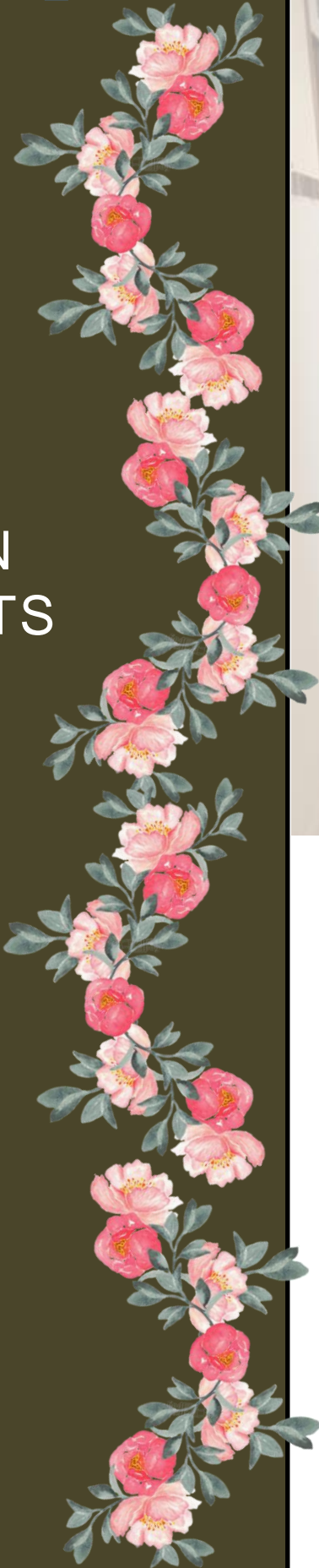


# Appel's Bulletin

Vol. 3

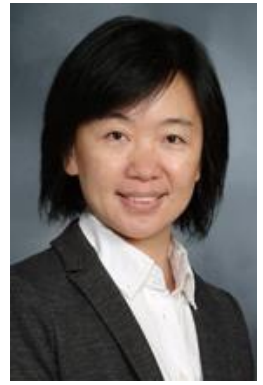
CO  
NT  
EN  
TS



- Interview with Dr. Wenjie Luo
- Staff Highlights- Man Ying
- New faculty member
- News in Appel
- Recent Publications
- Birthdays!
- Recommendations

# Interview- Dr. Wenjie Luo

Wenjie, you did your postdoctoral training in the laboratory of Dr. Paul Greengard, Nobel Prize winner. Can you describe how was your experience? Would you like to share any anecdote while you were working in his laboratory?



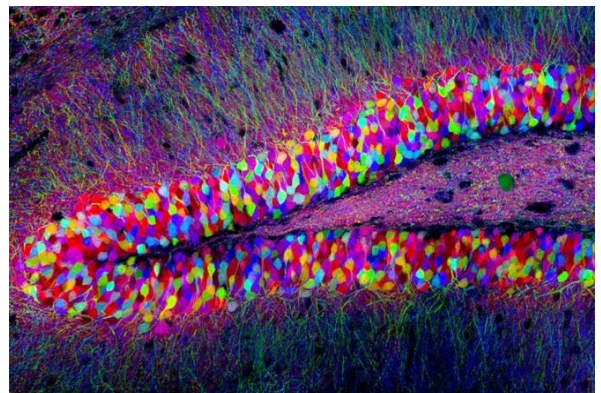
Dr. Wenjie Luo  
Assistant Professor  
of Neuroscience

[wel2009@med.cornell.edu](mailto:wel2009@med.cornell.edu)

*Those years are one of the most memorable ones in my life. I was interviewed by Paul right after his Nobel Prize winning news was announced. The whole lab was completely in a celebrating mode. Today I still clearly remember how he looked on my interview day, with extremely bright eyes and warm smile. His sharp questions yet with stronger encouragement and lots of funny jokes made me decide immediately to choose his lab for my postdoctoral training. Paul inspired me in science in many ways, which played the most important role in my long science journey till today. Paul has a strong scientific style of simplicity. He likes to write in a simple and accurate way without a single extra word. Frequently, he would spend a whole Saturday working on our manuscripts, editing line by line and word by word. Paul loves art and music. We were frequently invited to Soho art salon activities for art exhibitions of his family and friends. Paul also routinely invited lab members lunch together with him in faculty club, talking about life and other fun things in a relaxed natural environment. From these conversations, we benefited from his views beyond science. Paul devoted his whole life to science and worked until his last day. There are so many things to say about Paul, who is not only a great scientist, but also a human being I respect. I miss you, Paul!*

What is your favorite part of the brain and why?

**Hippocampus.** *It is the most beautiful brain region with such an elegant shape yet complex network. Just like its name derived the Greek hippokampus (hippos, meaning “horse,” and kampos, meaning “sea monster”), it always reminds me the cute sear horse each time I looked at it under microscope. The brainbow technology further reveals its beauty. You can see those lineup neurons in dentate gyrus stretching out to touch their team mates in hippocampal activity relay. These amazing images inspire many artists to produce many beautiful artworks. Each time I go to neuroscience conference, I will walk around in the art exhibition area and relax myself with those beautiful arts derived from hippocampi.*



Hippocampus by Family Weissman

# Interview- Dr. Wenjie Luo

You have shown us your passion about photography in previous Appel's bulletin. How did you develop an interest in photography?

*I started to develop this interest about 3-4 years ago. I joined an online workshop and picked some very basic skills how to arrange the objects and light in your photo frame. During those days, I took pictures using my phone in my daily commuting route between Penn station and work. It could be a random object on street, an old garage door on street, a homeless man sitting on stairs feeding city pigeons, or a bike parking lonely on street. I would spend my whole train riding time from Penn to home to edit those pictures in a way expressing my tiny thoughts behind. During weekends, I would go to my community and look for something interesting to me. When I bend myself down to take a picture of a stone, a flower or leaf, I like to lower the lens at the same level as them. I believe that, when we look at them closely at their level, we will feel something different from looking at them as human being. This is the most attractive part of photography; it can bring spiritual enjoyment and surprise to me.*



Photography by Wenjie Luo

What is your favorite book?

**M**y favorite book is "The Power of Now" by Eckhart Tolle. It enlightened me in many ways and helped me find my deepest self.

What is your favorite place in New York City?

**C**entral Park. It is a perfect integration of nature and humanity.



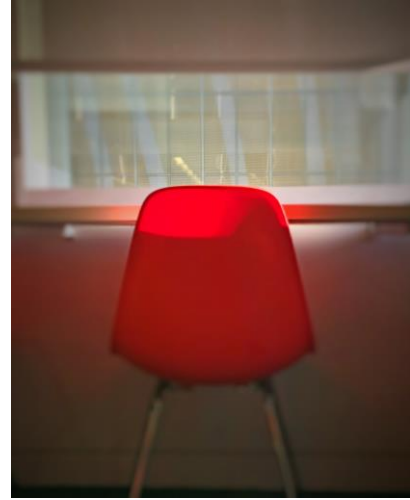
Photography by Wenjie Luo



# Interview- Dr. Wenjie Luo

Can you share with us your future projects in Alzheimer's disease?

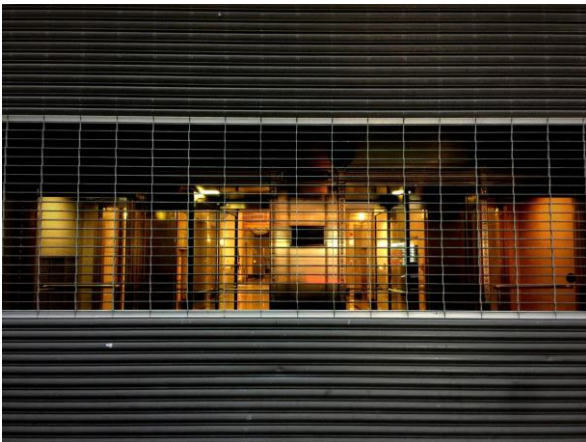
*I am super interested in how lipid metabolism contributes to pathogenesis of AD. Genome-wide association studies and microglia single-cell analyses have revealed that microglia transform from a homeostatic status into a unique disease status under neurodegenerative conditions. These disease-associated microglia have signature transcriptomic changes reflecting reprogramming of multiple cellular metabolic pathways. One of these pathways is lipid metabolic pathway. Our next challenge question is how these metabolic changes control microglial responses to disease condition, in an either adaptive and maladaptive manner, and contribute to disease progress. We will try to address these questions using AD mouse amyloid or tau mouse models and focusing on AD risk genes associated with lipid metabolism, such as APOE, TREM2, TYROBP, as well as other understudied lipid gene such as CH25H.*



Photography by Wenjie Luo

Finally, can you share any advice to those who would like to peruse a career in Neuroscience?

***Follow your interest, keep your curiosity, discover the mysteries of nature in brain with your eyes and your heart.***



Photography by Wenjie Luo

By Guillermo Coronas  
Laboratory Manager  
Appel Institute  
[guc9014@med.cornell.edu](mailto:guc9014@med.cornell.edu)

# Staff Highlights



**Man Ying Wong, M.S.**  
Senior Research Specialist  
Appel Institute  
[maw2046@med.cornell.edu](mailto:maw2046@med.cornell.edu)

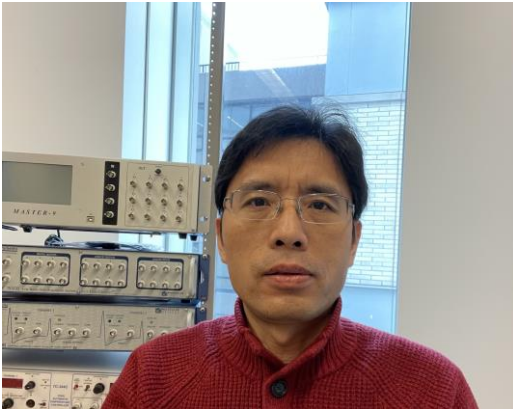
**M**y name is Man Ying Wong, I am a senior research specialist in the Gan Lab. I received my B.S. in Biochemistry from Stony Brook University and M.S. in Pharmacology from New York Medical College. I received a scholarship award from the Gates Millennium Scholar Program throughout my study. I joined the Weill Cornell community in 2011 with service in the Appel Institute for six years. It has been ten fruitful years at Weill Cornell, and I am blessed to have met and worked with many great trainers and mentors who have given so much scientific and personal guidance.

I once heard that running experiment is like cooking. The path to become a “chef” was not as easy as I have imagined. I was clueless when I was holding the pipette for the first time. My whole plate of assay had different volumes of 100 ul. I wrinkled my first western blot so badly that I could not image or analyze. I told myself I must conquer the fear of mice so that I could continue to pursue working in the science field. My science experience did not get interesting until I hopped on an internship with the National Space Biomedical Research Institute (NSBRI) at Baylor College of Medicine, where I was placed to work at the National Aeronautics and Space Administration (NASA) for a summer. Not only I studied the pharmacokinetics and pharmacodynamics of drugs during spaceflights, I also had the opportunity to visit the astronauts training center and labs where space shuttles were built, and I was invited to seminars by astronauts.

Before joining Appel, I worked in the Translational Research Program in Department of Pathology where I worked on numerous projects with immunohistochemistry staining. Upon joining Appel in 2014, I have been given many more opportunities to strengthen my scientific skills. I was trained with techniques on biochemical assays, animal surgery, microscopy, and cell culture. I picked up many tricks and tips from experts of these techniques.

Outside of lab, I enjoy traveling. Thailand is definitely my favorite place. During my free time, I like to search for travelling deals. I enjoy very much on searching and planning travelling routes. Looking forward to see everyone around and I would love to share my tips on different techniques and travelling experience.

# Welcome to Appel



**Dr. Mingrui Zhao**  
Associate Professor

[miz2003@med.cornell.edu](mailto:miz2003@med.cornell.edu)

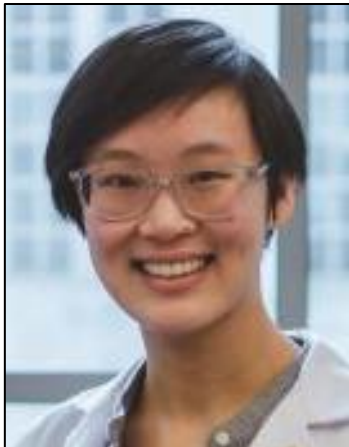
Mingrui Zhao is an Associate Professor of Research in Neuroscience in the Robert Appel Alzheimer's Disease Research Institute. He obtained his Ph.D. in neuropharmacology from the Chinese Academy of Medical Sciences and Peking Union Medical College in China. His postdoctoral trainings were done in Dr. Tracey Shors's lab at Rutgers, Dr. Bai Lu's lab at NICHD, and Dr. Theodore Schwartz's lab at Weill Cornell Medicine. Dr. Zhao's previous research focused on optical brain mapping in epilepsy, the neocortical microcircuitry in epilepsy, and the neurovascular coupling mechanisms of neurological diseases. His current research interest is in applying cutting edge electrophysiological and imaging methods to study molecular mechanisms of Alzheimer's disease including  $A\beta$ -induced aberrant neuronal activity, the miscommunications between neurons and microglia, modulation of gamma oscillations, and the imaging of neurotransmitter and neuromodulator dynamics using genetically encoded indicators.

# News

## Orr Lab



Neuroscience graduate student **Daniel Barnett** joined the lab for his thesis work on mitochondrial signaling mechanisms.



Tri-I MD/PhD student **Constance Zhou** is currently rotating in the lab; she has interests in glial-neuronal interactions.

The Orr lab was selected for funding from the **ADDF and AFTD foundations** for a drug discovery project focusing on **FTD pathology** and related disorders.

Appel Institute's **Subhash Sinha** is co-PI, and **Lei Xie** is a consultant on this project, so it is a highly collaborative endeavor in the Institute.



Alzheimer's  
Drug Discovery  
Foundation

We are growing our team and currently recruiting for **open postdoctoral positions** in our lab. Those interested in this opportunity can visit <https://www.orrlaboratory.com/labnews>



# News

## Gan Lab



Congratulations to **Sadaf Amin, Ph.D.**, from the Gan's lab for receiving the Bright Focus Award for her work "Studying the role of a novel innate immunity pathway in inducing brain inflammation and damage in Alzheimer's Disease".

*This research aims to study the molecular pathways that govern senescence and inflammation in Alzheimer's disease (AD). Cellular senescence is a state of growth arrest in response to stress. Cells in the body can become senescent in aging and many disease conditions. These cells induce chronic inflammation which damages their surrounding tissue. There is evidence that senescent cells increase in AD brains. Importantly, treatment of AD mouse models with drugs that selectively kill senescent cells has been shown to ameliorate the neurological and cognitive deficits in these mice. These promising preliminary results underline the need to study the mechanisms of senescence and inflammation in human post-mortem AD brains and mouse models. My research will focus on specific inflammatory pathways that are activated during senescence and cause tissue damage. I hope that my work will lead to a better understanding of the biology of AD and identify novel therapeutic targets to limit brain cell damage in humans suffering from AD.*



# News

## Burré Lab



Congratulations to **Virginia Gao, M.D., Ph.D.**, from the Burré lab for receiving the Leon Levy Fellowship in Neuroscience. Her proposal, “Mechanisms of  $\alpha$ -synuclein-mediated pathology in the central and enteric nervous system in Parkinson’s disease,” seeks to understand how biochemical changes in the gut and brain contribute to disease pathogenesis using animal models and human subjects.

# Recent Publications

## Burré Lab

Article



SOURCE  
DATA



TRANSPARENT  
PROCESS



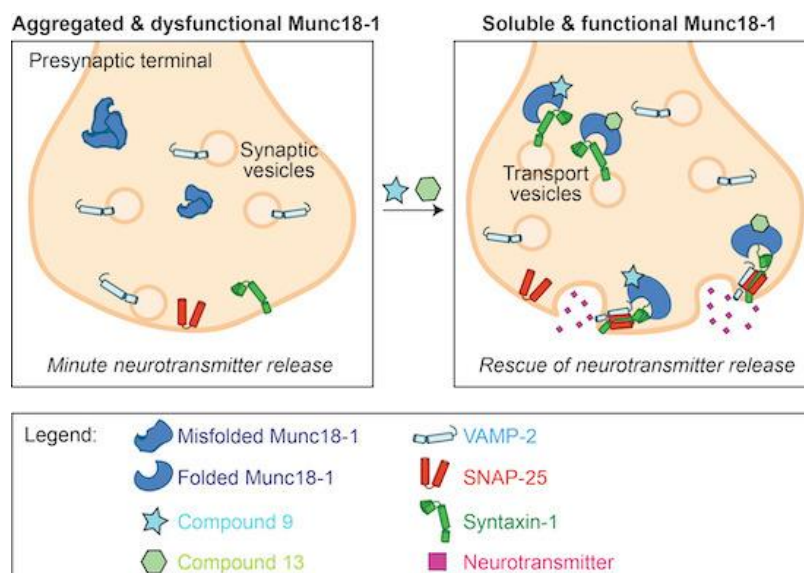
OPEN  
ACCESS

EMBO  
Molecular Medicine

## Targeted stabilization of Munc18-1 function via pharmacological chaperones

Debra Abramov<sup>\*</sup> , Noah Guy Lewis Guiberson , Andrew Daab<sup>†</sup>, Yoonmi Na, Gregory A Petsko<sup>‡</sup>, Manu Sharma & Jacqueline Burré<sup>\*\*\*</sup>

Heterozygous *de novo* mutations in the neuronal protein Munc18-1 cause syndromic neurological symptoms, including severe epilepsy, intellectual disability, developmental delay, ataxia, and tremor. No disease-modifying therapy exists to treat these disorders, and while chemical chaperones have been shown to alleviate neuronal dysfunction caused by missense mutations in Munc18-1, their required high concentrations and potential toxicity necessitate a Munc18-1-targeted therapy. Munc18-1 is essential for neurotransmitter release, and mutations in Munc18-1 have been shown to cause neuronal dysfunction via aggregation and co-aggregation of the wild-type protein, reducing functional Munc18-1 levels well below hemizygous levels. Here, we identify two pharmacological chaperones via structure-based drug design, that bind to wild-type and mutant Munc18-1, and revert Munc18-1 aggregation and neuronal dysfunction *in vitro* and *in vivo*, providing the first targeted treatment strategy for these severe pediatric encephalopathies.



# Recent Publications

Gan Lab



Biological Psychiatry


Available online 8 January 2021

In Press, Journal Pre-proof ?

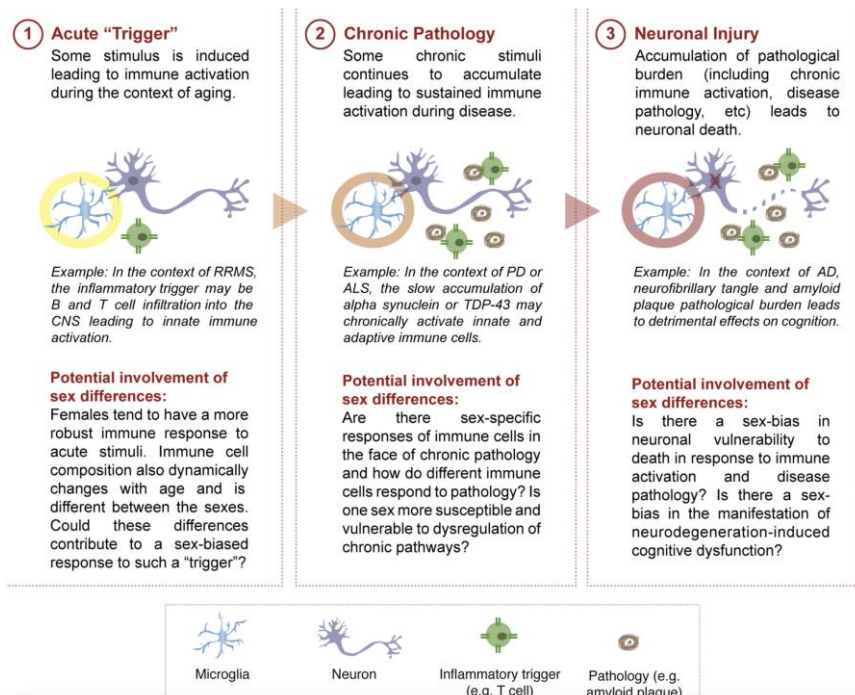


Review

## Sex differences in neurodegeneration: the role of the immune system in humans

Chloe Lopez-Lee<sup>1, 2</sup>, Lay Kodama<sup>2, 3</sup>  , Li Gan<sup>1, 2</sup>  

Growing evidence supports significant involvement of immune dysfunction in the etiology of neurodegenerative diseases, several of which also display prominent sex differences across prevalence, pathology, and symptomology. In this review, we summarize evidence from human studies of established and recent findings of sex differences in Multiple Sclerosis, Alzheimer's Disease, Parkinson's Disease, and Amyotrophic Lateral Sclerosis, and discuss how sex-specific CNS innate immune activity could contribute to downstream sex differences in these diseases. We examine human genomic and transcriptomics studies in each neurodegenerative disease through the lens of sex differences in the neuroimmune system and highlight the importance of stratifying sex in clinical and translational research studies. Finally, we discuss the limitations of the existing studies, and outline recommendations for further advancing sex-based analyses to uncover novel disease mechanisms that could ultimately help treat both sexes.



# Birthdays



**April**

**20<sup>th</sup> Debby**  
**30<sup>th</sup> Silvie**



# Safety recommendations

Clean your hands often

Put distance between yourself and other people (at least 6 feet)

Cover your mouth and nose with a mask when around others

Clean and disinfect frequently touched objects and surfaces daily

# Collaborations

Would you like to recommend a book, a movie or an inspiring quote?

You can participate!

Contact: [guc9014@med.cornell.edu](mailto:guc9014@med.cornell.edu)