# NIH-FDA IIG

National Institutes of Health // Food and Drug Administration // Immunology Interest Group

# NEWSLETTER

## MAY 2022

## PUBLICATIONS

### NF-kB, a culprit of both inflamm-ageing and declining immunity?

Songkiatisak P, Rahman SMT, Aqdas M, Sung MH.
Immun Ageing. 2022 May 17;19(1):20.
DOI: 10.1186/s12979-022-00277-w. PMID: 35581646.
*With its diverse functions, NF-kB has the potential to serve as linkages between known hallmarks of ageing. However, the complexity of NF-kB dimer composition, dynamic signaling, and tissue-specific actions has received relatively little attention in ageing research. Here, we discuss some areas of further research that may shed light on the impact of NF-kB in healthy ageing and longevity.*

### Universal antigen encoding of T cell activation from high-dimensional cytokine dynamics.

Achar SR, Bourassa FXP, Rademaker TJ, Lee A, Kondo T, Salazar-Cavazos E, Davies JS, Taylor N, François P, Altan-Bonnet G.
Science. 2022 May 20;376(6595):880-884.
DOI: 10.1126/science.abl5311. PMID: 35587980.
*We combined robotics, machine learning and theoretical modeling to build a quantitative model of antigen discrimination by T cells. High-dimensional dynamics of cytokine secretion could be compressed into a 1D model that classifies CD8+ T cell responses to antigen, according to antigen quality, independently of the immunological context (antigen quantity, T cell precursor frequency, antigen presenting cells etc.). We derived further insight about the competition between positive and negative feedbacks that regulates TCR signaling.*

*Accompanying comment: T cell immune responses deciphered.*

### Postmitotic G1 phase survivin drives mitogen-independent cell division of B lymphocytes.

Singh A, Spitzer MH, Joy JP, Kaileh M, Qiu X, Nolan GP, Sen R.
Proc Natl Acad Sci U S A. 2022 May 3;119(18):e2115567119.
DOI: 10.1073/pnas.2115567119. PMID: 35476510.
*B lymphocytes undergo multiple mitotic divisions, termed clonal expansion, to expand antigen-specific cells that mediate effective immunity. Here we demonstrate that B cells that have undergone one cell division continue to proliferate even in absence of further mitogenic signals. This mitogen-independent proliferation is accompanied by an altered G1 phase marked by transcriptomic and proteomic features of G2/M. Survivin, a G2/M-specific oncogene, is required in G1 to achieve mitogen-independent proliferation.*

### A phenotypic signature that identifies neoantigen-reactive T cells in fresh human lung cancers.

Hanada KI, Zhao C, Gil-Hoyos R, Gartner JJ, Chow-Parmer C, Lowery FJ, Krishna S, Prickett TD, Kivitz S, Parkhurst MR, Wong N, Rae Z, Kelly MC, Goff SL, Robbins PF, Rosenberg SA, Yang JC.
Cancer Cell. 2022 May 9;40(5):479-493.e6.
DOI: 10.1016/j.ccell.2022.03.012. PMID: 35452604.
*T cells in fresh NSCLC tumor were analyzed by CITE-seq with TCR-seq and the signature that can identify both CD4 and CD8 neoantigen-reactive T cells was developed. This method can expedite the personalized neoantigen-reactive T cell therapy.*

**Continued>>**

## A Randomized Phase II Trial of mFOLFOX6 + Bevacizumab Alone or with AdCEA Vaccine + Avelumab Immunotherapy for Untreated Metastatic Colorectal Cancer

Redman JM, Tsai YT, Weinberg BA, Donahue RN, Gandhy S, Gatti-Mays ME, Abdul Sater H, Bilusic M, Cordes LM, Steinberg SM, Marte JL, Jochems C, Kim SS, Marshall JL, McMahon S, Redmond E, Schlom J, Gulley JL, Strauss J. Oncologist. 2022 Mar 11;27(3):198-209.
DOI: 10.1093/oncolo/oyab046. PMID: 35274710.

*This study randomized patients to FOLFOX + bevacizumab standard of care (SOC) or SOC + avelumab + CEA-targeted vaccine (SOC + IO) for first-line treatment of microsatellite-stable metastatic colorectal cancer. SOC + IO did not improve progression-free survival or objective response rate compared to SOC alone in this small, randomized trial. However, the SOC + IO regimen yielded biological activity in the form of substantial increases in multifunctional CD4+ and CD8+ T cells specific for the cascade antigens MUC1 and brachyury. Identifying therapeutic regimens that can harness these cells and lead to improved clinical outcomes is key, as is further investigation of the potential biomarkers of response identified in this study.*



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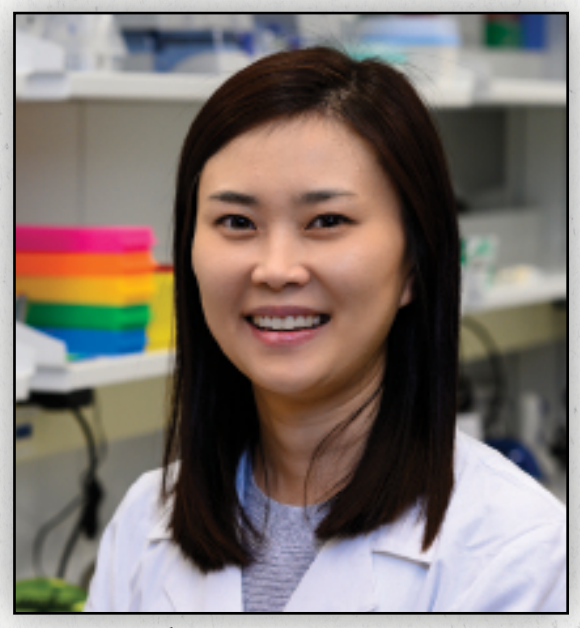
# Immunology Interest Group

# SPOTLIGHT

**Dr. Yoo is a Stadtman Investigator in the Chemical Biology Laboratory and Head of the Chemical Immunology Section at the Center for Cancer Research, NCI. To learn more about her work visit: https://ccr.cancer.gov/staff-directory/euna-yoo**

***Tell us about your science.***

Our laboratory develops chemical approaches to study and manipulate the human immune system to impact cancer biology, diagnosis, and treatment. We use synthetic chemistry, biochemical and phenotypic screening, and chemoproteomics to develop chemical probes that specifically detect and perturb key immune signaling pathways. In particular, our research focuses on defining the function of immunomodulatory proteases in cancer.



Euna Yoo, Ph.D.

***What event(s) lead to your career in science and interest in immunology?***

Immunology was one of my favorite courses I took in college. I was fascinated by the myriad of cell types that function together under the umbrella of immune system and complex chain of events that induce proper immune responses. For my graduate research, I joined the lab that investigates toll-like receptor agonists as vaccine adjuvants and realized that chemical developments have long assisted important discoveries in immunology. During my postdoctoral training, I became interested in understanding the role of specific enzymes during immune activation and tolerance.

***How has a mentor or colleague substantially influenced your career trajectory?***

I have been very fortunate to have great mentors and colleagues throughout my career in science. My postdoc mentor Dr. Matt Bogyo provided a research environment where I could be both independent and collaborative. His mentorship and all the interactions that I had with collaborators and colleagues in his lab paved the way for me to become a PI.

***In what area(s) do you expect significant research/medical advances in the next 5-10 years?***

I think cancer immunotherapies will continue to have significant impact. I expect that with advancements of genetic testing and diagnostic imaging, personalized medicine will be more widely implemented.

***What do you value most about the NIH-FDA Immunology community?***

The NIH-FDA Immunology community is a great place where scientists exchange ideas and develop new interactions.

***How do you spend your free time?***

I enjoy running, hiking, walking around town, and going to museums.



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# Immunology Interest Group

# SPOTLIGHT

**Dr. Bhattarai is a Principal Investigator in the Division of Cellular and Gene Therapies, Office of Tissues and Advanced Therapies in CBER, FDA. To learn more about his work visit: [https://www.fda.gov/vaccines-blood-biologics/biologics-research-projects/assessing-immunogenicity-products-gene-therapy-and-t-cell-therapy](https://www.fda.gov/vaccines-blood-biologics/biologics-research-projects/assessing-immunogenicity-products-gene-therapy-and-t-cell-therapy)**

Nirjal Bhattarai, Ph.D.

***Tell us about your science.***

My lab studies immunogenicity and inflammatory toxicities associated with gene therapy products. We are interested in understanding immune responses to gene therapy vectors such as AAV and developing novel strategies to reduce immunogenicity of these vectors. We are also working on understanding mechanisms for inflammatory toxicities often seen with cell-based gene therapy products such as CAR-T cells. Our overall goal is to understand underlying mechanisms contributing to these challenges in gene therapy and help develop novel ways to mitigate the risks and improve safety and efficacy of gene therapy products.

***What event(s) lead to your career in science and interest in immunology?***

I don't remember exactly when I became interested in science, but it started quite early. I was always fascinated by the universe, and how certain things work in certain ways within the universe. Science was the way for me to get answers to those questions, although I did not understand most of those concepts back in the days (and still don't understand much!). This also triggered a curiosity to engage in scientific research, but growing up in Kathmandu, Nepal in 90s where scientific research was limited, I did not get any opportunity. This led me to come to US for college where I was able to do research. After college, I worked with a virologist developing novel immunoassays to detect viruses. This experience was very rewarding, which led me to choose a career in virology/immunology.

***How has a mentor or colleague substantially influenced your career trajectory?***

My graduate school mentor, Dr. Jack Stapleton (University of Iowa) has significantly influenced my career. Although, he was my mentor, he treated me like a friend, and we always had open and candid discussions about science, lab, projects and life. He always supported my ideas, and even when most of the times they did not work, he always motivated me to ask new questions and try new experiments. He was very kind and demonstrated excellence in mentoring and motivating young scientists. As a practicing physician, even though he used to have long days in hospital, he always made time to visit lab and discuss research with me. His passion and motivation towards research were very contagious, it sparked an interest in me to not only peruse research, but also mentor and motivate next generation of scientists.

***In what area(s) do you expect significant research/medical advances in the next 5-10 years?***

I think gene therapy is really going mature in next decade or so. The field is developing very innovative therapies to treat and cure previously untreatable or incurable diseases. I think we will find solutions to many problems we face today through gene therapy, and we will be able to change lives of people around the world. This is really a exciting time.

***What do you value most about the NIH-FDA Immunology community?***

I deeply value friendship, collaboration, information exchange, and the support that I get from this community. This is really an unique relationship we have between two premier institutes, and this has benefited many of us - I look forward to many more exciting things that will come from this community.

***How do you spend your free time?***

I have yet not grown up from my time as a kid looking up in the sky and thinking about universe. So, whenever I get "free" time, I try to read about latest research on universe. I also like history, as it is very good teacher, so I read about ancient civilizations, empires, etc. Over the years, I have realized that there is no such thing called "free" time. Time is the most valuable thing we all have, and we should all use our time wisely and try doing things that make us happy. For me that is spending time with family and friends.



*Continued>>*

# NIA Fellow Receives Nathan W. Shock Award

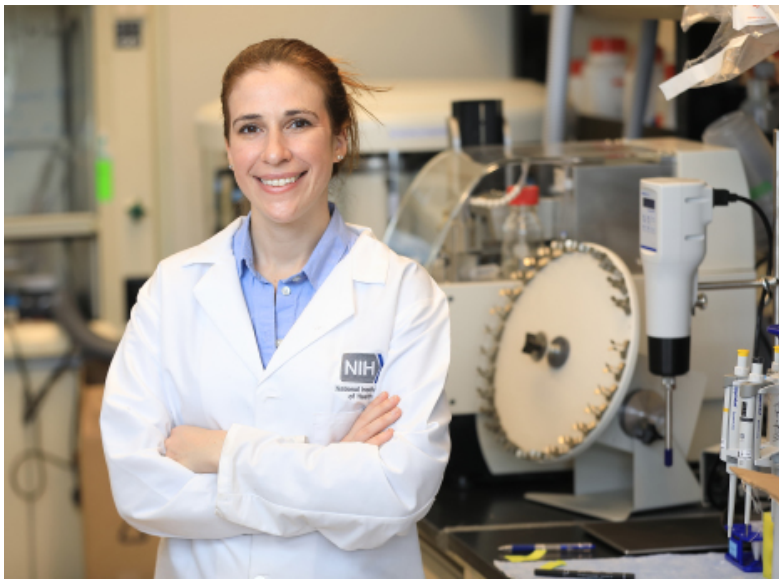
Dr. Shah Md Toufiqur Rahman, Ph.D., a post-doctoral fellow working to understand tissue-specific NF-kappaB signaling dynamics and it's dysregulation with aging in the Transcription Systems Dynamics and Biology Unit, Laboratory of Molecular Biology and Immunology, NIA led by Myong-Hee Sung Ph.D. Dr. Rahman received the Nathan W. Shock Award, the highest recognition at the 2022 National Institute on Aging Intramural Research Program Scientific Retreat.

Dr. Rahman presented a TED talk and poster related to this work entitled, "NF-κB reporter mouse models: a new tool for monitoring endogenous NF-κB activity at single-cell resolution."

Shah Md Toufiqur Rahman, Ph.D.

# Kaitlyn Sadtler Selected as World Economic Forum Young Global Leader and Receives Honorary Degree

Dr. Kaitlyn Sadtler, Ph.D. Earl Stadtman Tenure-Track Investigator and Chief of the Section for Immunoengineering was named a World Economic Forum Young Global Leader in 2022. The World Economic Forum selects the Young Global Leaders among the world's most promising and driven researchers, innovative entrepreneurs, activists and promising political leaders between the ages of 30 and 40.




Kaitlyn Sadtler, Ph,D

Since starting her laboratory at the NIH in 2019, Dr. Sadtler has lent her lab's expertise to the fight against COVID-19, launching the NIH Serologic Survey, detecting 16.8 million undiagnosed SARS-CoV-2 infections in the US via remote blood sampling and antibody testing. This work continues as the team works to map the spread of the pandemic in the US.

In May, Dr. Sadtler received an honorary degree and spoke during the 2022 University of Maryland Baltimore County's commencement ceremonies addressing graduates in the College of Natural and Mathematical Sciences, College of Engineering and Information Technology, and Division of Undergraduate Academic Affairs.



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# Bench-to-Bedside in Action

## Translating immunology to transform clinical care

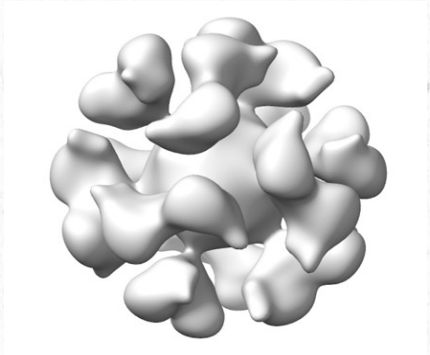
Harnessing fundamental knowledge to advance our understanding of disease and develop novel treatment strategies is a major mission of the NIH. Each month we highlight interesting clinical trials taking place at the NIH Clinical Center that are doing just that.

### Safety and Immunogenicity of an Epstein-Barr Virus (EBV) gp350-Ferritin Nanoparticle Vaccine in Healthy Adults With or Without EBV Infection

PI: Jessica R Durkee-Shock, M.D.

Epstein-Barr virus (EBV) infects more than 90% of the world's population and is the leading cause of infectious mononucleosis. Ten percent of those with infectious mononucleosis will have fatigue lasting 6 months or longer, and 1% of individuals may have serious complications including hepatitis, neurologic disease, or severe hematologic abnormalities. In addition, EBV is an oncogenic virus, associated with several multiple malignancies including gastric cancer, nasopharyngeal carcinoma, and lymphomas. Finally, EBV has been implicated in multiple autoimmune diseases, including a strong epidemiologic association with multiple sclerosis. An effective EBV vaccine could decrease the morbidity associated with infectious mononucleosis, as well as prevent future cancers and autoimmune disease.

In collaboration with the Vaccine Research Center, the Laboratory of Infectious Diseases developed a EBV gp350 ferritin nanoparticle vaccine candidate. EBV infects B cells where it establishes a lifelong infection. EBV gp350 is the principal target of antibodies that neutralize B cell infection with EBV. Use of a ferritin nanoparticle platform improves antigen presentation and immune stimulation due to high density of antigen and optimal distancing to cross link and stimulate B cells. The vaccine is adjuvanted with Matrix-M1, manufactured by Novavax, which is a potent saponin-based adjuvant. Taken together, this adjuvanted EBV gp350 ferritin nanoparticle vaccine has demonstrated greatly improved immunogenicity in animal models compared with soluble EBV gp350 used in previous vaccine trials.



Cryo-EM image of gp350-ferritin nanoparticle vaccine. Credit: Geng Meng (Purdue Univ.)

Study team from left to right:
Anna Hostal, Wei Bu PhD, Maria Ploussiou RN, Jeff Cohen MD, Jessica Durkee-Shock MD, Krista Gangler RN, and Kelly Liepshutz PA
Not shown: Kayla Morgan RN

Our recently launched, first-in-human Phase I clinical trial investigating EBV gp350 ferritin nanoparticle vaccine will study the safety and immunogenicity, both cellular and humoral, of the vaccine. Twenty individuals with prior EBV infection and 20 EBV seronegative individuals will be enrolled. Healthy volunteers will receive 3 vaccine doses over 6 months and will be followed for adverse events, including reactogenicity and autoimmunity, as well as durability of immune response for up to 30 months.

To learn more about this study, please visit: https://clinicaltrials.gov/ct2/show/NCT04645147



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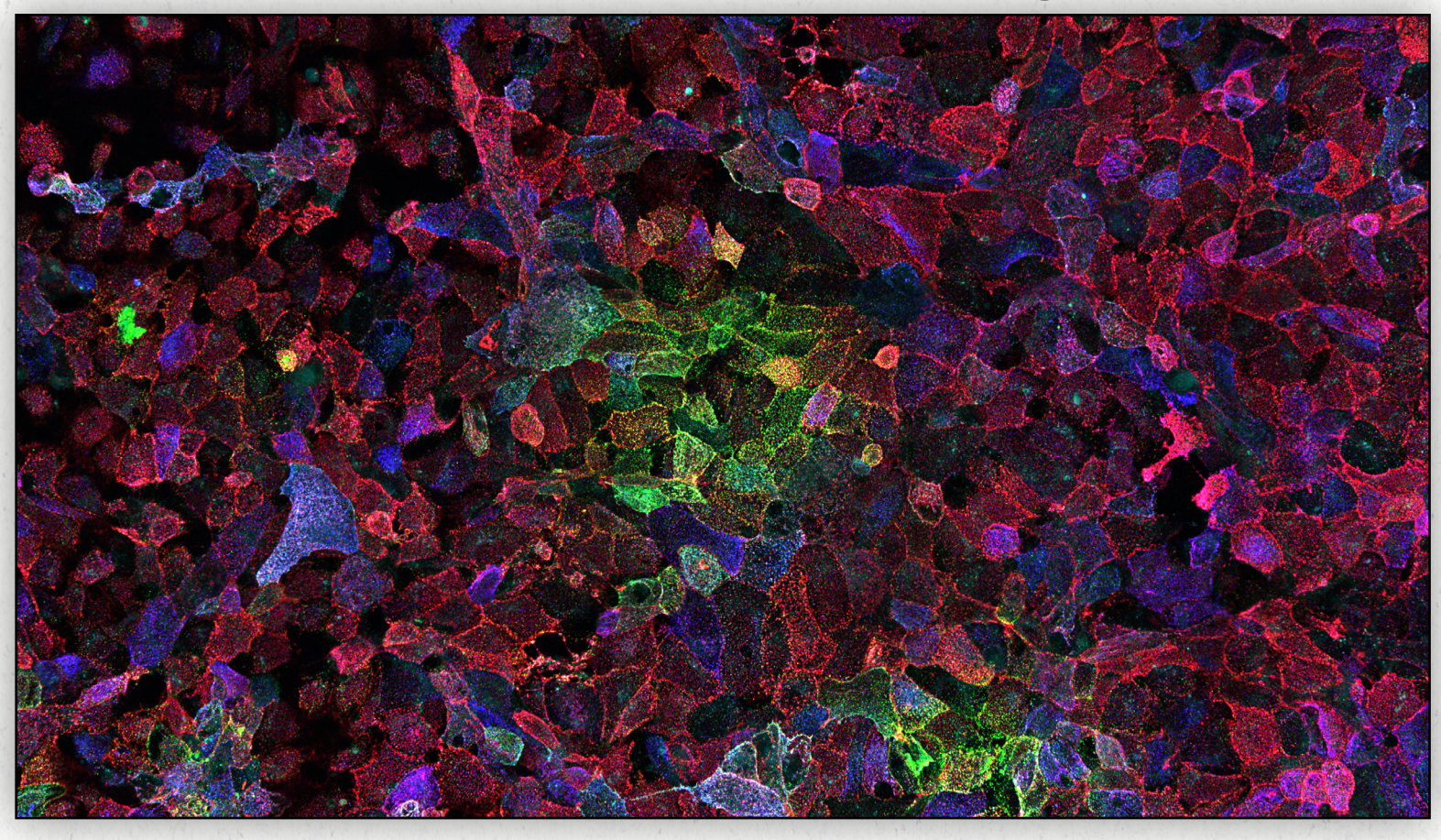
# Cell surface SARS-CoV-2 Nucleocapsid Protein during infection



Infected Vero cells with SARS-CoV-2 show surface nucleocapsid protein (green), spike (blue) and heparan sulfate (red), after live staining with monoclonal antibodies at 24 h post-infection. The nucleocapsid (N) protein is the most abundantly expressed viral protein during infection, which induces strong antibody and T cell responses. N has been canonically considered to be strictly localized intracellularly. However, cell surface N proteins of different RNA viruses have been reported to induce immunosuppression, also serving as antibody targets. For the first time, here we show a human coronavirus N protein being localized on the cell surface of infected and non-infected neighboring cells, by electrostatically associating with heparan sulfate. These findings, together with the ability of N to bind human chemokines and inhibit chemokine-mediated leukocyte migration, indicate that cell surface N may play an important role in host adaptive immunity to SARS-CoV-2 and in manipulating innate immunity at the early stages of infection.

Image credit:
Alberto D. Lopez-Munoz, Ph.D., M.Sc.
Postdoctoral Fellow
Cellular Biology Section, Laboratory of Viral Diseases
National Institute of Allergy and Infectious Diseases



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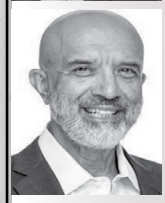
# Immunology Interest Group
# SEMINAR SERIES

## June 2022

June 1, 2022
**Joonsoo Kang**
Regulation of mucocutaneous inflammation and innate lymphocytes by cholesterol metabolites

June 8, 2022
**Akiko Iwasaki**
Immune response to SARS-CoV-2

June 15, 2022
**Gillian Griffiths****
Identifying novel genes that impact T cell effector function



June 22, 2022
**Vishva Dixit**
Why so many ways to die?

June 29, 2022
**Hans-Reimer Rodewald**
Deconvolution of hematopoiesis and immune responses by Polylox barcoding

# Missed a seminar?

## Catch up on prior talks at...

https://www.niaid.nih.gov/research/immunology-seminars

**FDA:** http://web.microsoftstream.com/channel/5c371a75-2d56-45d3-9f86-7bacc3015066

*Recordings are generally available 1-2 weeks after the presentation.



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# Join the List Serve!
## Immunology Interest Group

Share with new colleagues and trainees
that join the lab:

Please visit the IIG website and (re)subscribe to the
IMMUNI-L NIH Listserv with your
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https://www.niaid.nih.gov/research/immunology-interest-group

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