Signals

THE INTERNATIONAL CYTOKINE AND INTERFERON SOCIETY NEWSLETTER

OCTOBER 2016 | VOLUME 4 | NO. 2

IN THIS ISSUE:

2016 ICIS

THE SEYMOUR AND VIVIAN MILSTEIN AWARD WINNERS for Excellence in Interferon and Cytokine Research

The Seymour and Vivian Milstein Award for Excellence in Interferon and Cytokine Research

http://www.milstein-award.org/

The Seymour and Vivian Milstein Award for Excellence in Interferon and Cytokine Research, represents the pinnacle of scientific achievement in interferon and cytokine research. 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.

DR. CARL NATHAN

Carl Nathan, MD is R.A. Rees Pritchett Professor and chairman of the Department of Microbiology and Immunology at Weill Cornell Medical College and co-chair of the Program in Immunology and Microbial Pathogenesis at Weill Graduate School of Medical Sciences of Cornell University.

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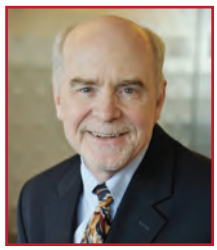

DR. JOHN O'SHEA

John J. O'Shea, M.D., graduated Phi Beta Kappa with a Bachelor of Science degree from St. Lawrence University, and received a Doctor of Medicine degree from the University of Cincinnati.

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DR. JAN VILCEK

Dr. Jan T. Vilcek, research professor at New York University School of Medicine, was born in Bratislava, Czechoslovakia (now Slovakia), where he also received his M.D. and Ph.D. degrees.

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Future Meetings

2016 Meeting
Cytokines 2016
Oct. 16-19, 2016
San Francisco, CA

Cytokines 2017
Oct. 29-Nov. 2, 2017
Kanazawa, Japan

Newsletter Editors

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ICIS
International Cytokine & Interferon Society

2016 ICIS
THE SEYMOUR AND VIVIAN MILSTEIN AWARD for Excellence in Interferon and Cytokine Research

DR. CARL NATHAN

After graduation from Harvard College and Harvard Medical School, he trained in internal medicine and oncology at Massachusetts General Hospital, the National Cancer Institute and Yale before joining the faculty of The Rockefeller University from 1977-1986. At Cornell since 1986, he has served as Stanton Griffis Distinguished Professor of Medicine, founding director of the Tri-Institutional MD-PhD Program, senior associate dean for research, acting dean, and leader of the planning team for and member of the Board of Directors of the Tri-Institutional Therapeutics Discovery Institute, a not-for-profit corporation owned by Weill Cornell Medical College, Memorial Sloan Kettering Cancer Center and The Rockefeller University. Nathan is a member of the National Academy of Sciences, the National Academy of Medicine and the American Academy of Arts and Sciences, a Fellow of the American Academy of Microbiology, associate scientific director of the Cancer Research Institute, a governor of the Tres Cantos Open Lab Foundation and on the scientific advisory boards of the Global Alliance for TB Drug Development, the American Asthma Foundation and the Rita Allen Foundation. He is a member of the national Pfizer Therapeutic Areas Scientific Advisory Panel and the Lurie Prize jury. He served for ten years on the SAB of the Cambridge Institute for Medical Research and the Board of Trustees of the Hospital for Special Surgery, where he chaired the Research Committee. He has been an editor of the Journal of Experimental Medicine since 1981 and joined the editorial board of the Proceedings of the National Academy of Sciences in 2014. He was awarded the Robert Koch Prize in 2009 for his work on tuberculosis and the Anthony Cerami Award in Translational Medicine in 2013.

Nathan is a member of the Bill and Melinda Gates Foundation's TB Drug Accelerator and Principal Investigator of the NIH-funded Tri-Institutional TB Research Unit. His research deals with the immunological and biochemical basis of host defense. He established that lymphocyte products activate macrophages, that interferon-gamma is a major macrophage activating factor, and that mechanisms of macrophage antimicrobial activity include induction of the respiratory burst and inducible nitric oxide synthase (iNOS). He and his colleagues purified, cloned, knocked out and characterized iNOS biochemically and functionally, discovered the cofactor role of tetrahydrobiopterin in NOS's and introduced iNOS as a therapeutic target. Although iNOS helps the host control *Mycobacterium tuberculosis* (Mtb), the leading cause of death from bacterial infection, Mtb resists sterilization by host immunity. Nathan's lab now focuses on the biochemical basis of this resistance. Genetic and chemical screens have identified enzymes that Mtb requires to survive during non-replicative states, including the mycobacterial proteasome. His group is identifying compounds that kill non-replicating bacteria while exploring new collaborative models between academia and industry to help invigorate antibiotic research and development.

See more at: www.nathanlab.org

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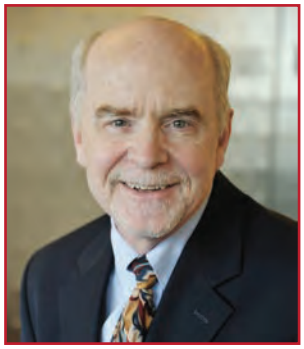

DR. JOHN O'SHEA

He then served as an intern and resident in Internal Medicine at the State University of New York Upstate Medical University in Syracuse, NY. He came to the National Institutes of Health (NIH) in 1981 for subspecialty training in Allergy and Immunology in the National Institute of Allergy and Infectious Diseases. He did additional postdoctoral work in the Cell Biology and Metabolism Branch in the National Institute of Child Health and Human Development. Dr. O'Shea is board certified in Internal Medicine and Allergy and Immunology.

He started his own group in the National Cancer Institute in 1989, and then moved to the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) in 1994 as Chief of the Lymphocyte Cell Biology Section of the Arthritis and Rheumatism Branch. He was appointed Chief of the Molecular Immunology and Inflammation Branch in 2002, and became Scientific Director and Director of the NIAMS Intramural Research Program in 2005. Dr. O'Shea also served as Acting Director of the NIH Center for Regenerative Medicine from 2009-2011. Dr. O'Shea is also an adjunct Professor in the Department of Pathology at the University of Pennsylvania.

Dr. O'Shea has received a number of awards, including: the U.S. Public Health Service Physician Researcher of the Year Award; the Paul Bunn Award in Infectious Disease; the Lee C. Howley Prize in Arthritis Research; the Irish Society for Immunology Public Lecture Award; a St. Lawrence University honorary degree; and the Ross Prize in Molecular Medicine. He has been the recipient of the National Institutes of Health Director's Award four times (1998, 2008, 2010, 2013). He was elected to the American Association of Physicians, the American Society for Clinical Investigation, and the Institute of Medicine/National Academy of Medicine. He is also an ISI Web of Knowledge "Highly Cited Researcher". He received the NIAMS Mentoring Award in 2003, and the NIH "Make a Difference" Office of Equal Opportunity Award in 2006. He was selected for the NYU Honors Lectureship, the Danny Thomas Lecture and more, and in 2015 delivered a Nobel Forum Lecture.

Dr. O'Shea has served on the editorial boards of multiple journals, including: *Immunity, Journal of Experimental Medicine, Journal of Biological Chemistry, Journal of* ***Immunology***, and *Blood*. He has been an invited lecturer at numerous universities and international meetings in the U.S., Canada, Europe and Asia.

Dr. O'Shea is one of the co-founders of the NIH/Oxford/Cambridge program in Biomedical Science, is a member of NIH-UPENN Immunology Program, and has served as a Howard Hughes Medical Institute Scholars Advisor.

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DR. JAN VILCEK

In 1964 he and his wife, Marica Vilcek, an art historian, defected from what was then communist Czechoslovakia. Upon immigrating to the United States in 1965, Dr. Vilcek joined the faculty of NYU School of Medicine.

Dr. Vilcek has devoted his scientific career to the study of cytokines. He was among the first scientists to investigate interferon. Subsequently, Dr. Vilcek focused his studies on another cytokine, called tumor necrosis factor (TNF). Dr. Vilcek's contributions to the understanding of proteins that control the body's defenses were instrumental in the development of the anti-inflammatory drug Remicade®, the first member of a new class of therapeutics called TNF blockers that are now widely used for the treatment of Crohn's disease, ulcerative colitis, rheumatoid arthritis, ankylosing spondylitis, psoriasis, and other chronic inflammatory disorders. Dr. Vilcek has published more than 350 papers in scholarly journals, and he holds 46 U.S. patents. His honors include the Albert Gallatin Medal from NYU, and honorary degrees from Comenius University in Bratislava, the CUNY Graduate Center in New York City, and NYU. He received the J. E. Purkyně Honorary Medal from the Czech Academy of Sciences, and the Outstanding American by Choice Award from the U.S. Citizenship and Immigration Services. In 2013, President Barack Obama named Dr. Vilcek a recipient of the National Medal of Technology and Innovation.

In 2000 Dr. Vilcek and his wife established the Vilcek Foundation, whose mission is to raise awareness of immigrant contributions in the United States and foster appreciation of the arts and sciences.

Dr. Vilcek's memoir *Love and Science* was published by *Seven Stories Press* in 2016. In it, Dr. Vilcek tells the story of his two intertwined journeys—one personal, the other scientific. The personal story is about his and his parents' survival during the Second World War, growing up in Communist Czechoslovakia, and arriving as a penniless immigrant in the U.S. The scientific story recounts how the vaunted cures for cancer that many saw in interferon and TNF never materialized, and how out of the ashes of that hope emerged treatments that revolutionized medicine and alleviated much suffering.

New ICIS Award:

THE ICIS-BIOLEGEND WILLIAM PAUL AWARD

BioLegend®
Enabling Legendary Discovery™

This new award 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 $2500 and a crystal block with the 3 D structure of IL-4, the cytokine most associated with Dr. Paul's research.

DR. RICHARD LOCKSLEY

Dr. Locksley is the Director of the Sandler Asthma Basic Research Center (SABRE) and a Howard Hughes Medical Institute Investigator. He is a Professor in the Departments of Medicine and Microbiology & Immunology. He received his undergraduate degree in biochemistry from Harvard and his M.D. from the University of Rochester. After completing his residency at UCSF, he trained in infectious diseases at the University of Washington. Prior to his position as director of the SABRE Center, Dr. Locksley served 18 years as the Chief of the Division of Infectious Diseases at UCSF Medical Center. Dr. Locksley is a fellow of the American Academy of Arts and Sciences.

Dr. Locksley's laboratory focuses on mechanisms by which the immune system becomes organized in stereotyped ways against discrete types of challenges. This involves the differentiation of naïve helper T cells to subsets that produce different kinds of cytokines, key effector molecules of the immune system. In turn, these different T cells subsets work with different kinds of innate cells, including neutrophils, eosinophils, macrophages and others, to mediate immunity. Properly executed, such responses mediate protection against infectious organisms or repair of damaged tissues, but, when dysregulated, these immune responses lead to disease, including asthma.

Dr. Locksley's laboratory investigates immunity using mice genetically engineered to report cytokines expressed during allergic immune responses. This approach reveals the shared expression of important cytokines by innate and adaptive immune cells. Using these methods, the laboratory participated in the discovery of Group 2 innate lymphoid cells, or ILC2s, which represent a previously unknown cell now implicated in allergic immunity. The ability to study the activation and organization of innate ILC2s uncovered a role for cells associated with allergy and asthma, such as eosinophils, in processes involved with basal metabolism and tissue homeostasis. Activation of ILC2s in the small intestine was implicated in alteration of the mucosa to a secretory phenotype characterized by high numbers of goblet cells and tuft cells. The latter, a previously mysterious epithelial cell of unknown function, was shown to be the source of IL-25, a cytokine capable of activating ILC2s and other immune cells associated with allergy and asthma, thus opening up entirely new avenues for discovery.

2016 ICIS AWARD WINNER

HONORARY LIFETIME MEMBERSHIP

Honorary Lifetime Membership Award

Nominations are solicited for Honorary Life Memberships in the ICIS. Each year an individual will be awarded Life Membership as a tribute to his/her contributions to the field. Nominees should be individuals who have made substantive contributions to the cytokine/chemokine/interferon field over much of their careers, either in basic, clinical or applied research. Honorary members are esteemed members of the Society and provide us with an historical perspective and valued research tradition. Honorary Life Members are accorded all rights and privileges of active members, are exempted from Society dues and annual meeting registration fees, and are listed in the dedicated Honorary Life Members section of the Society web site.

DR. HOWARD YOUNG

Howard Young joined the National Cancer Institute in 1983 as an independent investigator and is now a Senior Investigator in the Cancer and Inflammation Program, Center for Cancer Research at the National Cancer Institute at Frederick, in Frederick, MD. He is a Past President of the International Society for Interferon and Cytokine Research, has served on the ICIS Council for the last 3 years and for over 15 years has been on the ICIS Membership Committee. He founded and currently edits the ICIS newsletter. He is a member of the American Academy of Microbiology, the Faculty of 1000 and he has also served as Chair of the Immunology Division of the American Society for Microbiology. He was co-founder and Chair of the NIH Cytokine Interest Group (2 times) and is now an elected member of the NIH Immunology Interest Group steering committee and the NIH Assembly of Scientists. He is a two-time Recipient - National Cancer Institute - of the NIH Director's Award for Mentoring and a Recipient - National Public Service Award from the American Society for Public Administration and the National Academy of Public Administration.

He has established an NIH Interferon Club and an NIH Microbiome Working Group, both designed to bring together investigators involved in interferon research or microbiome research in order to promote interactions and collaborations across the NIH.

He has been working on varying aspects of innate immunity for over 30 years, and has a long history of studying cytokine gene expression and signaling, the biology and molecular biology of NK cells, the generation and analysis of murine macrophage cell lines and immune signaling networks; all of which has resulted in over 300 publications. His initial studies involved molecular characterization of the transcriptional regulation of Interferon-γ and was the first investigator to demonstrate epigenetic control of IFN-γ expression as mediated by methylation of a core regulatory element in the IFN-γ promoter. Following these studies, his laboratory began to focus on the effects of IFN-γ on the host. Given that the IFN-γ gene has been cloned from many different species, sequence comparisons have revealed that the AU rich element in the 3'UTR of the gene is more conserved than the coding region. Based on this evolutionary conservation, he asked a very basic research question, i.e. what are the consequences to the host if the conserved ARE region is removed. He found that low levels of circulating IFN-γ are observed in this mouse, consistent with levels that are observed in patients who have chronic inflammation. Analysis of the mouse has revealed differences in the phenotype dependent on the mouse genetic background. On the Balb/c background he reported that the mice develop aplastic anemia as well as accumulation of calcium in the liver and kidneys, resulting in death by 8 weeks of age. In contrast, on the BL/6 genetic background, the mice develop a lupus like condition as well as primary biliary cholangitis (PBC). Furthermore, the PBC has a female bias and is the first mouse model to mimic the human disease with respect to gender differences. These findings thus represent a novel mouse model of disease that will be important in developing new therapeutic approaches, as current treatments are inadequate and non-specific.

THE ICIS SLIDE REPOSITORY

Ever see a slide in a talk that you wish you could use for your own presentation? Well now this may be possible through the ICIS Slide Repository. All ICIS Members can go in and post slides that they have developed or download slides that others have provided to the membership. OVER 500 SLIDES ARE AVAILABLE!!!!!! For this member only feature, you need to have your ICIS member number so if you are not sure what that is, please contact the membership office. We urge members to upload general slides that other members can use for lectures, classes, seminars, etc. Slides are not to be changed without permission from the donor and all copyright permissions must be obtained. The repository now has a useful search capability that allows you to find slides on a particular topic. If you have trouble uploading or downloading slides, please contact Howard Young at younghow@mail.nih.gov

MEMBERS IN THE NEWS

Eleanor Fish was inducted as a Fellow into the African Academy of Sciences.

Richard Flavell received the AAI Mentoring award at the 2016 AAI meeting in Seattle.

AMERICAN SOCIETY FOR MICROBIOLOGY ICAAC YOUNG INVESTIGATOR AWARDS

Recognizes and reward early career scientists for research excellence and potential in microbiology and infectious disease.

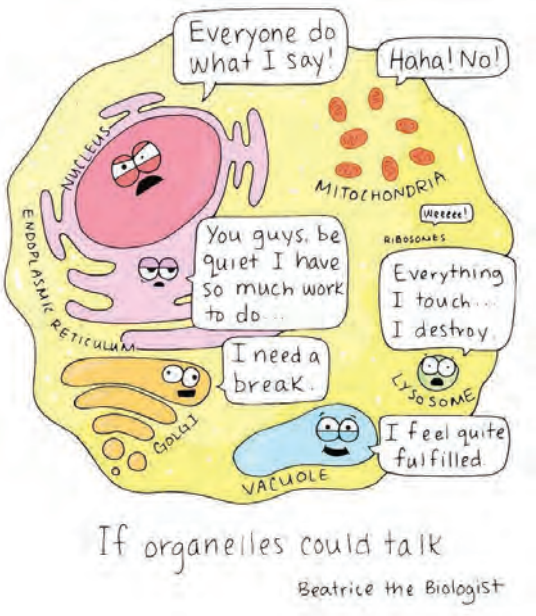
2016 Winners & ICIS members: Dusan Bogunovic, Stacy Horner

Stacy Horner with Dr. Lynn Enquist, ASM President (R), and Dr. Ned Ruby (L), Committee on Awards Chair

Dusan Bogunovic

www.asm.org/index.php/2016-awards

www.asmmicrobe.org/index.php/abstracts-and-travel-awards/travel-award-recipients#YoungInvestigator



http://www.beatricebiologist.com/

San Francisco Trivia

http://www.sfgate.com/bayarea/article/Test-your-knowledge-of-Bay-Area-trivia-2726362.php

1 Even casual movie fans know that Clint Eastwood is the title character in "Dirty Harry." But who was originally supposed to be the San Francisco police inspector?
2 While we're at it, the villain in "Dirty Harry" was loosely based on the Zodiac, one of the most famous killers in San Francisco history. According to the most generally accepted police estimate, how many people did the Zodiac kill in San Francisco?
3 Before Sacramento became the state capital in 1854, the capital shifted among three Bay Area cities. Name them.
4 Where can you find the world's oldest working lightbulb?
5 What 6-foot-2-inch girl captained her basketball team at the Branson School in Ross in 1928 and 1929?
6 We all know where Tony Bennett left his heart, but where is the heart of San Bruno?
7 What young comedian was heckled so badly during an appearance with Barbra Streisand at San Francisco's hungry i in the early 1960s that, as the San Francisco Examiner put it, "He was reduced to something pale, quivering and not quite human, his back to the audience, elbows on the piano, mumbling material to the brick wall"?
8 Thirty years ago, the Eugene O'Neill Foundation helped to save the Tao House in Danville from being demolished. Why?
9 What does San Francisco author Amy Tan have in common with bestselling authors Stephen King, Scott Turow and Mitch Albom, plus syndicated columnist Dave Barry and "Simpsons" creator Matt Groening?
10 What's the easiest way to walk from San Francisco to Alameda County without crossing a bridge?
11 Where is Wyatt Earp buried?
12 What is unique about Tuffy, one of the dogs buried in the Benicia Army Cemetery?
13 Why would Mill Valley's 2AM Club look familiar to fans of Huey Lewis and the News?
14 What was Li'l Folks?
15 In "Foul Play," a 1978 comedy starring Chevy Chase and Goldie Hawn, there's a plot to assassinate the pope in San Francisco. Who portrayed the pope?
16 Which current Bay Area resident was the youngest performer ever to win an Oscar?
17 Which San Francisco mayor became a Union general in the Civil War?
18 Where did Charlie Chaplin make several films, including "The Tramp"?
19 Why was the name of San Francisco's Pacific Street changed to Pacific Avenue?
20 What city's motto is "Climate Best by Government Test," and what the heck does that mean?
21 In San Francisco, a couple of streets just west of St. Mary's Park are in an unusual shape. Why?
22 In the 1969 graduating class at Redwood High School in Larkspur, who was voted "Least Likely to Succeed"?
23 On Memorial Day 1977, a large protest was held to support installing suicide barriers on the Golden Gate Bridge. Which key speaker in support of the barriers ended up becoming world famous?
24 In Alfred Hitchcock's "The Birds," one crucial building was Bodega Bay School. What's the school's real name, and where is it?
25 Who were Mother McCree's Uptown Jug Champions?
26 What brothers were part of the Blue Velvets, entertaining classmates at El Cerrito's Portola Junior High and El Cerrito High in the late 1950s and early 1960s?
27 TV trivia from the 1980s: The mansion in "Dynasty," the winery in "Falcon Crest" and the hotel in "Hotel" are all in the Bay Area. What are their real-life names and locations?
28 San Francisco used to be referred to as the Barbary Coast. Why?
29 What was the original name of the Oakland Raiders?
30 More Oakland sports: When the A's had their glory years in the early 1970s, they had famous players such as Reggie Jackson and Vida Blue and Rollie Fingers. But the most famous person from the team turned out to be a ballgirl, Debbie Sivyer. Why?

ANSWERS ARE ON PAGE 29

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.

Annabell Bachem
Australia

Shawn Beug
Children's Hospital of Eastern Ontario Research Institute
Canada

David Brooks
Princess Margaret Cancer Center
Canada

Anna Cardus Figueras
Cardiff Univ School of Med Inst of Infection & Immunity
United Kingdom

Kwan Chow
University of Washington
USA

Simone Dallari
Zuniga
USA

Pratik Deb
Rutgers New Jersey Medical School
USA

Joseph deCourcey
Trinity College Dublin Biochemistry and Immunology
Ireland

Virginie Deswaerte
Hudson Inst of Medical Research
Australia

Lydia Dyck
Trinity College Dublin
Ireland

Emily Eshleman
University of Colorado School of Medicine
USA

Eric Feeley
Duke Univ
USA

Ryan Finethy
Duke University
USA

Mariafausta Fischietti
Northwestern University
USA

Adriana Forero
USA

Katherin Gibbert
Germany

Misty Good
USA

Raffi Gugasyan
Burnet Institute
Australia

David Hare
McMaster Univ Dept of Pathology & Molecular Med
Canada

Eda Holl
Duke University
USA

Shawn Jeffries
Eli Lilly & Company
USA

Ewa Kosciuczuk
Northwestern University Robert H. Lurie Comprehensive Cancer
USA

Dan Li
Feinstein Institute for Medical Research
USA

Edmond Linossi
Walter and Eliza Hall Institute of Medical Research
Australia

Xiaodan Lu
China

Jason Lynch
University of Queensland
Australia

Samuel Maldonado
Rutgers New Jersey Medical School
USA

Constance McElrath
Rutgers University
USA

Amina Negash
University of Washington
USA

Adeola Obajemu
NCI/NIH
USA

Lisa Osborne
University of British Columbia
Canada

Genevieve Pepin
Hudson Institute
Australia

Maya Poffenberger
McGill University
Canada

Shauna Quinn
Prof. Kingston Mills
Ireland

Mathilde Raverdeau
Trinity Biomedical Sciences Institute
Ireland

Scott Read
Westmead Institute of Medical Research
USA

Yrina Rochman
Cincinnati Children's Hospital Medical Center
USA

Diana Saleiro
Northwestern University
USA

Laura Snell
Princess Margaret Cancer Centre
Canada

Jonas Van Audenaerde
University of Antwerp
Belgium

Barney Viengkhou
The University of Sydney
Australia

Robert Walsh
Trinity College Dublin
Ireland

Xin Wang
Lerner Res. Inst Cleveland Clinic Dept of Molecular Genetics
USA

Fang Wang
National Institutes of Health
USA

Rhiannon Werder
Australia

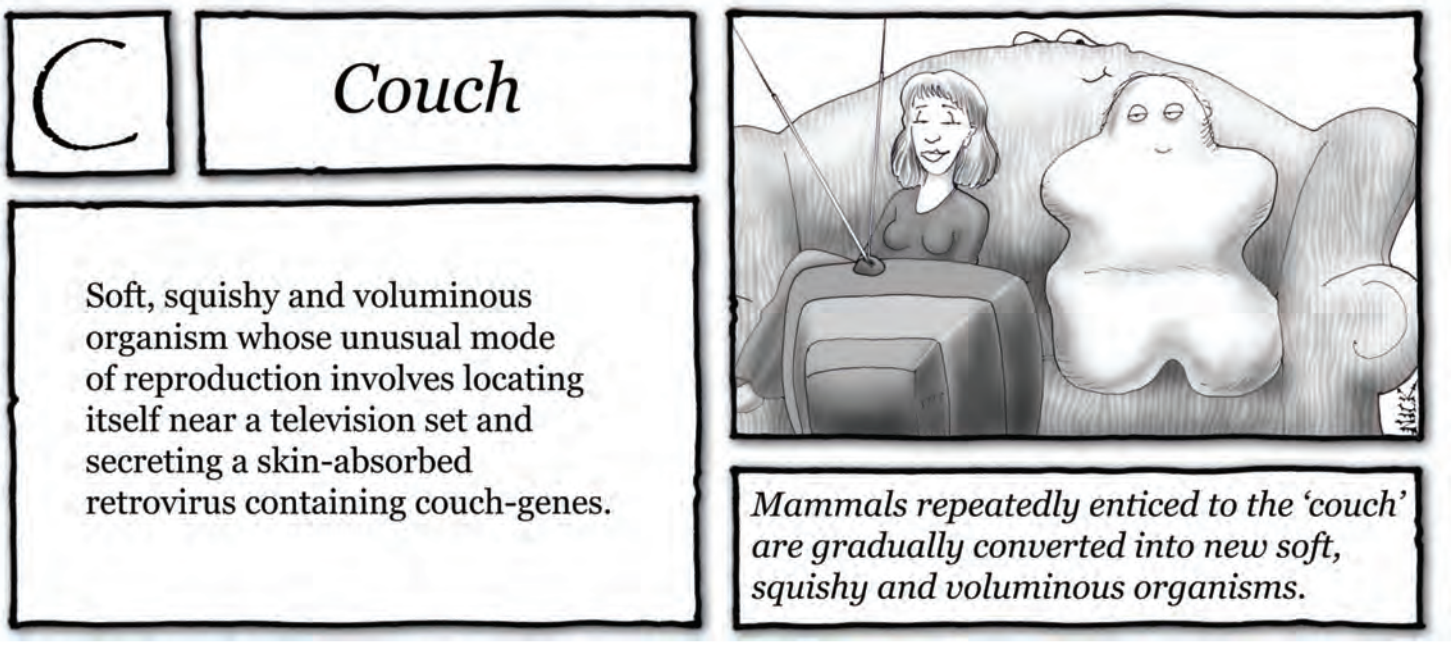
Phillip West
University of Sydney
Australia

Christoph Wilhelm
Germany

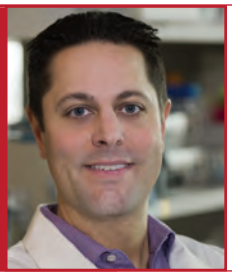
Kurt Wong
Synthetic Genomics
USA

Junji Xing
Immunobiology & Transplantation Research
USA

Lauren Zenewicz
University of Oklahoma Health Sciences Center
USA



New Member MINIBIOs *by Haiying Li*



David Brooks, Ph.D
Associate Professor
Princess Margaret Cancer Center, University Health Network
Department of Immunology, University of Toronto
Toronto, Ontario, Canada

Dr. Brooks attended graduate school at UCLA in the laboratory of Dr. Jerome Zack exploring HIV latency and therapeutic approaches to eliminate it. Dr. Brooks then did a postdoctoral fellowship in the laboratory of Dr. Michael Oldstone exploring the cytokine signals that drive immune dysfunction in persistent virus infection. Dr. Brooks joined the faculty position at UCLA in 2008 and became a tenured Associate Professor in 2015. Dr. Brooks moved his laboratory in 2015 and is currently a Senior Scientist and the Scotiabank Research Chair at the Princess Margaret Cancer Center, and an Associate Professor in the Department of Immunology at the University of Toronto. The Brooks laboratory is focused on uncovering and understanding the mechanisms of inflammation and immunosuppression that potentiate dysfunctional immunity during persistent virus infections and cancer; and how to modify the immune response to fight these diseases.

Lauren A. Zenewicz, Ph.D.
Assistant Professor
The University of Oklahoma Health Sciences Center
Department of Microbiology and Immunology
Oklahoma City, OK, USA

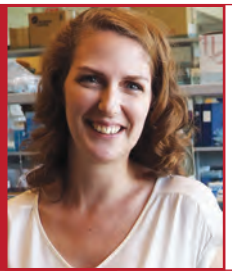
Dr. Lauren A. Zenewicz is an Assistant Professor of Microbiology and Immunology at the University of Oklahoma Health Sciences Center. She completed her doctoral training in bacterial pathogenesis at the University of Pennsylvania where, under Hao Shen, Ph.D. , she examined how similar virulence factors of Listeria monocotygenes and Bacillus anthracis modulated innate and adaptive immune responses. As a post-doctoral fellow with Richard A. Flavell, Ph.D., F.R.S., in the Department of Immunobiology at Yale University, she began her studies on interleukin-22 (IL-22), an important cytokine in modulating tissue responses during inflammation. Her research revealed both a protective and pathologic role for IL-22 in the inflamed gastrointestinal tract. Her studies also showed that IL-22 has effects on the host microbiota, causing changes in flora composition that can lead to exacerbated colitis. Through her research, Dr. Zenewicz identified that both T cells and innate lymphocytes are an important source of IL-22. Her laboratory is now focused on investigating the role of environmental factors in the regulation of IL-22 expression in T cells and innate lymphocytes.

Raffi Gugasyan, Ph.D..
Head: Lymphocyte Biology Laboratory
Centre for Biomedical Research
Burnet Institute
Melbourne, Australia

Dr. Gugasyan completed his Ph.D in Immunology at the Walter and Eliza Hall Institute, Melbourne, Australia. He then obtained his postdoctoral training in the laboratory of Emil Unanue at Washington University School of Medicine, St. Louis, M.O., USA. He is currently a Senior Research Fellow at the Burnet Institute in Melbourne, Australia and has an Adjunct appointment in the Department of Immunology, Monash University. His laboratory is focused on NF-κB and MAPK signaling pathways in lymphocytes, and the biology of inflammatory cytokines, that are involved in immunodeficiency and autoimmune diseases.

Eda Holl, PhD
Assistant Professor
Department of Surgery
Duke University
Durham, NC, USA

Dr. Holl completed her PhD in Microbiology and Immunology at the University of North Carolina-Chapel Hill in 2010 in the laboratory of Dr. Jenny Ting. She then obtained postdoctoral training in the laboratory of Dr. Bruce Sullenger at Duke University. During her postdoctoral training Dr. Holl was part of the Duke Translational Research Institute where she conducted research in the field of inflammation. Her studies focused on the mechanisms that control aberrant inflammation and discovery of polymer compounds that modulate signaling through TLR receptors. In 2014, she accepted a faculty position in the Department of Surgery at Duke University where she has been conducting research and clinical trials for novel cancer immunotherapies. Her most recent work focuses on utilizing oncolytic virus therapeutic agents to directly lyse solid tumors as well induce a long lasting immune response to prevent cancer recurrence.



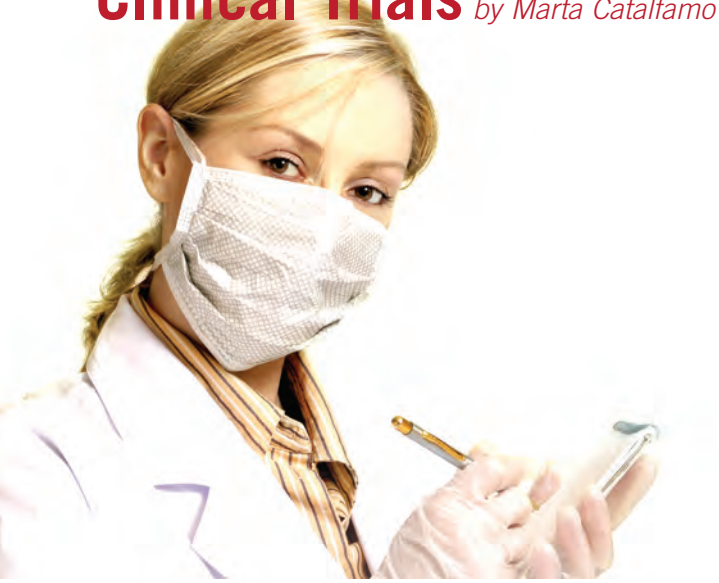
Lisa Osborne, Ph.D.
Assistant Professor
Department of Microbiology & Immunology
University of British Columbia
Vancouver, B.C.

Dr Osborne completed her graduate training at the University of British Columbia, investigating how signals from a stromal cell-derived cytokine, interleukin (IL)-7, support generation of host-protective immune responses. During her postdoctoral studies at the University of Pennsylvania, she investigated the immunological mechanisms that coordinate immunity to intestinal viral infection. In 2015, she started her lab in the Department of Immunology at the University of British Columbia. Her current research goals include defining mechanisms by which host-derived cytokine networks regulate diverse members of the intestinal ecosystem (viruses, bacteria and helminthic worms) in the context of infection and pathologic inflammation.

Misty Good, MD
Assistant Professor of Pediatrics
University of Pittsburgh School of Medicine
Children's Hospital of Pittsburg
Pittsburgh, PA, USA

Dr. Misty Good is a Neonatologist physician-scientist and Assistant Professor of Pediatrics in the Division of Newborn Medicine at Children's Hospital of Pittsburgh and the University of Pittsburgh School of Medicine. She received her Bachelor's degree from University of Southern California and earned her Masters of Science while completing medical school at American University of the Caribbean School of Medicine. Dr. Good completed her pediatrics training and chief residency at Children's Hospital of Illinois at the University of Illinois School of Medicine and completed her Neonatal-Perinatal Medicine and post-doctoral fellowship at Children's Hospital of Pittsburgh and University of Pittsburgh School of Medicine. Dr. Good's laboratory focuses on the cellular and molecular mechanisms involved in the development of the gastrointestinal disease affecting premature infants called necrotizing enterocolitis (NEC). Utilizing a mouse model of NEC, she is dissecting the mechanisms by which breast milk protects against the disease. A current focus of her laboratory seeks to better understand the intestinal mucosal host defense involved in NEC pathogenesis, to gain insights that will lead to the development of novel therapeutics for the disease. Additionally, Dr. Good has ongoing translational research studies evaluating the differences in the biological signature of premature infants with and without necrotizing enterocolitis, with the long term goal of determining which infants are the most susceptible to the disease, affording the opportunity to intervene earlier in the disease course, and institute strategies that may prevent the development of this devastating disease altogether.

Clinical Trials *by Marta Catalfamo*



Comparison of High-dose IL-2 and High-dose IL-2 With Radiation Therapy in Patients With Metastatic Melanoma. (SBRT/IL-2)
Principal Investigators: Brendan Curti, M.D, Steven K. Seung, M.D, Marka Crittenden, MD, PhD. Providence Health & Services. Providence Cancer Center. Portland, Oregon, 97213. United States
Contact: Christopher Fountain, R.N. Providence Health & Services. Portland, Oregon, 97213. United States. Phone: 503-215-2691
ClinicalTrials.gov Identifier: NCT01416831

Phase I/II Study of De-immunized DI-Leu16-IL2 Immunocytokine Administered Subcutaneously in Patients With B-cell NHL (DI-Leu16-IL2)
Principal Investigator: Ryotaro Nakamura, MD. City of Hope. Duarte, California 91010. United States.
Contact: Michelle Nelken. Phone: 617-755-4149
ClinicalTrials.gov Identifier: NCT01874288

MT2014-25: Haplo NK With SQ IL-15 in Adult Relapsed or Refractory AML Patients
Principal Investigator: Jeffrey Miller, MD. Masonic Cancer Center at University of Minnesota. Minneapolis, Minnesota 55455. United States.
Contact: Timothy Krepski. Masonic Cancer Center at University of Minnesota. Minneapolis, Minnesota 55455. United States. Phone: 612-273-2800
ClinicalTrials.gov Identifier: NCT02395822

IL-23/IL-12 Imbalance and T Lymphocyte Polarization in HIV Infection (INTESTIPAX)
Principal Investigator: Odile Launay, Pr. Centre d'Investigation Clinique BT505, Hôpital Cochin. Paris 75014. France.
Contact: Corinne Desaint. Centre d'Investigation Clinique BT505, Hôpital Cochin. Paris 75014. France. Phone: 01 58 41 28 59
ClinicalTrials.gov Identifier: NCT01942655

Anti-IL-17 a New Treatment for Contact Dermatititis
Principal Investigator: Tanja Todberg, MD. Department of Dermato-Allergolog. University of Copenhagen. Hellerup 2900. Denmark.
Contact: Tanja Todberg, MD. Phone: 0045 38673207
ClinicalTrials.gov Identifier: NCT02778711

Anti-IL-5 Therapy in Bullous Pemphigoid (BP)
Principal Investigator: Dagmar Simon, MD. Dep. of Dermatology. Bern University Hospital. Bern 3010. Switzerland.
Contact: Dagmar Simon, MD. Phone: 41 31 632 22 78
ClinicalTrials.gov Identifier: NCT01705795

IL-7 and IL-7R Expression in Peripheral Blood Mononuclear Cells, Peripheral Blood Monocytes or Differentiated Macrophages of Rheumatoid Arthritis Patients With Active vs. Inactive Disease Treated With DMARD and/or CIMZIA
Principal Investigator: Shiva Shahrara, PhD. Outpatient Care Center. University of Illinois at Chicago. Chicago, Illinois 60612. United States.
Contact: Shiva Shahrara, PhD. Phone: 312-413-7529.
ClinicalTrials.gov Identifier: NCT02451748

Effects of IL-1 Beta on the HPA-axis in Obese Persons (CortIL)
Principal Investigator: Mirjam Christ-Crain, MD. University Hopsital Basel. Basel. Switzerland.
Contact: Mirjam Christ-Crain, MD. Phone: 061 265 25 25
ClinicalTrials.gov Identifier: NCT02227420

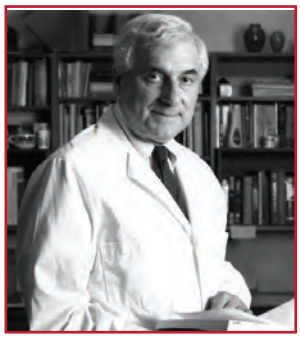
IL1-TRAP, Rilonacept, in Systemic Sclerosis
Principal Investigator: Robert Lafyatis, MD. Boston University Medical Center. Boston, Massachusetts 02118. United States.
Contact: Jessica Ziemek. Boston University Medical Center. Boston, Massachusetts 02118. United States. Phone: 617-638-5383
ClinicalTrials.gov Identifier: NCT01538719

Effect of IL-1β Inhibition on Inflammation and Cardiovascular Risk
Principal Investigator: Priscilla Hsue, MD. San Francisco General Hospital. University of California, San Francisco, California 94110. United States.
Contact: Danny Li. San Francisco General Hospital. University of California, San Francisco, California 94110. United States. Phone: 415-206-5801
ClinicalTrials.gov Identifier: NCT02272946

A Study to Investigate the Safety and Efficacy of an Anti-IFN mAb in Children Affected by Primary Haemophagocytic Lymphohistiocytosis
Principal Investigator: Multicenter. United States: Colorado, Delaware, Delaware, North Carolina, Ohio, Texas, Utah. Austria, Germany, Italy, Spain, Sweden, and Turkey.
Contact: Cristina de Min, MD. NovImmune SA. Chemin des Aulx 14, 1228 Plan-les-Ouates, Switzerland. Phone: +41-22-593- ext 5116
ClinicalTrials.gov Identifier: NCT01818492

Ruxolitinib Phosphate (Oral JAK Inhibitor INCB18424) in Treating Patients With Relapsed or Refractory Diffuse Large B-Cell or Peripheral T-Cell Non-Hodgkin Lymphoma
Principal Investigator: Julie M Vose, MD. University of Nebraska Medical Center. Omaha, Nebraska, United States.
Contact: Susan Blumel, RN. University of Nebraska Medical Center. Omaha, Nebraska, United States. Phone: 402-559-9183
ClinicalTrials.gov Identifier: NCT01431209

JAK-2 Inhibitor Before Donor Stem Cell Transplant in Treating Patients With Primary or Secondary Myelofibrosis
Principal Investigator: Rachel Salit, MD. Fred Hutch/University of Washington Cancer Consortium. Seattle, Washington 98109. United States.
Contact: Rachel B. Salit, MD. Phone: 206-667-1317
ClinicalTrials.gov Identifier: NCT02251821



SYSTEMIC LUPUS ERYTHEMATOSIS (SLE) PATIENTS PRODUCE AN INTERFERON α

by Bob Friedman

With the availability of anifrolumab an anti-interferonα receptor monoclonal antibody for the treatment of moderate to severe SLE, it might be of interest to explore the reasoning that led to this antibody's use in the treatment of this disease. In early 1982 I became aware of two publications reporting that SLE patients produced interferon in their serum during the course of their disease (1, 2). One identified the interferon in these patients as being IFNγ on the basis of its sensitivity to pH 2 (2).

From the time I was medical student, I had been quite interested in autoimmune diseases such as SLE, and my lab was studying interferons. Since I was in the Arthritis Institute at NIH which has an excellent SLE clinic, and one of my friends, Dr. David Koffler, was studying SLE at Rockefeller University, I had access to two rich sources of serum from SLE patients. Two of the scientists in my unit at the time, Olivia Preble and Roberta Black, expressed interest in the problem, so I requested some samples of serum from patients at various stages of the disease.

We proceeded to test the sera we had obtained for antiviral activity, and almost all of them had some. Indeed, high titers of interferon were often observed, especially in patients suffering exacerbations of their disease. We then attempted to characterize the interferon observed, and found that its antiviral activity was destroyed by low pH, as previously reported. Of course, we wanted to characterize the interferon we had observed further, since we had antibodies to each of the major forms of interferon known at the time. And at this point we hit a snag for the antiviral activity was neutralized only by antibody to IFNα. When you have results that differ from those of labs you know are quite careful, you get more than a little nervous. So, in order to firm up our observation, I contacted Jan Vilcek at NYU Medical School, who had antibody columns which bound IFNα, to ascertain whether he was able to check our tentative observation about exactly which form of interferon the SLE patients were producing. Jan quickly confirmed that it was IFNα, and was indeed inactivated at pH 2. We reported this unexpected result in Science (3). The effects of IFNα on the immune system are indeed similar to those observed in SLE patients.

This result had at least one unexpected follow up. Jan described the result our labs had found to Joseph Sonnabend, one of the earliest physicians treating AIDS patients in New York City. Joseph pointed out that some of the immunologic abnormalities he was observing in his AIDS patients resembled those seen in SLE, and therefore, it might be interesting to check whether such patients were also producing and acid-labile IFNα. We were able to obtain sera from some symptomatic AIDS patients, and found that 60% of them were indeed producing an interferon with the same characteristics at the SLE patients, that is, neutralized by antibody to IFNα and pH 2 labile (4).

1. Skurkovich, S. & Eremkina, E.I. Ann. Allergy 3:356, 1979.
2. Hooks, J.J. et al, N. Eng. J. Med. 301: 5, 1979.
3. Preble, O.T. et al Science 216: 429, 1982.
4. DeStefano, E. et al, J. Infectious Dis. 146: 451, 1982

Comments on the discovery of Interferon-gamma

Dear Howard,

I see in the latest ICIS Newsletter there is an article entitled "Discovery of IFN-gamma" by Julius Youngner. The following comments may be relevant and of interest to you.

In 1964, Kia Naficy and I published an article in the Proc. Soc. Eptl. Biol. and Med. v117, pg 285 entitled "Recovery of an Interferon-Like substance from Cerebrospinal Fluid"

We stated in the Discussion:

"The biologic properties of the inhibitor which we have recovered from the CSF, insofar as determined, suggested that they were identical to those of interferon. We have utilized the term" interferon-like" since at pH 2.0-2.2 a loss of activity was observed, whereas interferon is reported to be stable at pH 2".

The following year, 1965, Wheelock E.F. published an article in Science 149,310 entitled "Interferon-Like inhibitor induced in human leukocytes by phytohemagglutinin."

Our observation of pH sensitivity of the viral inhibitor was cited and given priority in William Stewarts Book "The Interferon System" Springer Verlag 1979 table 9, pg. 146

I refer to our observation and its probable relationship to Interferon gamma in a recent article in the J. of Interferon and Cytokine research 27:447, 2007 entitled "Interferon: An Unfolding Tale"

Several years later at a conference, I mentioned our observations of the pH sensitivity of the interferon-like inhibitor in C.S.F. to Julie Youngner who told me that he had been unaware of our findings.

With best wishes,
Ion Gresser

http://www.lab-initio.com/index.html

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Kim BH, Chee JD, Bradfield CJ, Park ES, Kumar P, MacMicking JD. *Nat Immunol.* 2016 Apr 19;17(5):481-9. doi: 10.1038/ni.3440.

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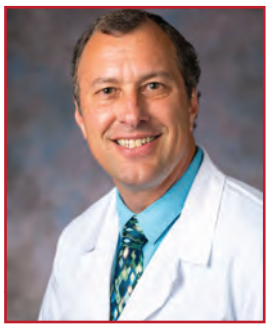

Designing NK cells for the Clinic & the impact of Cytokines: an interview with Dr. Dean Lee

By Annette Khaled

Dean Lee, MD, PhD, has just been named the director of the Cellular Therapy and Cancer Immunotherapy Program for Nationwide Children's Hospital's Division of Hematology/Oncology/BMT and Center for Childhood Cancer and Blood Diseases. Dr. Lee will also serve as the Director of Cellular Therapy at The Ohio State University Comprehensive Cancer Center.

(AK) What are the current issues around NK cells and cellular immunotherapy?
(DL) The overarching theme that is solved is the issue of growing NK cells and generating up numbers. So there's a lot of work now trying to understand the heterogeneity within NK cells and identify specific subpopulations that we can focus on for either a particular type of tumor or for an infectious disease on an individual basis. For example, I can say that your tumor expresses this NK ligand and therefore these subsets of NK cells would be most effective and then focus on expanding that subset rather than the whole bulk. There's new data from high parameter flow cytometry, like CyTOF. Now we're understanding that the average person may have 10,000 different NK cells. Some of those are going to be the ones that are most important for particular purpose.

(AK) What's the background for that finding?
(DL) This was found using the current available antibodies for NK cell surface receptors, including all the antibodies that will discriminate between different KIRs. We know that even though you may have 15 potential KIRS to choose from, any one NK cell will express one or two or three KIRs and in all possible combinations. So with just the combinatorial variability, you have 15 (basically) to the power of two, which gives you a lot of potential. In addition, you have the all NKG2 receptors. So flow cytometer with CyTOF lets you do around 40 or 45 parameters, which when whittled down into every possible combination, the average per person may have around 6-10,000 different NK cells with some people having up to 30,000 different NK cell types.

(AK) That's powerful information. Do you have a specific type of cancer you're focusing on with this technology?
(DL) Most of my work has been in AML. However, what we're looking at for this part of the project is a broad panel of different pediatric cancers. I decided to do that so we would get as a wide of representation of potential NK cell actions as possible. There are two approaches. One is to do it intelligently. Look at the tumor and identify a particular tumor type. This tumor expresses these NK ligands therefore we will select NK cells that express these receptors. Another way to say this is prospectively – identify the ligands on the tumors and select the NK cells that have these. The other way to do it is blindly. We don't know what ligands the tumors express and we don't even have all the interactions with NK cells worked out yet… So let's just interact this big bulk number of NK cells with the tumors, select the ones that respond, then grow the responders and leave the non-responders behind. Both of these approaches have different pros and cons, depending on the setting. At the moment, it surprises us that neither one seems to really do much better. It seems that the function of NK cells is already high, given the right target, that when you try to manipulate you don't get a whole lot of extra benefit. But we haven't done this in an animal model. Most work has been in vitro so far.

(AK) Is there specific strategy that you are thinking of for the clinical application of this therapy with NK cells?
(DL) Probably three areas. One of the most promising is combining it in the context of other therapies like stem cell transplant. If you are already delivering high dose chemotherapy, reducing bulk disease, and you're restoring a new immune system, then let's put in a focused number of the best NK cells that are going to consolidate remission and help immune reconstitution. Another way is to just broadly help immune reconstitution after chemotherapy. We know that NK cells are really sensitive to chemotherapy, yet right after chemotherapy is when tumors cells are most sensitive, when these are most stressed and primed. I have this hope someday, that maybe the first thing that happens, when you come into the cancer hospital with a new diagnosis, is that we take a tube of blood and build a bank of your own NK cells. Then every time you get chemotherapy, we give back your NK cells. You know, we give chemo and give back platelets, and we give chemo and

restore your red blood cells. But we don't do anything with your white blood cells or immune system. In terms of tumor control actually what you need is a good functioning anti-tumor response during that window after chemotherapy - when you are most susceptible and most likely to benefit. Then the last setting is this sort of general adoptive immunotherapy usually combined with some other kind of sensitizing agent or targeting antibody. We know that rituximab works really well by itself. In some settings, you don't have to give chemo in order to make rituximab work. But you do have to have functioning NK cells to make rituximab work. So perhaps there are certain settings where combining NK cells with a targeting antibody will further enhance the benefit of that antibody.

(AK)Is there a place in cellular immunotherapy for cytokines?
(DL) Yes, there is a lot of work being done. So where we really started understanding NK cell therapy was with IL-2 therapy. People starting playing with IL-2 and giving it to patients and thought initially that it was a T cell response. Then they realized that IL-2 activates NK cells – that's part of the reason why it (IL-2) works. More recently, the understanding of how much NK cells need IL-15 for good maturation of function has helped get IL-15 into the clinic. So once the NCI made the commitment to develop IL-15 at a clinical grade in order to do clinical trials, they looked throughout the clinical trial networks and selected some targets trials to test, which were really based on understanding NK cell function and how we could augment that using IL-15. However, both of them (IL-2 and IL-15) have been pretty toxic. Systemic use of cytokines may need more work in terms of figuring out how to direct the cytokine to the tissue that is needed most, rather than globally affecting all tissue. Altor's (Altor Bioscience Corp) work generating the high affinity IL-15 receptor cytokine is going to be real important – seeing how that works out. Seems to have much less toxicity than just IL-15 itself and yet maintains all the immune stimulating function. Another example are immuno-cytokines where you are combining cytokines with targeting antibodies. Other ways to limit the scope of what the cytokine stimulates will be important in getting more targeted benefit with less systemic toxicity.

(AK) How have you been using cytokines for cellular therapy?
(DL) Our focus has just been during expansion of NK cells and in genetically engineering the feeder cells (that expand the NK cells) to express the cytokines that we want. That's been the mostly in the form of membrane-bound cytokines that we engineer the feeder cells with. I haven't done as much clinical research - looking at giving it (cytokines) to patients – it's mainly been in the in vitro setting.

(AK) What you think are the major problems or challenges of getting cellular therapy into the clinic?
(DL) One (problem) is the feeder cell itself……getting a version that is easy to use and that we can distribute to other sites. For a lot of reasons, every time we move forward with the feeder cell itself, we get locked up around IP issues that have made it harder to further develop with academic institutions – also avoiding commercial interests. Another (problem) is GMP space and right now I think that all of cell therapy is struggling with the problem of how to get enough manufacturing ability to broadly serve the community with cell therapies. We can barely manufacture enough cells in our GMP facility for our own phase 1 trials. So companies like Novartis just built this huge GMP facility to move forward with their CAR-T cell therapies and we'll have to see how well that really translates. Can the rest of the cell therapy community really move forward enough to keep pace? It's not like you could just hand it (feeder cell manufacturing) over to a drug company and say – now make this in your drug facility. There haven't been large-scale commercial facilities for growing these cells with the exception of just a few companies like Dendreon and Novartis. The other hurdles for cellular therapies is where they fit and what kind of the things to combine it with. We certainly learned 40-50 years ago that one drug at a time was not going to work to cure cancer – you have to figure how to combine it and how often to give it and at what does and what frequency. Now we've got to figure those same things out with cell therapy.

(AK) Now that you are leading these immunotherapy programs at Nationwide Children and Ohio State cancer center – what do you want to do next?
(DL) Part of the reason that this was an appealing move for me was the opportunity to build a GMP program from the ground up. Most of the advances have been done in places that have been doing this for 20 years and we now have some really good tools for growing therapeutic cells in closed systems. We need to pay attention to new technology that can help optimize and enable higher throughput, rather than growing everything in flasks like we have over the last 30 years, which takes a lot of labor and is prone to a lot of mistakes and is prone to contamination. So trying to scale those things up with new technology that enables manufacturing in a much more consistent manner in a closed facility with safe production. So that was one of one of the things I wanted to accomplish here. I think the second is to start looking beyond just oncology and try to figure out where else is there a need for cell therapies - in the immunodeficiency space or in infectious diseases - where there's opportunities to help non-cancer patients.

Are there any final thoughts you'd like to add?
It's a really exciting time for cell therapy. From the perspective of cytokines, it is really the extension of all the hard work that was done in the past around cytokines. If we hadn't understood the importance of cytokines for different cell types, we wouldn't be able to nowadays generate the cells needed for cellular immunotherapy.

WWW

Human Protein Atlas

A Tissue-Based Map of the Human Proteome
http://www.proteinatlas.org/index.php

Here, we summarize our current knowledge regarding the human proteome mainly achieved through antibody-based methods combined with transcriptomics analysis across all major tissues and organs of the human body. A large number of lists can be accessed with direct links to gene-specific images of the corresponding proteins in the different tissues and organs.

The Immunology Link

http://www.immunologylink.com/

The Immunology Link is an immunology, cell biology, biotechnology, and molecular biology research resource, which provides information for graduate and medical students, post-doctoral fellows, clinical fellows, faculty in immunology, and research scientists in basic medical sciences and biotechnology.

Visit our site for online job and journal searches, to find a graduate program, to find an address of a scientist, for antibody resources, finding immunochemicals, information on knockout/transgenic mouse strains, and for many other useful databases.

ImmPort

https://immport.niaid.nih.gov/immportWeb/home/home.do?loginType=full

The Immunology Database and Analysis Portal (ImmPort) is a long-term, sustainable data warehouse for the purpose of promoting re-use of immunological data generated by NIAID DAIT and DMID funded investigators. ImmPort supports analysis of flow cytometry results and HLA genetic associations.

The goals of the ImmPort system are to:
- Accelerate a more collaborative and coordinated research environment
- Create an integrated database that broadens the usefulness of scientific data and advances hypothesis-driven and hypothesis-generating research
- Advance the pace and quality of scientific discovery while extending the value of scientific data in all areas of immunological research
- Integrate relevant data sets from participating laboratories, public and government databases, and private data sources
- Promote rapid availability of important findings, making new discoveries available to the research community for further analysis and interpretation
- Provide analysis tools to advance immunological research

Immuno-Navigator

A database for gene coexpression in the immune system
http://sysimm.ifrec.osaka-u.ac.jp/immuno-navigator/

The Immuno-Navigator database is a large collection of cell type-specific gene expression and co-expression data for cells of the immune system. At present, Immuno-Navigator contains co-expression data based on 3,434 samples, obtained from 24 mouse cell types, from 261 studies in total. Several co-expression databases have already been established, such as ATTED-II, COXPRESdb, HGCA, and STARNET2. In contrast with the above databases, Immuno-Navigator provides co-expression data in a cell type-specific way. A second difference lies in the processing of the gene expression data for batch effects, prior to the calculation of correlation data. Immuno-Navigator contains several functions for the analysis of gene expression and co-expression for single genes, pairs of genes, and sets of genes.

Immune Polymorphism DB

http://www.ebi.ac.uk/ipd/

The Immuno Polymorphism Database (IPD), was developed in 2003 to provide a centralized system for the study of polymorphism in genes of the immune system. The IPD project was established by the HLA Informatics Group of the Anthony Nolan Research Institute in close collaboration with the European Bioinformatics Institute.

InnateDB

http://www.innatedb.ca/

InnateDB is a publicly available database of the genes, proteins, experimentally-verified interactions and signaling pathways involved in the innate immune response of humans, mice and bovines to microbial infection. The database captures an improved coverage of the innate immunity interactome by integrating known interactions and pathways from major public databases together with

manually-curated data into a centralized resource. To date, 18,780 interactions have been manually curated by the InnateDB curation team. The database can be mined as a knowledgebase or used with our integrated bioinformatics and visualization tools for the systems level analysis of the innate immune response.

InterPro: protein sequence analysis & classification

http://www.ebi.ac.uk/interpro/index.html

InterPro provides functional analysis of proteins by classifying them into families and predicting domains and important sites. We combine protein signatures from a number of member databases into a single searchable resource, capitalizing on their individual strengths to produce a powerful integrated database and diagnostic tool.

Lymph TF DB

http://www.iupui.edu/~tfinterx/

This website is designed as a portal of information regarding transcription factor (TF) activity in the developing B and T cells (lymphocytes) in the mouse. This topic has been studied for some time, and a large number of TFs have been identified as crucial to the process. In addition to new TFs being identified and studied, differential activities, developmental stage-specific timing, modifications and cooperative functions of established TFs during lymphocyte development are continually being described. This site is designed as a repository of such information published in peer-reviewed journals. The many interactions are meant to be displayed in a biologically meaningful way so that information on timing of a TF's activity on target genes can be accessed at a glance. Queries can be run to search for TF-target gene interactions and their corresponding developmental stages. A TF-TF interaction query (run from the TF Activity page) can provide clues to the transcriptional regulatory networks active in lymphocyte development. In addition, a graphical representation of target genes' promoter region (from -8 kb upstream to +2 kb downstream of the transcription start site) where some TF binding sites are mapped can be viewed. The relevant sequence is mapped to graphical outputs of CpG content and matrix associated region (MAR) analysis and a simple drag and click tool can be employed to retrieve any portion of the sequence. Immunologists, other biological researchers and bioinformaticians are encouraged to submit any relevant information that can be added to the database.

MUGEN Mouse DB

http://195.251.21.2/mugen/mde.jsp

Welcome to the MUGEN Mouse Database (MMdb) a fully searchable database of murine models of immune processes and immunological diseases. The MMdb is being developed within the context of the MUGEN network of Excellence, a consortium of 21 leading research institutes and universities, and currently holds all mutant mouse models that were developed within the consortium. Its primary aim is to enable information exchange between participating institutions on mouse strain characteristics and availability. More importantly, it aims to create a mouse-centric international forum on modelling of immunological diseases and pave the way to systems biology of the mouse by correlating various genotypic and phenotypic characteristics.

PhosphoNet

Human Phosphosite Knowledgebase
http://www.phosphonet.ca/

PhosphoNET is an open-access, online resource developed by Kinexus Bioinformatics Corporation to foster the study of cell signaling systems to advance biomedical research in academia and industry. PhosphoNET is the world's largest repository of known and predicted information on human phosphorylation sites, their evolutionary conservation, the identities of protein kinases that may target these sites and related phosphosites. PhosphoNET presently holds data on over 950,000 known and putative phosphorylation sites (P-sites) in over 21,000 human proteins that have been collected from the scientific literature and other reputable websites. Over 19% of these phosphosites have been experimentally validated. The rest have been predicted with a novel P-Site Predictor algorithm developed at Kinexus with academic partners at the University of British Columbia and Simon Fraser University.

With the Kinase Predictor module, listings are provided for the top 50 human protein kinases that are likely to phosphorylate each of these phosphosites using another proprietary kinase substrate prediction algorithm developed at Kinexus. Our kinase substrate predictions are based on deduced consensus phosphorylation site amino acid frequency scoring matrices that we have determined for each of ~500 different human protein kinases. The specificity matrices are generated directly from the primary amino acid sequences of the catalytic domains of these kinases, and when available, have proven to correlate strongly with substrate prediction matrices based on alignment of known substrates of these kinases. The higher the score, the better the prospect that a kinase will phosphorylate a given site. Over 30 million kinase-substrate phosphosite pairs are quantified in PhosphoNET.

THE DISCOVERY OF INTERLEUKIN-2 AND LONG-TERM GROWTH OF FUNCTIONAL T-LYMPHOCYTES

Francis Ruscetti

It is indeed gratifying to have this article appear in the newsletter following Dr. Julius Youngner's description of the interferon gamma discovery. When Sandra and I came to the University of Pittsburgh to begin our graduate studies in 1968, Dr. Youngner was chairman of the microbiology department at the medical school and by the time I completed my studies, I was keenly aware of his and Dr. Salvin's then unpublished data on interferon gamma, which presaged my developing views on humoral regulation.

In the 1970s, there was still considerable debate about the growth potential of lymphoid cells, with many investigators believing that small lymphocytes were terminal end-stage cells with no real function. Fortunately, during my time as an instructor at Pitt, my interest in the new field of in vitro hematopoiesis driven by growth factors allowed Paul Chervenick and I to show that activated T cells released hematopoietic growth factors (1), although reviewers repeatedly informed us that T cells do not make such factors. Ray Cypress and I demonstrated growth factor specificity by using parasite-infected rats that developed eosinophilia to discover an eosinophilic-specific factor (now IL-5) for the growth of eosinophils in these infected rats (2).

Based on my experience with myeloid growth factors, Robert Gallo, who wanted to identify a means of growing human myeloid cells long-term in order to discover and culture human retroviruses, offered me a postdoctoral fellowship in his laboratory at the National Cancer Institute (NCI). When I arrived at NCI, the project on growing myeloid cells had also been given to Doris Morgan. We chose mitogen activated human peripheral blood mononuclear cells (PBMCs) as a source of myeloid growth factors even though neither the blastogenic factors nor the colony-stimulating factors previously discovered from PBMCs gave any hint of long-term growth potential. Human bone marrow cells used as a source of myeloid progenitors were cultured under many variations with repeated additions of cell free supernatants from PHA stimulated PBMCs from several different donors providing a strong mixed-lymphocyte reaction (MLR) (3, 4). Despite months of attempts to grow myeloid cells, the immature and mature myeloid elements rapidly died leaving only lymphoid cells. At that time, only EBV-transformed B cells and leukemic cells proliferated in suspension culture but these cells were all exogenous factor-independent. Although, at that time, there were few methods to identify human T lymphocytes, I found that these proliferating cells were pure cultures of sheep erythrocyte (E) rosette forming T cells, which could be maintained and expanded continuously for 9 months solely by the repeated addition of T cell growth factor (TCGF now IL-2). We reported TCGF/IL-2 as a factor capable of enerating normal T cells in large quantities and predicted that these factor-dependent normal T cells would provide an excellent tool for molecular immunological studies of the growth and differentiation of T cells and could be utilized in the treatment of cancer patients. The immunological studies on IL-2 were primarily initiated by Kendall Smith and his colleagues. The availability of IL-2 made it possible to study cloned T cells with a single antigenic specificity (5). This has led to an understanding of how T cells recognize antigens and the identification of receptors for IL-2 and antigens.

Given the serendipitous nature of science, Robert Gallo was initially disappointed that this approach yielded the "wrong" (non-myeloid) cell for the purpose of cultivating human retroviruses. However, Bernie Poiesz and I used our IL2/T cell growth discovery to provide the necessary culture methodology that led to the discoveries of the first diseases causing human retroviruses, HTLV-1 (6) and HIV-1 (7).

In retrospect, the potential of long term growth of T cells and subsequently other cell types (8), including immature myeloid cells, the original cellular target, was more important than the discovery of a single growth factor. Joe Gootenberg and I demonstrated the presence of another distinct human TCGF (now IL-15) in lymphoma cells (9). These observations on T cell growth also led to the unanticipated identification of TH1 and TH2 polarized T cell types and the many T cell subsets that followed. Furthermore, recent studies led to the surprising observation that IL-2 is a stimulator of T regulatory cells (Tregs) (10). IL-2 is necessary for the development, survival and expansion of Tregs that repress self-reactive lymphocyte responses. Consequently, we now know that cytokines like IL-2 regulate the ying and yang of effector and suppressive immune responses. All of these discoveries have led to the tremendous increase in attempts to use immuno-therapy for treatment of chronic diseases.

It is particularly gratifying that our report of the discovery of IL-2 eventually sparked great interest in growth regulation of lymphocytes and as a result, merited being featured as a "Pillar of Immunology" by the Journal of Immunology in 2007 (4). Subsequently, at the 100th anniversary meeting of the AAI, it was selected as the second most important paper published in JI over that period. As with any scientific discovery, some people do not get sufficient credit and I would like to recognize Ray Kiefer, the late Alan Wu and Bob Gallagher for their contributions to these studies.

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Lab Happiness

This recipe was in the newsletter many years ago but it will still make your lab very happy (unless you have some labmates that have lost their chocolate gene). Members are encouraged to send other recipes that have been found to improve lab morale.

BLACK BOTTOM CUPCAKES

8 oz cream cheese
1 egg
1/3 cup sugar
1/8 tsp. salt
1 6-oz pkg. Chocolate chips (dark is better)

1 ½ cup sifted all purpose flour
1 cup sugar
1 tsp. baking soda
¼ cup cocoa
½ tsp salt
1 cup H20
1/3 cup oil
1 tblsp vinegar
1 tsp. Vanilla

Place cream cheese, egg, sugar and salt in a bowl. Beat well and stir in chocolate chips. Set aside. Beat all remaining ingredients until blended. Fill cupcake liners 1/3 full. Top each with a heaping teaspoon of cream cheese mixture. Bake at 350 degrees for 25-30 minutes. Makes about 18 cupcakes but they will disappear fast.

Special Thanks to David Artis for his outstanding efforts and dedication on behalf of the ICIS for Cytokines2016

サイトカイン2016用ICISの代わりに彼の卓越した献身と取り組みについてデビッド・アルティスへのスペシャルサンaクス

Gracias especiales a David Artis por sus esfuerzos y la dedicación de las instalaciones nombre de la CIHI de citoquinas 2016

Un ringraziamento speciale a David Artis per il suo straordinario impegno e dedizione da impianto conto del CIHI per citochine 2016

Merci spécial à David Artis pour son dévouement exceptionnel et efforts en faveur de l'ICIS pour Cytokines 201

特别感谢大卫·阿蒂斯为他卓著的奉献和努力的ICIS代的细胞因子2016年

Besonderer Dank geht an David Artis für seine herausragenden Engagement und Einsatz für die ICIS für Cytokine 2016

사이토 카인 2016에 대한 ICIS의 대신에 특별 그의 뛰어난 헌신에 대한 데이비드 아티스에게 감사와 노력

תודות מיוחדת לדוד סיטרא רובע תואצוי תוריסמה ולש ופודה ICIS סעטמ סיצמאמ ביניקוטיצ רובע2016ם

Особая благодарность David Artis за его выдающуюся самоотверженность и усилия по оказанию помощи ИОПП для цитокинами 2016 года

شكر خاص لديفيد ارتيس لتفانيه المتميز والجهود نيابة عن ICIS للسيتوكينات 2016

2017 ICIS Meeting

www.icis2017japan.com

Meetings of Interest

Abstract Submission Deadline: 30 November 2016

SPECIAL FOCUS
Development and Maintenance of Immune Activation and Tolerance.

FACTS & FIGURES
600 - 800 participants, more than 40 international speakers in 12 plenary symposia, more than 250 abstracts, 3 poster sessions with buffet, 12-16 workshops, 12-16 best workshop presentation awards, 25 travel grants, 5 poster prizes

EARLY REGISTRATION AT REDUCED PRICE & ABSTRACT SUBMISSION
1 October - 30 November 2016

TOPICS

Basic Mechanisms

- Innate immune response
- Dendritic cell subsets and immune regulation
- B cell subsets and immune regulation
- NK cells and NK-T cells
- Eosinophils, Basophils and Neutrophils
- Innate lymphoid cells
- Transcriptional regulation of immune responses
- Development of effector and regulatory T cells
- T and B cell memory and immune regulation
- Effector mechanisms in immune response
- Chemokines and receptors in immune response
- Apoptosis in the regulation of immune responses
- Mechanisms of immune privilege
- The role of microRNAs in immune regulation and effector functions
- Immune regulatory mechanisms related to resident tissue cells
- Epigenetic-mediated immune response and immune memory
- Metabolism and immunity

Focus on clinical application, drug discovery and novel biotechnological developments

- Hygiene hypothesis in immune regulation
- Regulatory and effector T cell subsets and cytokines: from bench to bedside
- Immune response to parasites
- Tumor antigen-specific immune regulation
- Autoimmunity
- Neuroimmunology
- Allergy and asthma
- Immune regulation in organ transplantation
- Experimental models of inducing and breaking peripheral tolerance
- Mucosal tolerance and intestinal homeostasis
- Development of novel vaccines and drugs
- "Biologicals", Immunomodulation in vivo
- Cellular therapies including stem cell therapies
- Regenerative medicine and immune system
- Precision Medicine

Meetings of Interest

The Beyond Sciences Initiative (BSI) announces:

Science & Society is an online, globally accessible conference providing academics from around the world an opportunity to present their research and network with a broad scientific audience. Online Registration & Abstract submissions: www.beyondsciences.org/conference2017/ Registration and Abstract submission are free of charge, and will remain open until November 30th, 2016.

TRINITY COLLEGE | Immunology UNIVERSITY OF TORONTO | BioLegend®

TNFSuperfamily2017

https://tnfsuperfamily2017.wordpress.com/

The 16th TNF Superfamily meeting will be held from 17-21st of April 2017 in Singapore. As in all previous meetings there will be an exciting scientific program that will cover all aspects of this fascinating family: the biology, the biochemistry, the clinical applications and pharmaceutical perspectives.

There will be a large percentage of talks set aside for selection from abstracts so that the most exciting and emerging areas can be presented at the meeting. And there will also be short talks set aside for junior scientists.

Singapore is a lively city to visit with many cultural diversions and innumerable and diverse eating opportunities. The Organizing Committee will capitalize on this to develop a social program that will enhance the scientific program giving plenty of time for attendees to interact and exchange ideas and share the excitement emanating from this area in an informal setting.

Lastly, Singapore really is a world class tourist destination and travel hub and in easy reach of many other beautiful South East Asian locations. Why not take this opportunity to discover this fascinating part of the world?

San Francisco Trivia Answers (from page 9)

1 Frank Sinatra. According to the Internet Movie Database (www.imdb.com), Sinatra injured his hand and had to back out, then the role was rejected by John Wayne, Steve McQueen and Paul Newman before Eastwood accepted it.

2 Just one: Taxi driver Paul Stine, at the corner of Cherry and Washington streets in 1969. The Zodiac also is suspected of killing three people in Vallejo and one near Lake Berryessa. In letters, he claimed far more victims, but these are the only five police have linked him with.

3 San Jose, Vallejo and Benicia.

4 The lightbulb is at the Livermore Fire Station, 4550 East Ave., and has been burning since 1901. It has been recognized by "The Guinness Book of World Records," and even has its own Web cam at www.centennialbulb.org/photos. htm.

5 Julia McWilliams, who later married and became far better known by her married name: Julia Child.

6 The streets around Cupid Row, which are in the shape of a heart.

7 Woody Allen.

8 O'Neill wrote his most famous plays there, including "The Iceman Cometh."

9 Tan and the others have all been members of the Rock Bottom Remainders, a rock music group. And no, they're not quitting their day jobs.

10 The far west end of the former Alameda Naval Air Station sticks so far into the bay that it is technically in San Francisco. So from there, it's not exactly hard to walk to Alameda County.

11 Hills of Eternity Memorial Park, a Jewish cemetery in Colma. Earp's wife, Josephine Marcus, was Jewish, and her family had a plot there. If you just can't get enough trivia about where various people are buried, check out www.findagrave.com.

12 Tuffy might well have been the only dog in Army history to be court- martialed. On patrol during World War II, Tuffy went after a girl who was running across the street and tore her trousers. After behaving himself for months, however, he was reinstated -- and eventually was buried with full military honors.

13 The 2AM Club, one of Lewis' favorite hangouts, is on the cover of the group's popular "Sports" album.

14 A comic drawn by Charles Schulz that was the precursor to Peanuts. When United Feature Syndicate picked up his work, it wanted to change the name because there were already strips called Little Folks and, of course, Li'l Abner. A collection of the Li'l Folks strips is available through the Charles M. Schulz Museum in Santa Rosa. According to the museum, Schulz never liked the Peanuts title.

15 Cyril Magnin, nicknamed "Mr. San Francisco," notable bon vivant and the city's chief of protocol years ago.

16 Woodside resident Shirley Temple Black. According to Guinness World Records, Shirley Temple was 6 years and 310 days old when she earned a special Oscar in 1935. If you just can't resist playing "Six Degrees of Separation," you wouldn't need much to connect Magnin, who appeared in only two films, with Temple, whose last major movie was in 1949. Billy Barty was in "Foul Play" with Magnin and in 1933's "Out All Night" with Temple. And in the real world, Black has been an ambassador and White House chief of protocol and has attended all sorts of Bay Area functions, so she would have crossed paths many times with Magnin, who died in 1988.

17 John Geary, San Francisco's first mayor.

18 Niles, the historic district of Fremont.

19 Because of its brothels and saloons near Kearny and Montgomery streets in the bawdy old days, Pacific Street was nicknamed "Terrific Street." Residents who lived in less colorful blocks wanted to be separated from the scum, so the Board of Supervisors passed a resolution in 1871 naming the section west of Larkin Street as Pacific Avenue. As the years went on and things cleaned up, the whole street eventually became Pacific Avenue in 1929.

20 Redwood City. According to the city's Web site, the U.S. and German governments evaluated meteorological data and identified that Redwood City was at the center of one of the world's three best climates (the Canary Islands and the Mediterranean coast of North Africa are the other two).

21 St. Mary's College used to be there, but eventually left the city, first for Oakland and then for Moraga. As a couple of streets were developed, they were put in the shape of a bell. What, you've never heard of the bells of St. Mary's?

22 Robin Williams.

23 The Rev. Jim Jones, the same man who ended up leading a mass suicide in Guyana 18 months later.

24 It's the Potter Schoolhouse, now a private residence, and it's actually in Bodega, several miles inland.

25 According to Janet Bailey's "The Great San Francisco Trivia & Fact Book" (Cumberland House), that was the first band that Jerry Garcia formed with Bob Weir and Ron McKernan -- before the Grateful Dead.

26 Tom and John Fogerty, who later went on to fame as part of Creedence Clearwater Revival.

27 The Filoli estate in Woodside, the Spring Mountain Vineyard in St. Helena and the Fairmont Hotel in San Francisco.

28 Deanna Kastler, the office administrator for the San Francisco Museum and Historical Society, says the most common theory involves a toast between two men during the Gold Rush era in the bawdy area around Broadway and Pacific. "Here's to the Barbary Coast," one said. "If the whiskey don't get you, the harlots and hoodlums will." The toast was because of San Francisco's similarity to the notorious Barbary Coast of northern Africa, a longtime haven for pirates.

29 The Oakland Señors. By the time they played their first game, though, the name had already been changed.

30 Debbie Sivyer married a Portola Valley investment adviser named Randall Fields. In 1977, she opened Mrs. Fields Chocolate Chippery in Palo Alto. And the rest is cookie history.

San Francisco

http://mentalfloss.com/article/54225/25-things-you-didnt-know-about-san-francisco

1. The Chinese fortune cookie was invented by a Japanese resident of San Francisco.
2. And Irish coffee? It was perfected and popularized in the City by the Bay.
3. Lombard Street gets all the love, but Filbert St. between Hyde and Leavenworth Streets is the steepest—31.5 degrees!
4. San Francisco was part of Mexico until the Mexican-American War in 1848.
5. During the Depression, not a single San Francisco-based bank failed.
6. Business was so good, the city constructed the Oakland Bay Bridge and the Golden Gate Bridge during the Depression.
7. When Al Capone was held at Alcatraz, he gave regular Sunday concerts with the inmate band, the Rock Islanders. He played the banjo.
8. In 1901, the city outlawed burials. Most of its cemeteries are in Colma, Calif. There, the dead outnumber the living by over 1000 to 1.
9. The "Summer of Love" actually started in the winter. The January 1967 Human Be-In at Golden Gate Park kicked it off.
10. Speaking of seasonal confusion, Mark Twain wasn't as down on San Francisco's weather as some people would have you believe. Twain never uttered the quote, "The coldest winter I ever spent was a summer in San Francisco."
11. The neighborhoods of Marina, Mission Bay, and Hunters Point are all built atop a landfill.
12. The first bubonic plague epidemic in the continental US broke out in SF's Chinatown in 1900.
13. As historical beginnings go, the United Nations Charter was drafted and ratified in San Francisco in 1945.
14. And as historic endings go, the Beatles gave their last full concert at Candlestick Park on August 29, 1966.

Fun Facts

15. San Francisco was huge on the mid-century treaty circuit. In 1951, the Treaty of San Francisco officially ended Japanese hostilities from World War II.
16. When prospectors caught gold fever and hightailed it to California, San Francisco's port became packed with abandoned ships. With demand to build the city booming, the ships were torn apart and repurposed into banks, businesses, and homes.
17. Decades later, in 1906, three quarters of the city was destroyed by an earthquake and fire.
18. Contemporary reports of the fire note that an unlikely hero helped save the city: Redwood trees. When fire hit buildings made of redwood, which has low resin content and a porous grain that takes in lots of water, they didn't go up in smoke.
19. In September 1859, San Francisco's favorite eccentric resident, Joshua Abraham Norton, declared himself America's emperor.
20. Emperor Norton had a following: Nearly 30,000 people later packed the streets for his funeral.
21. The bear on California's state flag is modeled after a California grizzly named Monarch, who was held at Golden Gate Park.
22. The U.S. Navy originally planned on painting the Golden Gate Bridge black with yellow stripes. The famed "International Orange" color was supposed to be a sealant.
23. In 1867, San Francisco instituted America's first "ugly law," which prohibited unsightly people from showing their faces in public. (It's since been repealed.)
24. The city's cable cars are the only National Historical Monument that can move.
25. The Liberty Bell once vacationed in San Francisco! When San Francisco hosted the Panama-Pacific International Exposition in 1915, America's most famous bell made a national train tour to be part of the fun. After the exposition ended, it returned to Philadelphia, where it's stayed ever since. Once you've seen San Francisco, why travel anywhere else?

REMEMBER TO **JOIN** THE INTERNATIONAL CYTOKINE AND INTERFERON SOCIETY OR **RENEW** YOUR MEMBERSHIP FOR 2017 OR BEYOND (3 YEAR, 5 YEAR, LIFETIME (AGE 55+) AND STUDENT MEMBERSHIPS ARE AVAILABLE)

Signals

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