Program in Cellular and Molecular Medicine
at Boston Children's Hospital

HARVARD MEDICAL SCHOOL
TEACHING HOSPITAL

May 2025, Volume 2

MAY 2025 NEWSLETTER

In this issue

Research Highlights……...2

Postdoctoral Fellow Awards……...3

New PCMM Postdoctoral Award Announcement……....4

Faculty News……..5

Happy spring PCMM —

We hope everyone's enjoying the warmer temperatures and having a productive spring. We would like to start highlighting recent publications from PCMM labs. In this first run, we're highlighting a publication from Dr. Yi Zhang's lab, by Dr. Yuting Wang et al, on blood stem cells' rejuvenating effects. If you'd like a particular publication from your lab highlighted in the upcoming newsletters, please contact Vera Gaun (vera.gaun@childrens.harvard.edu).

Additionally, the last PCMM seminar of the academic year is this week:

Anthony Hyman, Ph.D.

Director and Research Group Leader, Max Planck Institute of Molecular Cell Biology and Genetics

"Phase separation in cell physiology and disease"

Thursday, May 8th, 2025 4:00pm
Armenise Amphitheater (210 Longwood Avenue)
(reception to follow in the Jeffrey Modell Center)
Zoom Link Passcode: 911162 **Host: Prof. Hao Wu**

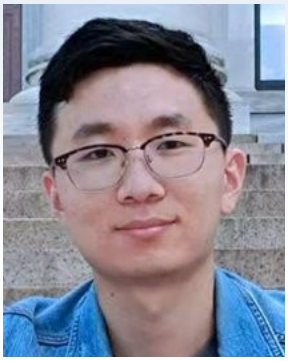
Research Highlights

Searching for rejuvenating blood stem cells

April 30th, 2025 by Vera Gaun

Aging results in a variety of processes, including stem cell quality decline. At the same time, it's been shown that transplanting blood stem cells (otherwise known as Hematopoietic Stem Cells or HSCs) from young to old mice results in rejuvenating effects. But, so far there's been no consensus on the specific factors involved in this systemic rejuvenation or the mechanisms behind it.

In a recent *Cell Research* publication from Dr. Yi Zhang's lab, Dr. Yuting Wang et al. have greatly added to the identification of the HSC populations: they have characterized the molecular, epigenetic, and functional differences of the young and aging blood stem cell populations. Using single cell RNA-seq, they have found that, while the young HSCs show homogeneity, the old HSCs show heterogeneity and can be grouped into several populations. Additionally, they've identified a reliable marker to distinguish the heterogeneous old HSC populations: the cell-surface marker CD150. Specifically, the "younger" old HSC subpopulation exhibits a low expression of CD150, whereas in the "older" old HSC subpopulation, the CD150 marker is high. Moreover, they demonstrated that transplanting the "younger" old CD150^{low} subpopulation into middle-aged mice positively impacts hematopoietic health, reduces epigenetic age, improves physical parameters, and extends lifespan by approximately 10%. Notably, they also showed that reducing the proportion of 'older' old CD150^{high} HSCs through transplantation can attenuate aging in older recipient mice. *(continued on page 3)*



Yuting Wang

Yi Zhang

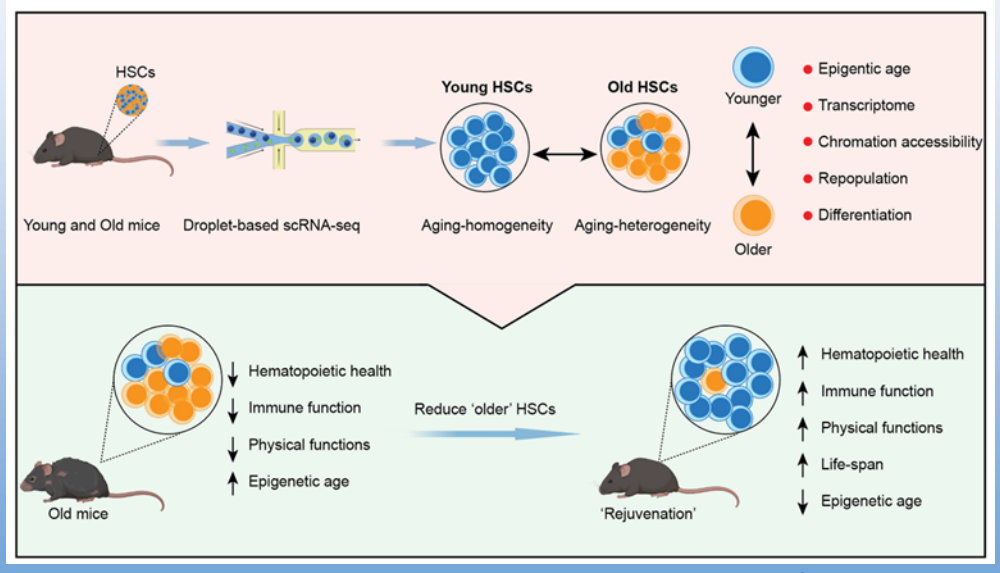


Image: courtesy of Dr. Yuting Wang

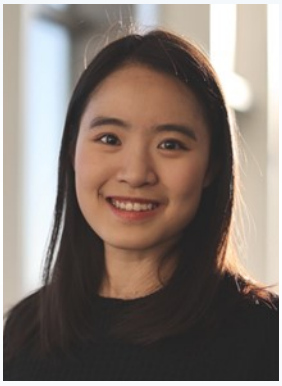
(continued from page 2)

Next Steps

Since blood stem cell transplantation is not possible in humans due to the potential immune system rejection, a viable strategy could be depleting the "older" CD150^{high} subpopulation of the old HSCs in elderly humans. The team is now working on a strategy of developing an anti-CD150 antibody conjugated to a toxic molecule in order to deplete this target HSC population. Dr. Wang comments: "Perhaps aging and death are inevitable, but the frailty and illness that often accompany aging are entirely avoidable. We hope our work can offer new ideas toward this shared goal of humanity."

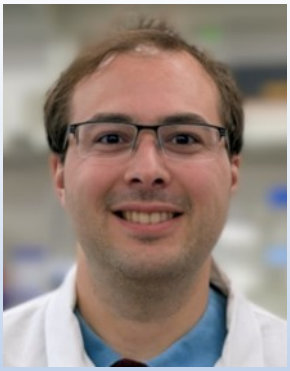
Yuting Wang, PhD, was the first author of the article, and Yi Zhang, PhD, was the senior author. Other authors include: Wenhao Zhang, PhD, Chao Zhang, PhD, Hoang Q. Tran Van, and Takashi Seino, PhD.

Postdoctoral Fellow Awards



Rena Ren, PhD, (Zhang Laboratory) has been awarded a Helen Hay Whitney Fellowship supported by HHMI. A long-held goal of biological research is to systematically measure protein translation with single-molecule spatial resolution of intact system in 3D. Existing methods such as ribosome profiling measure protein translation as an average of many cells or in low-throughput single cells and lack spatial resolution. Rena previously developed a highly multiplexed, ribosome-bound mRNA imaging and sequencing technique called RIBOmap and applied it in cells and tissues to profile translation events with spatial coordinates. As a Helen Hay Whitney Fellow, Rena is developing a new version of RIBOmap technology tailored to map RNA translation status in intact, pre-implantation embryos. This work will be valuable for understanding biological development and paving ways to reveal early cell-fate decisions using a new modality.

Julian Ehrmann, PhD, (Wu Laboratory) has received an NIH T32 Ruth L. Kirschstein Postdoctoral National Research Service Award to study molecular drivers of chronic inflammation. Causative for Crohn's disease, the sensor protein NOD2 is also found overexpressed in nephropathy and serves as an unfavorable disease progression marker. Typically dormant until detection of cytosolic bacteria, premature and chronic NOD2 activation drives pro-inflammatory IL-18 cytokine release. To better understand how NOD2 patient mutations and aberrant expression can drive inflammation, he aims to determine multiple functional states in the NOD2 pathway using cryo-EM and in vitro reconstitution. Further, the project seeks to screen for small molecules that disrupt NOD2 activation, possibly allowing for pharmacological dampening of inflammation.



Jonas Zähringer, Ph.D, (Ha Laboratory) was awarded the Feodor-Lynen Fellowship by the Alexander von Humboldt foundation. His research focuses on integrins—essential proteins that enable cells to sense and respond to mechanical forces in their environment. These proteins play key roles in immune regulation, tissue repair, and cancer progression. Despite their importance, the mechanisms by which mechanical forces activate integrin signaling remain poorly understood. Recent research suggests that integrins undergo force-dependent conformational changes that initiate signaling and tune ligand binding. Using single-molecules fluorescence and DNA origami nanotechnology, he will interrogate the relationship between mechanical force and integrin conformations. By shedding light on how mechanical signals activate integrins, he may open new paths for therapeutic targets.

New PCMM Postdoctoral Award Announcement

The 2025 Jeffrey, Vicki, and Fred Modell Lecture Award

Members of the PCMM community,

We are pleased to announce the establishment of a new award for PCMM postdoctoral fellows, which will replace the Jeffrey Modell Award. This inaugural award for 2025, made possible through the generosity of the Jeffrey Modell Foundation, will be The Jeffrey, Vicki, and Fred Modell Lecture Award, an annual prize open to PCMM postdocs. The winner of the annual competition will receive $1,000 and a plaque and will present a lecture at the PCMM retreat.

Eligibility:

• The Jeffrey, Vicki, and Fred Modell Lecture Award is open to postdoctoral fellows at PCMM. This award is not intended for graduate students or instructors.

• The lecture award will be judged on the basis of the description of the nominee's research **performed at PCMM**.

• More than one submission will be accepted from each PCMM laboratory from eligible applicants.

Nomination format:

• A CV that is NO LONGER than two pages (Arial 11 point with 0.5 inch margins on all sides) with the following information:

Name, address, phone number, and email
Education and training (undergraduate, graduate, and postgraduate institutions with degrees awarded and years attended)
Honors and awards
Publications and patents (NIH biosketch format suggested)
Conferences and presentations

• Nomination must be accompanied by a one-page reference letter from the nominee's PCMM PI.

• An essay (1200 words maximum) written in English by the nominee explaining their PCMM research to a broad audience with scientific interest, with an optional secondary essay describing mentoring, service, and/or outreach (300 words maximum)

Submission and review:

• PIs (not fellows) must email completed applications to James Falvo at james.falvo@childrens.harvard.edu no later than midnight, **Friday, June 27, 2025**.

Nominations will be reviewed, and the winner determined, by the PCMM Scientific Advisory Board.

Faculty News

Timothy Springer Receives the Stein & Moore Award

Tim Springer, PhD, has been named the 2025 recipient of the Stein & Moore Award from The Protein Society. From the Society's website, the award "recognizes eminent leaders in protein science who have made sustained, high-impact research contributions to the field… Dr. Springer was the first to discover that T-cell antigen-specific responses require cell-recognition receptors. His fundamental research has also paved the way to developing first therapeutics directed to cell-recognition molecules – an LFA-3 ectodomain-Fc fusion (Amevive), an LFA-1 antibody (Raptiva) for psoriasis, and an integrin α4β7 antibody (Entyvio) for ulcerative colitis."

Denisa Wagner Receives an Outstanding Mentor Award

Denisa Wagner, PhD has been named a 2025 recipient of the Outstanding Mentor Award from the International Society on Thrombosis and Haemostasis (ISTH). The ISTH web site notes that the society "launched the Outstanding Mentor Awards in 2024 to recognize individuals who have demonstrated an ongoing commitment to cultivate and mentor early career professionals in the thrombosis and hemostasis field." Dr. Wagner commented: "It has been the greatest pleasure of my career as a professor to interact with and mentor my students and postdoctoral fellows in research and discovery. The vast majority have gone on to highly successful scientific careers and are now based all over the world, with some already in leadership positions."

Tom Kirchhausen Elected to American Academy of Arts and Sciences

Tom Kirchhausen, PhD was one of almost 250 individuals elected to the American Academy of Arts and Sciences in 2025. The American Academy of Arts and Sciences honors excellence and convenes leaders from every field of human endeavor to examine new ideas and address issues of importance to the nation and the world. His laboratory's descriptions of complex intracellular processes at remarkable spatial and temporal resolutions have set new standards for understanding membrane dynamics in cells, by bridging from atomic detail to cell morphology through implementation of frontier imaging technologies, such as lattice light-sheet microscopy. Dr. Kirchhausen's creative studies of clathrin-mediated endocytosis have transformed our understanding of the molecular machinery that moves cargo (including viruses) from one membrane-bound intracellular compartment to another.