cells that are otherwise insensitive to IL-2 owing to their low expression of IL-2Rα (which stabilizes IL-2 interaction with IL-2Rβ). Indeed, Super2 showed superior expansion of cytotoxic T cells relative to regulatory T cells than did IL-2 and also reduced pulmonary toxicity in preclinical tumor models (*6*). Building on this work, an entirely new cytokine termed "neo-2/15" was designed in silico that signals through the shared chains of IL-2 and IL-15 receptors (the heterodimer of IL-2Rβ and IL-2Rγc) but has no binding sites for their respective private chains (IL-2Rα and IL-15Rα). Bypassing the private receptors allows neo-2/15 to preferentially signal to antitumor lymphocytes. In preclinical tumor models, neo-2/15 shows superior therapeutic activity to IL-2 and reduced toxicity (*7*). Recent efforts in cytokine engineering have also resulted in a "decoy-

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resistant" IL-18 (DR-18), which maintains native IL-18 signaling but is impervious to inhibition by IL-18 binding peptide (IL-18BP), an endogenous secreted antagonist for wild-type IL-18 (*8*). Unlike IL-18, DR-18 showed effective antitumor effects in mice resistant to immune-checkpoint therapies. Clinical examples of designer cytokines include Pitrakinra, an engineered IL-4 variant that acts as an antagonist. In completed phase 2 trials, Pitrakinra showed some benefits for treating IL–4-associated asthma, with fewer adverse events (*9*).

A more radical emerging approach to limiting detrimental cytokine action is to engineer orthogonal cytokine-receptor pairs. This approach entails changing both the cytokine molecule and the way a target cell recognizes the engineered cytokine—an approach that fits well with engineered immune cell therapies [such as adoptive transfer of chimeric antigen receptor (CAR) T cells], which already involves a commitment to engineering a target effector immune cell. For example, to precisely target IL-2 functions to specific target T cells, an orthogonal IL-2/IL-2R pair (ortho2 and ortho2R, respectively) was developed (*10*). Ortho2 is a mutant IL-2 that can no longer bind to the native IL-2R; similarly, ortho2R is a mutant IL-2R that does not recognize the native IL-2. The ortho2/2R pair are engineered to only interact with each other. Thus, ortho2 stimulates only the complementary T cells that have been engineered to express ortho2R. Although engineering perfect orthogonal pairs with wild-type like potency remains a challenge, this pioneering work shows the power of the approach. In mouse models, ortho2 cytokine-receptor pairs show a high degree of specificity and orthogonality in vivo, suggesting that ortho2 may be a powerful tool to precisely control the proliferation of engineered cells while remaining inert to the endogenous immune system. This concept can be broadly applied to other cytokines and could be used to control CAR T cells or any other engineered therapeutic cell.

Moving beyond cytokines that already exist in nature, non-natural cytokines, or "synthekines," have also been described (*11*). These synthekines do not bind to natural cytokine receptor pairings, but instead assemble non-natural receptor heterodimers that lead to previously undescribed responses. Together, these important advances demonstrate the possibility of going beyond the proteins that our genomes naturally encode and open exciting therapeutic opportunities.

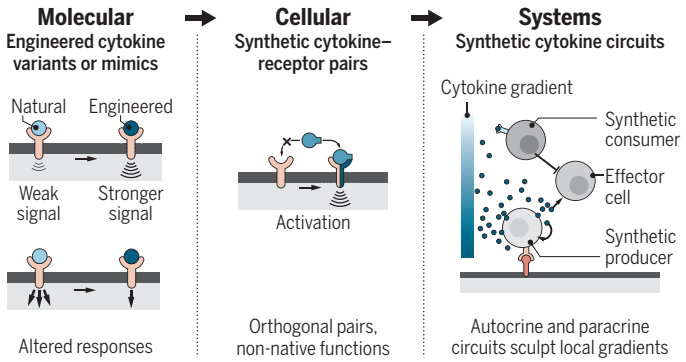
An even higher level of emerging engineering involves the creation of new multicellular cytokine systems and circuits. The highly localized action of cytokines originates from the ability of specific cells to read local signals that control both the production and consumption of cytokines—in essence, the immune system sculpts spatial gradients and niches using source and sink cells (in addition to effector cells that read the gradients) (*12*). With our mechanistic understanding of cellular biology and cell-cell communication, it may now be possible to rationally sculpt cytokine gradients, using cells that are synthetically engineered to act as sources and sinks. Engineering such gradients will likely require dynamic and discrete combinations of agonists and antagonists in the forms of cytokines, inhibitors, and cytokine receptors.

An early approach to engineering "source cells" has been to design CAR T cells to express proinflammatory cytokines (e.g., IL-12), either constitutively or under a CAR-controlled promoter (*13*). Engineering of cytokine consuming "sink" cells can also be a complementary powerful tool for sculpting cytokine milieus. A recent example of this nascent concept is engineered T cells constitutively expressing a nonsignaling membrane-bound IL-6R to effectively deplete IL-6 and thus reduce IL-6–mediated toxicity in mice (*14*). More controlled approaches are emerging in which modular sensing receptors, such as synNotch receptors (*15*), can be used to induce cytokine secretion or consumption in response to local disease or tissue antigen signals, yielding the potential of highly localized and programmable sink or source cells. Such engineered cellular delivery systems may offer one of the best ways to autonomously target and modulate local disease environments (including metastases) to drive antitumor responses and to remodel immunosuppressive responses, especially when combined with engineered autocrine or paracrine signaling that can locally amplify activity through positive feedback. Conversely, similar approaches could be used to create locally suppressed microenvironments in the case of autoimmunity.

These concepts are still at an early stage, and much experimental and theoretical validation are needed before they can reach the clinic. As a therapy, it is also important to critically evaluate the timing of intervention during disease progression. Ultimately, these multicellular cytokine control circuits may allow modulation of the expansion and death of engineered and host cells, and tuning the amplitude and duration of cytokines in a precisely targeted local environment. The future for engineered cytokines and cellular circuits is promising given that they could have many advantages compared to current cytokine therapies, including higher specificity, local and tissue-specific actions, and reduced off-target effects. It is expected that these strategies will be broadly impactful in treating other diseases involving inflammatory imbalances, such as autoimmunity, fibrosis, and tissue or wound regeneration. As more attempts are made to sculpt local cytokine microenvironments, deeper understanding of the language and grammar of cytokine-based communication will be gained. ■

Engineering cytokine communication

Emerging protein- and cell-engineering technologies may provide multiple levels at which to program cytokine-driven immune responses. These tools may lead to powerful therapeutics and improve understanding of cytokine-based communication.



GRAPHIC: V. ALTOUNIAN/*SCIENCE*

REFERENCES AND NOTES

1. J. A. Klapper *et al.*, *Cancer* **113**, 293 (2008).
2. D. H. Charych *et al.*, *Clin. Cancer Res.* **22**, 680 (2016).
3. H. B. Lowman, J. A. Wells, *J. Mol. Biol.* **234**, 564 (1993).
4. A. B. Shanafelt *et al.*, *Nat. Biotechnol.* **18**, 1197 (2000).
5. K. Margolin *et al.*, *Clin. Cancer Res.* **13**, 3312 (2007).
6. A. M. Levin *et al.*, *Nature* **484**, 529 (2012).
7. D.-A. DSilva *et al*, *Nature* **565**, 186 (2019).
8. T. Zhou *et al.*, *Nature* **583**, 609 (2020).
9. S. Wenzel, D. Wilbraham, R. Fuller, E. B. Getz, M. Longphre, *Lancet* **370**, 1422 (2007).
10. J. T. Sockolosky *et al.*, *Science* **359**, 1037 (2018).
11. I. Moraga *et al.*, *eLife* **6**, e22882 (2017).
12. A. Oyler-Yaniv *et al.*, *Immunity* **46**, 609 (2017).
13. O. O. Yeku, T. J. Purdon, M. Koneru, D. Spriggs, R. J. Brentjens, *Sci. Rep.* **7**, 10541 (2017).
14. A. H. J. Tan, N. Vinanica, D. Campana, *Blood Adv.* **4**, 1419 (2020).
15. K. T. Roybal *et al.*, *Cell* **167**, 419 (2016).

ACKNOWLEDGMENTS

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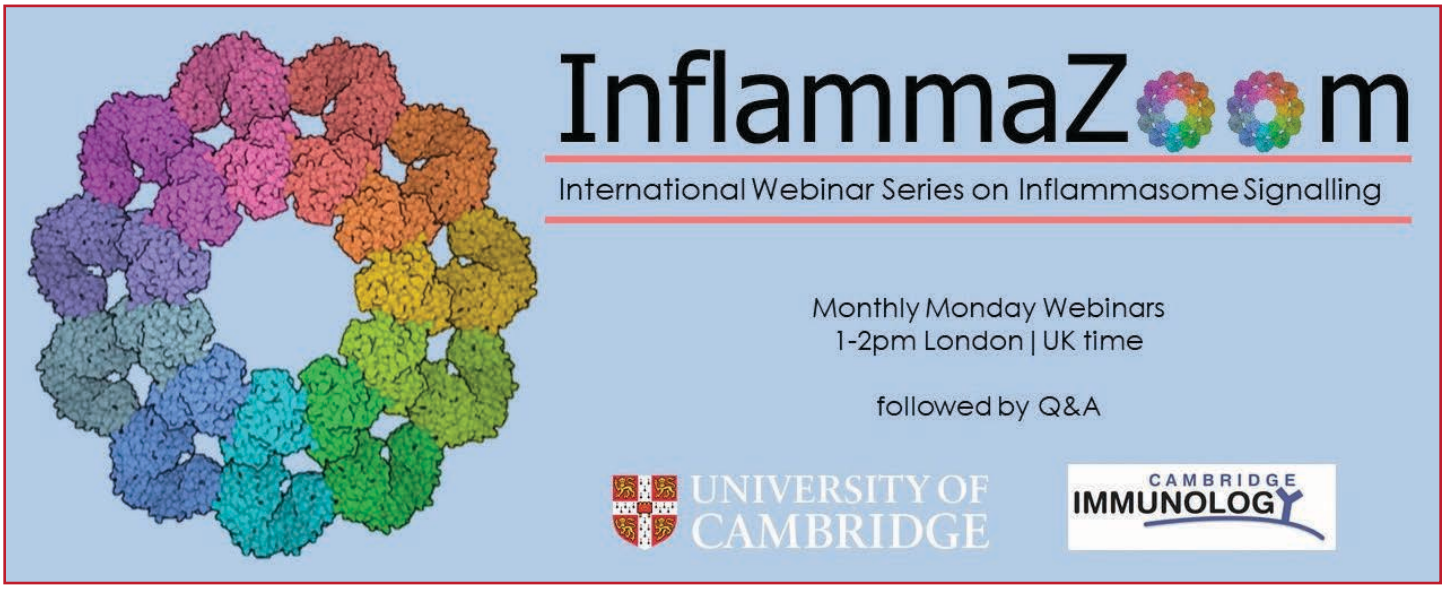
Science

Engineering cytokines and cytokine circuits

Aileen W. Li and Wendell A. Lim

Science **370** (6520), 1034-1035.
DOI: 10.1126/science.abb5607



InflammaZoom is an international webinar series on Innate Immunity and Inflammasome biology and was established in June 2020 by Professor Clare Bryant (Cambridge Immunology Network chair) to ensure that communication of outstanding science in this area would continue in the face of the pandemic.

InflammaZoom Upcoming Talks

24 MAY Michael Heneka (University of Bonn, DZNE) and Etienne Meunier (IPBS University of Toulouse)

14 JUN Vijay Rathinam (UConn Health) and Thiru Kanneganti (St. Jude Children's Research Hospital)

Global Immunotalks Live on Wednesdays at 12:00 Eastern Time

TRIALS OF INTERFERON LAMBDA FOR SARS-COV-2 /COVID-19: A STATUS REPORT

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This work was supported by the Intramural Research Program of the National Institutes of Health, National Cancer Institute, Division of Cancer Epidemiology and Genetics. The content of this publication and the opinions expressed reflect those of the individual author solely and do not necessarily reflect the views or policies of the Department of Health and Human Services, the National Institutes of Health or the National Cancer Institute nor does mention of trade names, commercial products, or organizations imply endorsement by the U.S. Government.

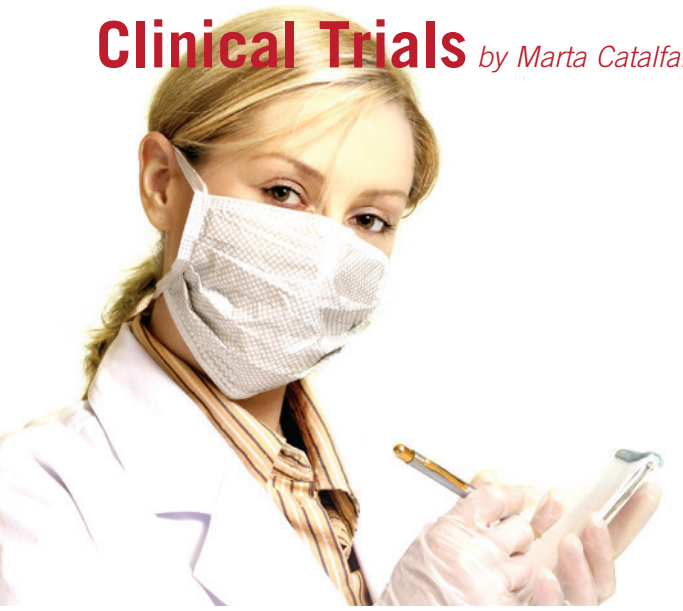
Early in the COVID-19 pandemic, several groups of scientists proposed IFN-λ as a potential therapy for SARS-CoV-2 infection (O'Brien et al., Clinical Infectious Diseases, 2020; Prokunina-Olsson et al., Journal of Experimental Medicine, 2020). That suggestion was based on evidence that the IFN-λ family provides important first-line immunological defense against viral respiratory tract infections and data indicating that SARS-CoV-2 induces weak expression of IFNs. There are no licensed IFN-λ therapeutics, however, pegylated-interferon lambda 1, which was shown to be safe and effective in testing among >3,000 patients with chronic viral hepatitis infections, is available as an investigational agent through Eiger Biopharmaceuticals. Several phase 2 clinical trials have been launched to assess the safety and efficacy of pegylated-IFN-λ1 for treatment or prevention of SARS-CoV-2 / COVID-19. Findings from two trials are now available.

Jordan Feld (University of Toronto) and colleagues conducted a double-blind, placebo-controlled randomized trial of pegylated-IFN-λ1 among outpatients with mild-to-moderate COVID-19 (NCT04354259; Feld et al., The Lancet Respiratory Medicine, 2021). Patients with laboratory-confirmed COVID-19 were randomly assigned to a single subcutaneous injection of 180 µg of pegylated-IFN-λ1 or to a placebo injection within 7 days of either symptom onset or, for asymptomatic patients, the first positive swab. The investigators recruited 30 patients per arm. At day 7 after injection, findings in the active treatment group compared to those who received placebo were: a 2.42 log greater decline in SARS-CoV-2 RNA copies per mL (p=0·004); a 4-fold greater likelihood of having undetectable virus (p=0.03); 80% frequency of undetectable virus, compared with 63% in the placebo group (p=0·15). Among those with a baseline viral level >106 copies per mL, 79% of the treatment group had undetectable virus on day 7, compared with 38% of the placebo group (p=0·01). Treatment was well tolerated, and adverse events were similar between groups. Mild, but transient, increases in aminotransferase levels were more frequent in the pegylated-IFN-λ1 group.

In a second trial, Prasanna Jagannathan (Stanford University) and colleagues enrolled 120 outpatients within 72 hours of diagnosis of mild-to-moderate COVID-19 (NCT04331899; Jagannathan et al., medRxiv, 2020). At enrollment, 41% of these subjects were SARS-CoV-2 IgG seropositive. Participants were randomized to receive a single injection of either pegylated-IFN-λ1 or a placebo. In this study, neither median time to cessation of viral shedding (7 days in each arm) nor symptom duration (8 days with treatment, 9 days with placebo) differed significantly between groups. Treatment with pegylated-IFN-λ1 was well-tolerated, however, elevated liver transaminases were more frequent in the active group (25%) compared to the placebo arm (8%; p=0.03).

While results of these two trials studies provide similarly encouraging results regarding the safety of a single injection of pegylated-IFN-λ1 in patients with SARS-CoV-2 infection, the papers reached different conclusions regarding the efficacy of that treatment of early COVID-19. Feld and colleagues determined that pegylated-IFN-λ1 accelerated viral clearance, especially in those with higher baseline viral levels, while Jagannathan et al concluded that this therapy did not shorten the duration of SARS-CoV-2 viral shedding. Clearly, more data are needed regarding the efficacy of pegylated-IFN-λ1 for SARS-CoV-2 / COVID-19. Given the observed safety profile and the encouraging results from Feld et al, a larger, phase 3 trial to more fully assess the effect of pegylated-IFN-λ1 on clearance of SARS-CoV-2 and the clinical course of infection would be welcome. Unfortunately, no such trial is currently in the works. Several additional phase 2 trials of pegylated-IFN-λ1 are listed as active on the ClinicalTrials.gov website. We look forward to those results.

Clinical Trials *by Marta Catalfamo*



Study of Intratumorally Administered Stimulator of Interferon Genes (STING) Agonist E7766 in Participants With Advanced Solid Tumors or Lymphomas - INSTAL-101

Principal Investigators: Beth Israel Deaconess Medical Center. Boston, Massachusetts, United States, 02215
Contact: Eisai Medical Information, Phone: 1-888-274-2378
ClinicalTrials.gov Identifier: NCT04144140

Study of SNX281 in Subjects With Advanced Solid Tumors and Lymphoma

Principal Investigators: Humphrey Gardner, Chief Medical Officer, MD, FCAP. Silicon Therapeutics. Boston, MA. United States, 02210
Contact: Salah Nabhan, MS Phone: 479)530-3530
ClinicalTrials.gov Identifier: NCT04609579

Nivolumab, Fluorouracil, and Interferon Alpha 2B for the Treatment of Unresectable Fibrolamellar Cancer

Principal Investigators: Sunyoung Lee, MD. M.D. Anderson Cancer Center. Houston, Texas, United States, 77030
Contact: Sunyoung Lee, Phone: 713-792-2828
ClinicalTrials.gov Identifier: NCT04380545

Melanoma Vaccine Against Neoantigen and Shared Antigens by CD40 Activation and TLR Agonists In Patients With Melanoma (Mel66)

Principal Investigators: Craig L Slingluff, Jr, Professor of Surgery; Director, Human Immune Therapy Center, University of Virginia. Charlottesville, Virginia, United States, 22908.
Contact: Adela Mahmutovic, BS Phone: 14349826714
ClinicalTrials.gov Identifier: NCT04364230

Clinical Study for the Treatment With Interferon-ß-1a (IFNß-1a) of COVID-19 Patients (INTERCOP)

Principal Investigators: Emanuele Bosi, Professor. IRCCS Ospedale San Raffaele. Milano, Italy, 20132
Contact: Patrizia Rovere Querini, Professor Phone: 00390226426768
ClinicalTrials.gov Identifier: NCT04449380

Rintatolimod and IFN Alpha-2b for the Treatment of Mild or Moderate COVID-19 Infection in Cancer Patients

Principal Investigators: Brahm H. Segal, MD. Roswell Park Cancer Institute. Buffalo, New York, United States, 14263
Contact: Pawel Kalinski, MD, Phone: 716-845-5721
ClinicalTrials.gov Identifier: NCT04379518

Study of SRF388 in Patients With Advanced Solid Tumors

Principal Investigators: Daniel Morgensztern, MD, Washington University School of Medicine - St. Louis. Saint Louis, Missouri, United States, 63110
Contact: Jessica Archambault, Phone: 314-362-8246
ClinicalTrials.gov Identifier: NCT04374877

Peg-Interferon Alpha 2b Combined With Two Intravenous Broadly HIV-1 Neutralizing Antibodies 3BNC117 and 10-1074 (BEAT-2) (BEAT-2)

Principal Investigators: Luis J Montaner, DVM, DPhil. The Wistar Institute. University of Pennsylvania. Philadelphia, Pennsylvania, United States, 19104
Contact: Pablo Tebas, M.D, Phone: 215-662-8217
ClinicalTrials.gov Identifier: NCT03588715

Human IL-15 (rhIL-15) and Obinutuzumab for Relapsed and Refractory Chronic Lymphocyte Leukemia

Principal Investigators: Milos Miljkovic, M.D. National Cancer Institute. National Institutes of Health Clinical Center. Bethesda, Maryland, United States, 20892
Contact: NCI Medical Oncology Referral Office, Phone: (240) 760-6050
ClinicalTrials.gov Identifier: NCT03759184

Use of the Interleukin-6 Inhibitor Clazakizumab in Patients With Life-threatening COVID-19 Infection

Principal Investigators: Nada Alachkar, MD. Johns Hopkins Hospital. Baltimore, Maryland, United States, 21287
Contact: Study Manager Phone: 4105508858
ClinicalTrials.gov Identifier: NCT04363502

Rintatolimod and IFN Alpha-2b for the Treatment of Mild or Moderate COVID-19 Infection in Cancer Patients'

Principal Investigators: Brahm H Segal, MD. Roswell Park Cancer Institute. Buffalo, New York, United States, 14263
Contact: Pawel Kalinski , MD Phone: 716-845-5721
ClinicalTrials.gov Identifier: NCT04379518

Interferon Lambda for Immediate Antiviral Therapy at Diagnosis in COVID-19 (ILIAD)

Principal Investigators: Jordan Feld, MD. Toronto General Hospital. Toronto, Ontario, Canada, M5G 2C4
Contact: Seham Noureldin, PhD, Phone: 416-340-4800 ext 8681
ClinicalTrials.gov Identifier: NCT04354259

Recombinant Interleukin-7 (CYT107) to Treat Patients With Refractory Nontuberculous Mycobacterial Lung Disease (IMPULSE-7)

Principal Investigators: Andrej SPEC, MD. Washington University. Saint Louis, Missouri, United States, 63110
Contact: Andrej SPEC, MD, Phone: 314-747-1725
ClinicalTrials.gov Identifier: NCT04154826

REVIEWS OF INTEREST

Contributed by Zhian Chen and Di Yu

PMID: 33649606
Neuromodulation by the immune system: a focus on cytokines.
Salvador AF, de Lima KA, Kipnis J.
Nat Rev Immunol. 2021 Mar 1. doi: 10.1038/s41577-021-00508-z. Online ahead of print. Review.

PMID: 33686279
TNF in the era of immune checkpoint inhibitors: friend or foe?
Chen AY, Wolchok JD, Bass AR.
Nat Rev Rheumatol. 2021 Mar 8. doi: 10.1038/s41584-021-00584-4. Online ahead of print. Review.

PMID: 33515492
Therapeutics targeting the IL-23 and IL-17 pathway in psoriasis.
Ghoreschi K, Balato A, Enerbäck C, Sabat R.
Lancet. 2021 Feb 20;397(10275):754-766. doi: 10.1016/S0140-6736(21)00184-7. Epub 2021 Jan 27. Review.

PMID: 33428453
Cytokine Regulation and Function in T Cells.
Dong C.
Annu Rev Immunol. 2021 Jan 11. doi: 10.1146/annurev-immunol-061020-053702. Online ahead of print.

PMID: 33577346
IL-17 in the Pathogenesis of Disease: Good Intentions Gone Awry.
Majumder S, McGeachy MJ.
Annu Rev Immunol. 2021 Feb 12. doi: 10.1146/annurev-immunol-101819-092536. Online ahead of print.

PMID: 33264572
Opposing Roles of Type I Interferons in Cancer Immunity.
Boukhaled GM, Harding S, Brooks DG.
Annu Rev Pathol. 2021 Jan 24;16:167-198. doi: 10.1146/annurev-pathol-031920-093932. Epub 2020 Dec 2.

PMID: 33158368
Engineering IL-2 to Give New Life to T Cell Immunotherapy.
Overwijk WW, Tagliaferri MA, Zalevsky J.
Annu Rev Med. 2021 Jan 27;72:281-311. doi: 10.1146/annurev-med-073118-011031. Epub 2020 Nov 6.

PMID: 33622601
Dual Nature of Type I Interferons in SARS-CoV-2-Induced Inflammation.
King C, Sprent J.
Trends Immunol. 2021 Feb 12:S1471-4906(21)00027-2. doi: 10.1016/j.it.2021.02.003. Online ahead of print. Free PMC article. Review.

PMID: 33546974
Impact of Type I Interferons on Susceptibility to Bacterial Pathogens.
Peignier A, Parker D.
Trends Microbiol. 2021 Feb 2:S0966-842X(21)00009-3. doi: 10.1016/j.tim.2021.01.007. Online ahead of print. Review.

PMID: 33478870
Roles of TGF- Superfamily Proteins in Extravillous Trophoblast Invasion.
Li Y, Yan J, Chang HM, Chen ZJ, Leung PCK.
Trends Endocrinol Metab. 2021 Mar;32(3):170-189. doi: 10.1016/j.tem.2020.12.005. Review.

PMID: 33358571
Targeting CTGF in Cancer: An Emerging Therapeutic Opportunity.
Shen YW, Zhou YD, Chen HZ, Luan X, Zhang WD.
Trends Cancer. 2020 Dec 23:S2405-8033(20)30312-5. doi: 10.1016/j.trecan.2020.12.001. Online ahead of print. Review.

PMID: 33172749
Insights Into Mechanisms of GDF15 and Receptor GFRAL: Therapeutic Targets.
Rochette L, Zeller M, Cottin Y, Vergely C.
Trends Endocrinol Metab. 2020 Dec;31(12):939-951. doi: 10.1016/j.tem.2020.10.004. Epub 2020 Nov 7. Review.

PMID: 33692481
Local and systemic effects of IL-17 in joint inflammation: a historical perspective from discovery to targeting.
Miossec P.
Cell Mol Immunol. 2021 Mar 10. doi: 10.1038/s41423-021-00644-5. Online ahead of print. Review.

PMID: 33039897
Cytokines and transcription factors in the differentiation of CD4+ T helper cell subsets and induction of tissue inflammation and autoimmunity.
Pawlak M, Ho AW, Kuchroo VK.
Curr Opin Immunol. 2020 Dec;67:57-67. doi: 10.1016/j.coi.2020.09.001. Epub 2020 Oct 8. Review.

REVIEWS OF INTEREST

Contributed by Zhian Chen and Di Yu

Continued

PMID: 32173514
The cytokine network in the pathogenesis of major depressive disorder. Close to translation?
Petralia MC, Mazzon E, Fagone P, Basile MS, Lenzo V, Quattropani MC, Di Nuovo S, Bendtzen K, Nicoletti F.
Autoimmun Rev. 2020 May;19(5):102504. doi: 10.1016/j.autrev.2020.102504. Epub 2020 Mar 13. Review.

PMID: 33482337
Interleukin 1α: a comprehensive review on the role of IL-1α in the pathogenesis and treatment of autoimmune and inflammatory diseases.
Cavalli G, Colafrancesco S, Emmi G, Imazio M, Lopalco G, Maggio MC, Sota J, Dinarello CA.
Autoimmun Rev. 2021 Mar;20(3):102763. doi: 10.1016/j.autrev.2021.102763. Epub 2021 Jan 20. Review.

PMID: 33476812
Pathophysiologic role of Interleukin-33/ST2 in Sjögren's syndrome.
Soyfoo MS, Nicaise C.
Autoimmun Rev. 2021 Mar;20(3):102756. doi: 10.1016/j.autrev.2021.102756. Epub 2021 Jan 18. Review.

PMID: 33485992
Exploring IL-17 in spondyloarthritis for development of novel treatments and biomarkers.
Groen SS, Sinkeviciute D, Bay-Jensen AC, Thudium CS, Karsdal MA, Thomsen SF, Schett G, Nielsen SH.
Autoimmun Rev. 2021 Mar;20(3):102760. doi: 10.1016/j.autrev.2021.102760. Epub 2021

PMID: 33333233
B cell activating factor (BAFF): Structure, functions, autoimmunity and clinical implications in Systemic Lupus Erythematosus (SLE).
Möckel T, Basta F, Weinmann-Menke J, Schwarting A.
Autoimmun Rev. 2021 Feb;20(2):102736. doi: 10.1016/j.autrev.2020.102736. Epub 2020 Dec 14. Review.

PMID: 33542718
Shared and Unique Features of Human Interferon-Beta and Interferon-Alpha Subtypes.
Wittling MC, Cahalan SR, Levenson EA, Rabin RL.Front *Immunol.* 2021 Jan 19;11:605673. doi: 10.3389/fimmu.2020.605673. eCollection 2020. Free PMC article. Review.

COVID-19 SPECIAL COLLECTION

PMID: 33075298
Cytokine elevation in severe and critical COVID-19: a rapid systematic review, meta-analysis, and comparison with other inflammatory syndromes.
Leisman DE, Ronner L, Pinotti R, Taylor MD, Sinha P, Calfee CS, Hirayama AV, Mastroiani F, Turtle CJ, Harhay MO, Legrand M, Deutschman CS.
Lancet Respir Med. 2020 Dec;8(12):1233-1244. doi: 10.1016/S2213-2600(20)30404-5. Epub 2020 Oct 16. Free PMC article.

PMID: 33850327
Is IL-6 a key cytokine target for therapy in COVID-19?
Jones SA, Hunter CA. *Nat Rev Immunol.* 2021 Apr 13:1-3. doi: 10.1038/s41577-021-00553-8. Online ahead of print.

PMID: 33264547
Cytokine Storm.
Fajgenbaum DC, June CH.
N Engl J Med. 2020 Dec 3;383(23):2255-2273. doi: 10.1056/NEJMra2026131. Free PMC article. Review. No abstract available.

PMID: 32425294
Weathering the COVID-19 storm: Lessons from hematologic cytokine syndromes.
England JT, Abdulla A, Biggs CM, Lee AYY, Hay KA, Hoiland RL, Wellington CL, Sekhon M, Jamal S, Shojania K, Chen LYC.
Blood Rev. 2021 Jan;45:100707. doi: 10.1016/j.blre.2020.100707. Epub 2020 May 15. Free PMC article. Review.

Preliminary predictive criteria for COVID-19 cytokine storm.
Caricchio R, Gallucci M, Dass C, Zhang X, Gallucci S, Fleece D, Bromberg M, Criner GJ; Temple University COVID-19 Research Group.
Ann Rheum Dis. 2021 Jan;80(1):88-95. doi: 10.1136/annrheumdis-2020-218323. Epub 2020 Sep 25. Review.

PMID: 32896310
The role of IL-6 and other mediators in the cytokine storm associated with SARS-CoV-2 infection.
Copaescu A, Smibert O, Gibson A, Phillips EJ, Trubiano JA.
J Allergy Clin Immunol. 2020 Sep;146(3):518-534.e1. doi: 10.1016/j.jaci.2020.07.001.PMID: Free PMC article. Review.

REVIEWS OF INTEREST

Contributed by Zhian Chen and Di Yu

Continued

PMID: 33007328
Highways to hell: Mechanism-based management of cytokine storm syndromes.
Canna SW, Cron RQ.
J Allergy Clin Immunol. 2020 Nov;146(5):949-959. doi: 10.1016/j.jaci.2020.09.016. Epub 2020 Sep 29. Free PMC article. Review.

PMID: 33214057
A Potential Role of Interleukin 10 in COVID-19 Pathogenesis.
Lu L, Zhang H, Dauphars DJ, He YW.
Trends Immunol. 2021 Jan;42(1):3-5. doi: 10.1016/j.it.2020.10.012. Epub 2020 Nov 2. Free PMC article. Review.

PMID: 33153908
Coronaviruses: Innate Immunity, Inflammasome Activation, Inflammatory Cell Death, and Cytokines.
Lee S, Channappanavar R, Kanneganti TD.
Trends Immunol. 2020 Dec;41(12):1083-1099. doi: 10.1016/j.it.2020.10.005. Epub 2020 Oct 15. Free PMC article. Review.

PMID: 33051104
A Cytokine Circus with a Viral Ringleader: SARS-CoV-2-Associated Cytokine Storm Syndromes.
Cabler SS, French AR, Orvedahl A.
Trends Mol Med. 2020 Dec;26(12):1078-1085. doi: 10.1016/j.molmed.2020.09.012. Epub 2020 Sep 30. Free PMC article. Review.

PMID: 33391477
Immunopathogenesis and treatment of cytokine storm in COVID-19.
Kim JS, Lee JY, Yang JW, Lee KH, Effenberger M, Szpirt W, Kronbichler A, Shin JI.
Theranostics. 2021 Jan 1;11(1):316-329. doi: 10.7150/thno.49713. eCollection 2021. Free PMC article. Review.

PMID: 32929876
The Longitudinal Immune Response to Coronavirus Disease 2019: Chasing the Cytokine Storm.
Chau AS, Weber AG, Maria NI, Narain S, Liu A, Hajizadeh N, Malhotra P, Bloom O, Marder G, Kaplan B.
Arthritis Rheumatol. 2021 Jan;73(1):23-35. doi: 10.1002/art.41526. Epub 2020 Dec 1. Review.

PMID: 32291137
Can we use interleukin-6 (IL-6) blockade for coronavirus disease 2019 (COVID-19)-induced cytokine release syndrome (CRS)?
Liu B, Li M, Zhou Z, Guan X, Xiang Y.
J Autoimmun. 2020 Jul;111:102452. doi: 10.1016/j.jaut.2020.102452. Epub 2020 Apr 10. Free PMC article. Review.

PMID: 32961074
Cytokine storm and COVID-19: a chronicle of pro-inflammatory cytokines.
Fara A, Mitrev Z, Rosalia RA, Assas BM.
Open Biol. 2020 Sep;10(9):200160. doi: 10.1098/rsob.200160. Epub 2020 Sep 23. Free PMC article. Review.

PMID: 33072097
COVID-19: In the Eye of the Cytokine Storm.
de la Rica R, Borges M, Gonzalez-Freire M.
Front Immunol. 2020 Sep 24;11:558898. doi: 10.3389/fimmu.2020.558898. eCollection 2020. Free PMC article. Review.

PMID: 33621130
Perspectives on Targeting IL-6 as a Potential Therapeutic Strategy for COVID-19.
Khaedir Y, Kartika R.
J Interferon Cytokine Res. 2021 Feb;41(2):37-43. doi: 10.1089/jir.2020.0135. Review.

PMID: 33113222
T cell immunobiology and cytokine storm of COVID-19.
Luo XH, Zhu Y, Mao J, Du RC.
Scand J Immunol. 2021 Mar;93(3):e12989. doi: 10.1111/sji.12989. Epub 2020 Nov 25. Free PMC article. Review.

PMID: 32794180
IL-18 and infections: Is there a role for targeted therapies?
Vecchié A, Bonaventura A, Toldo S, Dagna L, Dinarello CA, Abbate A.
J Cell Physiol. 2021 Mar;236(3):1638-1657. doi: 10.1002/jcp.30008. Epub 2020 Aug 13. Review.

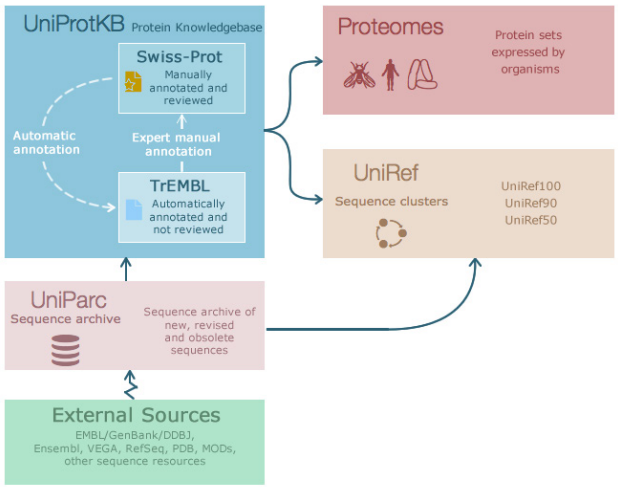
WWW

Contributions from Supreet Agarwal

Uniprot

https://www.uniprot.org/

The Universal Protein Resource (UniProt) is a comprehensive resource for protein sequence and annotation data. The UniProt databases are the UniProt Knowledgebase (UniProtKB), the UniProt Reference Clusters (UniRef), and the UniProt Archive (UniParc). The UniProt consortium and host institutions EMBL-EBI, SIB and PIR are committed to the long-term preservation of the UniProt databases.



UniProt is a collaboration between the European Bioinformatics Institute (EMBL-EBI), the SIB Swiss Institute of Bioinformatics and the Protein Information Resource (PIR). Across the three institutes more than 100 people are involved through different tasks such as database curation, software development and support.

EMBL-EBI and SIB together used to produce Swiss-Prot and TrEMBL, while PIR produced the Protein Sequence Database (PIR-PSD). These two data sets coexisted with different protein sequence coverage and annotation priorities. TrEMBL (Translated EMBL Nucleotide Sequence Data Library) was originally created because sequence data was being generated at a pace that exceeded Swiss-Prot's ability to keep up. Meanwhile, PIR maintained the PIR-PSD and related databases, including iProClass, a database of protein sequences and curated families. In 2002 the three institutes decided to pool their resources and expertise and formed the UniProt consortium.

The UniProt consortium is headed by Alex Bateman, Alan Bridge and Cathy Wu, supported by key staff, and receives valuable input from an independent Scientific Advisory Board.

The Gene Transcription Regulation Database (GTRD)

http://gtrd.biouml.org/

The most complete collection of uniformly processed ChIP-seq data on identification of transcription factor binding sites for human and mouse. Convenient web interface with advanced search, browsing and genome browser based on the BioUML platform. For support or any questions contact gtrd@biosoft.ru

Mouse Gene Expression Database

www.informatics.jax.org/expression.shtml

GXD collects and integrates the gene expression information in MGI. Its primary emphasis is on endogenous gene expression during mouse development

- GXD stores primary data from different types of expression assays. By integrating these data, GXD provides, as data accumulate, increasingly complete information about the expression profiles of transcripts and proteins in different mouse strains and mutants. (See details.)
- GXD describes expression patterns using an extensive, hierarchically-structured dictionary of anatomical terms. In this way, expression results from assays with differing spatial resolution are recorded in a standardized and integrated manner and expression patterns can be queried at different levels of detail. The records are complemented with digitized images of the original expression data. The Mouse Developmental Anatomy Ontology was developed in collaboration with the Edinburgh Mouse Atlas Project (EMAP).
- GXD places the gene expression data in the larger biological context by establishing and maintaining interconnections with many other resources. Integration with MGD enables a combined analysis of genotype, sequence, expression, and phenotype data. Links to PubMed, Online Mendelian Inheritance in Man (OMIM), sequence databases, and databases from other species further enhance the utility of GXD.

Protac Database

http://cadd.zju.edu.cn/protacdb/

PROTAC-DB is a public, web-accessible database. The **chemical structures, biological activities, physiochemical properties** of these compounds are manually extracted from the literature or calculated by some programs. Here, the biological activities of PROTACs contain the **degradation capacity, binding affinities and cellular activities**. The detailed information is as follows.

- **Degradation capacity:** In general, **DC50** (concentration that resulted in a 50% targeted protein degradation) and **Dmax** (maximal levels of protein degradation) are utilized to quantify the power of targeted protein degradation of PROTACs. However, since a large number of PROTACs lacked the above data, the **percent degradation** was integrated to the database, if it was assessed at least with two concentrations and each concentration was measured with at least two independent experiments. Further, the **Western blotting (WB) figures** were also collected by us to show the degradation capacities of PROTACs.

WWW

Continued

But the WB figures are only displayed on the detailed information pages of PROTACs, not on its list pages.

- **Binding affinities:** The binding affinities between **PROTACs and targeted proteins, PROTACs and E3 ligases, the formation of ternary complexes** are collected into PROTAC-DB. The binding affinities of the formation of ternary complexes are employed to assess the capacity of PROTAC-induced complex formation with E3 ligase and targeted protein. It can be determined through some assays between E3 ligase (targeted protein) and the complex of PROTAC and targeted protein (E3 ligase). There are four types of values, including Kd, Ki, IC50 and EC50. Only Kd and IC50 will be displayed on the list pages and the other are shown on the detailed information pages. In addition, for the biophysical binding data, ΔG, ΔH, -TΔS, t1/2, kon and koff are also collected into the database and only displayed on the detailed information page.
- **Cellular activities:** IC50, EC50, GI50, ED50 and GR50 are collected into PROTAC-DB. Similarly, ED50 and GR50 are only displayed on the detailed information pages, not on the list pages.

Moreover, the biological activities of warheads and E3 ligands are also collected. We will constantly add new data and improve the usability of the interface. For feedback, suggestions, errors or bug reports, please contact us.

PheLiGe

https://phelige.com

PheLiGe is a web-service that provides access to publicly available results from human genetic association studies. By serving information and tools for investigation of (regional) genotype-phenotype associations across phenome, this service aims to provide a researcher with an insight into biological function affected by variation in question, to help formulating aetiologic hypothesis and inform functional studies. Web-service allows for exploration of genome-wide and regional associations, finding phenotypes associated to a genetic variant, and comparison of associations patterns between different traits to assertain whether a co-association is due to pleiotropy or linkage.

You can access the database via a web-interface with three tabs: *Analysis*, *GWAS/cis-QTL Descriptors*, *Associations*. In the *Associations* tab you can search for phenotypic associations observed for an SNP of interest, directly or via a proxy variant in LD. The search results will be presented as a table with several pages and sorted by association p-value. Moreover, on this tab you can select two regions for following colocalisation analysis. In the Analysis tab, regional patterns of association are compared using the θ metric, and hypothesise on whether the overlapping signals are due to pleiotropy or linkage disequilibrium. In the *GWAS/cis-QTL* Descriptors tab, you can access association study meta-data, search for specific association studies and investigate interactive Manhattan plot of a trait of interest.

European Nucleotide Archive

https://www.ebi.ac.uk/ena

The European Nucleotide Archive (ENA) provides a comprehensive record of the world's nucleotide sequencing information, covering raw sequencing data, sequence assembly information and functional annotation. More about ENA.

Access to ENA data is provided through the browser, through search tools, through large scale file download and through the API.

MITOCARTA3.0: AN INVENTORY OF MAMMALIAN MITOCHONDRIAL GENES

https://www.broadinstitute.org/mitocarta/mitocarta30-inventory-mammalian-mitochondrial-proteins-and-pathways

MitoCarta3.0 is an inventory of 1136 human and 1140 mouse genes encoding proteins with strong support of mitochondrial localization, now with sub-mitochondrial compartment and pathway annotations. To generate this inventory, we performed mass spectrometry of mitochondria isolated from fourteen tissues, assessed protein localization through large-scale GFP tagging/microscopy, and integrated these results with six other genome-scale datasets of mitochondrial localization, using a Bayesian approach. MitoCarta3.0, released 2020, uses manual literature curation to revise the previous MitoCarta2.0 inventory (78 added and 100 removed genes), provide annotation of sub-mitochondrial localization, and assign genes to a custom ontology of 149 mitochondrial pathways.

WWW

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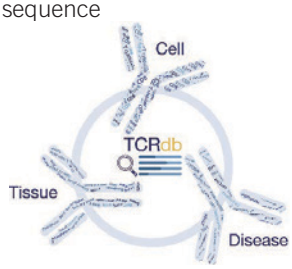
TCRdb

A comprehensive database of human T-cell receptor (TCR) sequence



http://bioinfo.life.hust.edu.cn/TCRdb/

TCRdb is a comprehensive T-cell receptor (TCR) database, the TCR on the surface of T cells recognize antigen and participate in the activation of T cells in immune response. The diversity and antigen specificity of TCRs are mainly determined by the high hypervariable complementarity-determining region 3 (CDR3). TCRdb contains processed sequences of TCRs CDR3 beta chain of human with different phenotypes. We provide an easy-to-use interface to query and browse the database, which will make TCRdb a very useful resource in T cell related researches.

What can users do in TCRdb

- Search identical/similar CDR3 sequences.
- Find disease/tissue/cell-specific TCR CDR3 sequences.
- Browse TCR CDR3 sequences in different diseases and tissues.

Promiscuous 2.0

http://bioinformatics.charite.de/promiscuous2

PROMISCUOUS2 is an one stop resource for drug-repositioning. The database can be used from experts by using the drug or target search as well as non experts, by browsing through the data via the Browse tab. Those functions are complemented by with the drug repositioning tab, where users can search for indications or atc-codes and will get “new” drugs proposed for their query.
The aim of this database is to provide a uniform data-set for drug repositioning and further analysis.

Our database PROMISCUOUS2 contains four different types of entities: Drugs, Proteins, side-effects and indications including relations between them for a global view. This is summarized in the network representation (see warfarin example network), where all information are highlighted and linked to the detail sites.

http://www.grndb.com

Gene regulatory networks are crucial for understanding the mechanism of gene expression regulation and expression heterogeneity. **GRNdb** is a freely accessible and user-friendly database for conveniently exploring and visualizing the predicted regulatory networks formed by transcription factors (TFs) and downstream target genes (termed regulons) based on large-scale RNA-seq data as well as the known TF-target relationships for various human and mouse conditions.

All the regulations in GRNdb are predicted from the omics data rather than being experimentally determined. Users can easily search, browse, and download the TF-target pairs and corresponding motifs of a variety of conditions at the single-cell or bulk level, as well as investigate the expression profile of a list of genes simultaneously and analyze the association between gene expression level and the patients’ survival of diverse TCGA cancers. We will continue to update GRNdb and add more datasets for different organisms.

iCSDB: an integrated database of CRISPR screens

https://www.kobic.re.kr/icsdb/

High-throughput screening based on CRISPR-Cas9 libraries has become an attractive and powerful technique to identify target genes for functional studies. However, accessibility of public data is limited due to the lack of user-friendly utilities and up-to-date resources covering experiments from third parties. Here, we describe iCSDB, an integrated database of CRISPR screening experiments using human cell lines. We compiled two major sources of CRISPR-Cas9 screening: the DepMap portal and BioGRID ORCS. DepMap portal itself is an integrated database that includes three large-scale projects of CRISPR screening. We additionally aggregated CRISPR screens from BioGRID ORCS that is a collection of screening results from PubMed articles. Currently, iCSDB contains 1375 genome-wide screens across 976 human cell lines, covering 28 tissues and 70 cancer types. Importantly, the batch effects from different CRISPR libraries were removed and the screening scores were converted into a single metric to estimate the knockout efficiency. Clinical and molecular information were also integrated to help users to select cell lines of interest readily. Furthermore, we have implemented various interactive tools and viewers to facilitate users to choose, examine and compare the screen results both at the gene and guide RNA levels.

WWW

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DualSeqDB

http://www.tartaglialab.com/dualseq

DualSeqDB is a manually curated database that contains data of gene expression changes in different bacterial infection models, measured by dual RNA-Seq. It comprises more than 250,000 entries, with information about bacterial and host gene expression levels under *in vivo* or *in vitro* conditions. The entries were produced by collecting raw sequencing data from 7 different studies where dual RNA-Sequencing was performed, and subsequently analyzing these data through a standardized pipeline. It includes information on 6 different strains of pathogenic bacteria and a variety of cell types and tissues in *Homo sapiens*, *Mus musculus* and *Macaca fascicularis* at different time-points.

Web based tools to analyze CRISPR screens

CRISPRAnalyzeR

http://crispr-analyzer.dkfz.de/

CRISPRAnalyzeR is a web-based analysis platform for pooled CRISPR screens. CRISPRAnalyzeR was developed with user experience in mind and provides you with a one-in-all data analysis workflow. And once you are finished, you can download all the data as well as your analysis as an interactive HTML report.
You can use our online web service, but also download CRISPRAnalyzeR to install it on your local computer or within your lab/institute. CRISPRAnalyzeR is open-source and free for non-commercial use, please check out the download pages below.

CRISPRCloud2

https://crispr.nrihub.org/

CRISPRCloud2 is a user-friendly, cloud-based, and analysis platform for the deconvolution of CRISPR(Clustered Regularly Interspaced Short Palindromic Repeats) pooled screening data. **CRISPRcloud2** serves a dual purpose of extracting, clustering and analyzing raw next generation sequencing files derived from pooled screening experiments while at the same time presenting them in a user-friendly way on a secure web-based platform.

2021 VILCEK AWARDS

VILCEK FOUNDATION PRIZEWINNERS IN BIOMEDICAL SCIENCE: VILCEK FOUNDATION HONORS OUTSTANDING IMMIGRANTS IN BIOMEDICAL SCIENCE

The Vilcek Foundation Prizes in Biomedical Science celebrate the contributions of immigrant scientists to biomedical research and discovery in the United States

The Vilcek Foundation has announced the recipients of the 2021 Vilcek Foundation Prizes in Biomedical Science. Ruth Lehmann, director of the Whitehead Institute for Biomedical Research is the recipient of the 2021 Vilcek Prize in Biomedical Science. The 2021 Vilcek Prizes for Creative Promise in Biomedical Science are presented to Mohamed Abou Donia, Ibrahim Cissé, and Silvi Rouskin.

Awarded annually, the prizes honor the foundation's mission of raising awareness of immigrant contributions in the United States and fostering appreciation of the sciences. The Vilcek Prize in Biomedical Science is awarded to a prominent foreign-born scientist with a demonstrated legacy of major accomplishments and contributions to the biomedical sciences. The Vilcek Prizes for Creative Promise honor young biomedical scientists whose early-career work demonstrates an innovative approach and represents a significant contribution to their field of study.

"The outstanding diversity of thought and innovation that immigrant scientists bring to the United States cannot be overstated," says Jan Vilcek, chairman and CEO of the Vilcek Foundation. "The United States has long been a beacon for scientists from around the globe, and many groundbreaking discoveries made in research laboratories in this country have been wrought by immigrant scientists."

Detailed profiles and video interviews with each of the 2021 Vilcek Foundation Prizewinners in Biomedical Science can be found on the Vilcek Foundation website. Highlights about each of this year's prizewinners and their accomplishments are included below. We congratulate all four of these outstanding scientists on their achievements and look forward to what comes next from each of them.

Ruth Lehmann
2021 VILCEK PRIZE IN BIOMEDICAL SCIENCE

Ruth Lehmann is a developmental geneticist and cell biologist, and the director of the Whitehead Institute for Biomedical Research in Cambridge, Massachusetts. Born in Cologne, Germany, Ruth discovered her love of research science and genetics while studying ecology on a Fulbright fellowship at the University of Washington in 1978. Ruth receives the Vilcek Prize in Biomedical Science for her foundational contributions to the understanding of primordial germ cells and the germ cell life cycle, and for her institutional leadership in the field.

Prizewinner Profile

Photo courtesy of Gretchen Ertl

Mohamed Abou Donia
2021 VILCEK PRIZE FOR CREATIVE PROMISE IN BIOMEDICAL SCIENCE

Mohamed Abou Donia receives the Vilcek Prize for Creative Promise in Biomedical Science for demonstrating the potential of the human microbiome as a source of novel drugs and uncovering the basis of microbiome-driven drug metabolism. Born in Ismailia, Egypt, Mohamed is an associate professor and director of the Donia Lab at Princeton University. Mohamed knew he wanted to pursue a career in research science after taking a summer research internship in the United States while studying pharmacy at Suez Canal University.

Prizewinner Profile

Photo courtesy of The Vilcek Foundation

2021 VILCEK AWARDS *CONTINUED*

Ibrahim Cissé

2021 VILCEK PRIZE FOR CREATIVE PROMISE IN BIOMEDICAL SCIENCE

Ibrahim Cissé is a professor of physics at CalTech. Born in Niger, he receives the Vilcek Prize for Creative Promise in Biomedical Science for the development of single-molecule and super-resolution approaches to study the dynamic nature of gene expression in living cells—including protein clustering, biomolecular condensation in transcription, and other processes.

Prizewinner Profile

Photo courtesy of The Vilcek Foundation

Silvi Rouskin

2021 VILCEK PRIZE FOR CREATIVE PROMISE IN BIOMEDICAL SCIENCE

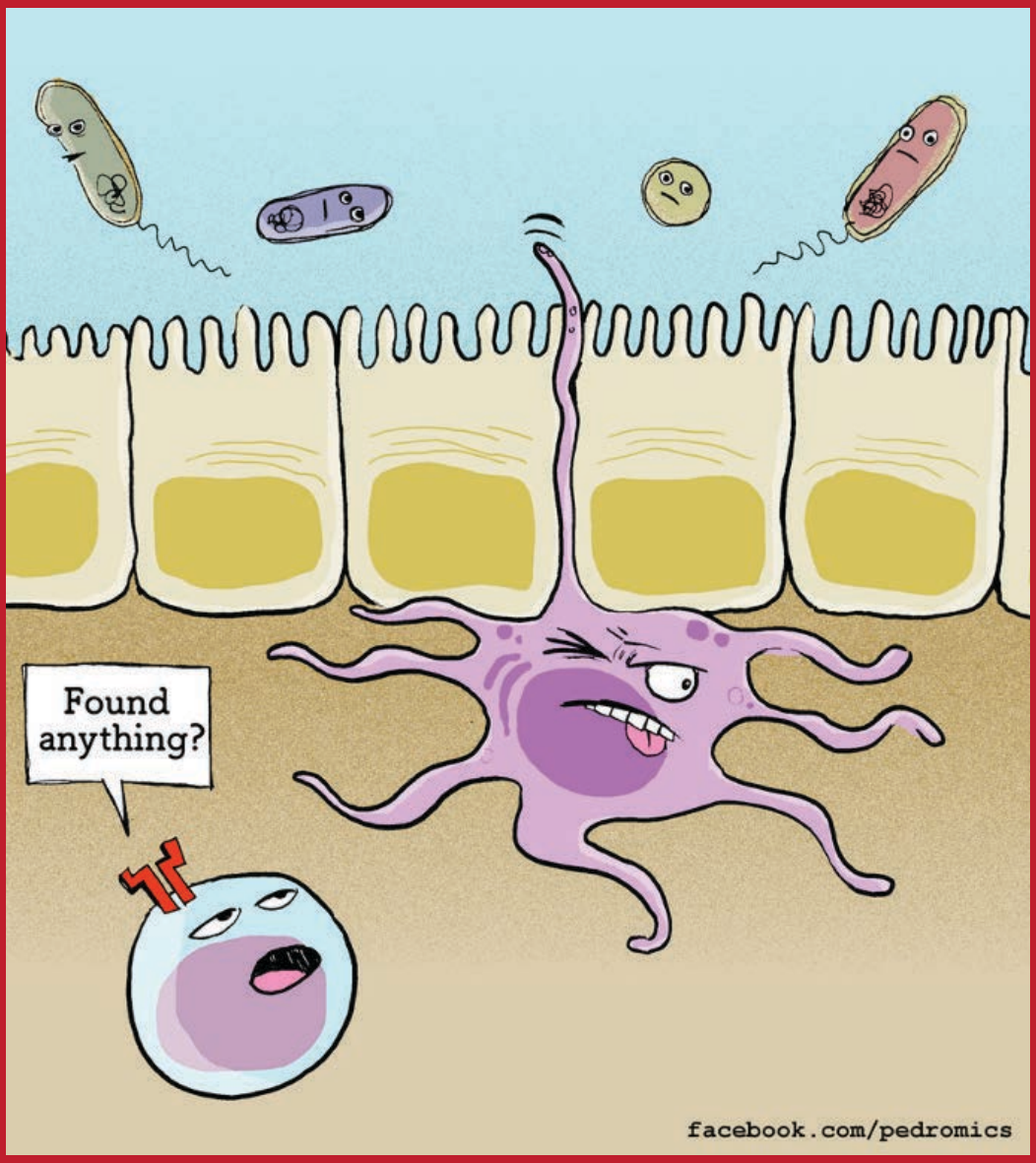
Silvi Rouskin is the Andria and Paul Heafy Whitehead Fellow at the Whitehead Institute for Biomedical Research. The Bulgarian-born molecular biologist receives the Vilcek Prize for Creative Promise in Biomedical Science for developing methods to unravel the shapes of RNA molecules inside cells and aiding the potential development of RNA-based therapeutics for viral diseases.

Prizewinner Profile

Photo courtesy of The Vilcek Foundation

IUIS-EFIS Webinar: Immunology in the time of COVID-19: achievements, challenges and opportunities

April 29, 2021 Free Registration!



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