

Celebrating 50 Years Muscle, Motors, and the Cytoskeleton

October 16, 2023

Gaulton Auditorium and Lobby
Biomedical Research Building (BRB II/III)
421 Curie Blvd., 1st Floor

Jean and Joseph Sanger Lecture in Muscle Biology:

James A. Spudich, PhD

Stanford University

"Myosin, the exquisite nanomachine: From basic science to biotech to medicines"

Andrew Somlyo Honorary Lectures:

Jennifer Lippincott-Schwartz, PhD

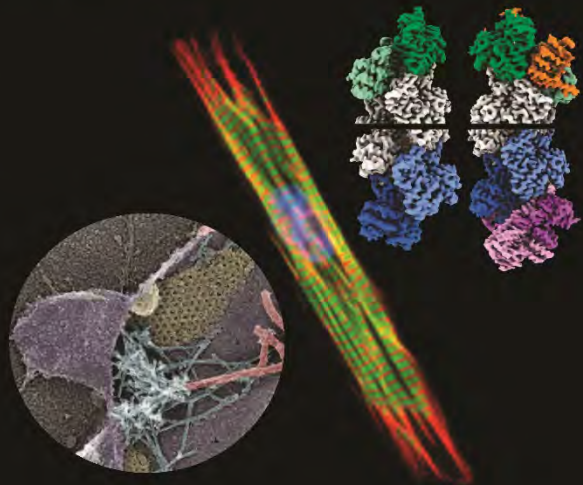
HHMI Janelia Research Campus

"How the cytoskeleton controls the structure and dynamics of the endoplasmic reticulum"

Andrew P. Carter, PhD

MRC Laboratory of Molecular Biology

"Cargo transport by dynein/dynactin"



Penn Speakers:

Sharlene M. Day, MD

Division of Cardiovascular Medicine

"Mechanisms of Myosin Binding Protein C Mutations in Hypertrophic Cardiomyopathy"

Roberto Dominguez, PhD

Department of Physiology

"Structural-Functional Mechanisms Controlling Actin Filament Barbed and Pointed End Dynamics"

Hansell H. Stedman, MD

Department of Surgery

"Gene Therapy for Inherited Muscle Disease: A Glimpse of the Summit Ridge from Everest Base Camp"

Xingyuan Fang (Svitkina Lab)

Department of Biology

"Mechanism of branched actin assembly in microtubule- and APC-dependent manner"

Adam Fenton (Holzbaur and Jongens Labs)

Department of Physiology

"FMRP-associated protein synthesis locally determines mitochondrial organization in neurons"

Jennifer Petrosino, PhD (Prosser Lab)

Department of Physiology

"The Hitchhiker's Guide to the Myocyte: Active transport of tRNAs facilitates distributed protein synthesis"

Qing Tang, PhD (Lakadamyali Lab)

Department of Physiology

"Insight into cytoskeleton sorting from microtubule deetyrosination"



Scan for schedule

www.med.upenn.edu/pmi

Poster session for all attendees

Pennsylvania Muscle Institute Annual Retreat and Symposium 2023

“Celebrating 50 Years of Muscle, Motors, and the Cytoskeleton”

Monday, October 16, 2023

Location: BRB Gaulton Auditorium & Lobby,
Biomedical Research Building (BRB II/III),
421 Curie Blvd., 1st Floor, Philadelphia, PA 19104

*Sponsored by the Physiological Society of Philadelphia and
the Pennsylvania Muscle Institute*

www.med.upenn.edu/pmi

Registration

8:30 – 9:00am

Registration Check-in, Poster Setup, Breakfast, Coffee

Location: BRB Gaulton Auditorium & Lobby*

**Table seating available in BRB 14th Floor Lounge*

9:00 – 9:15am

Welcome

E. Michael Ostap, PhD

Director, Pennsylvania Muscle Institute

Professor of Physiology

University of Pennsylvania

Jonathan A. Epstein, MD

Executive Vice Dean and Chief Scientific Officer, Perelman School of
Medicine at the University of Pennsylvania

Senior Vice President and Chief Scientific Officer, University of
Pennsylvania Health System

William Wikoff Smith Professor of Medicine (Cardiology) and Cell and
Developmental Biology

University of Pennsylvania

9:15 – 9:30am

50 Years of Progress at the PMI

E. Michael Ostap, PhD

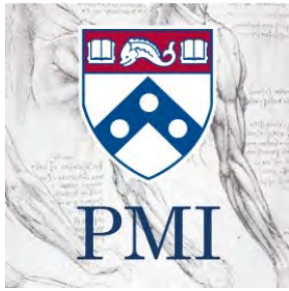
Director, Pennsylvania Muscle Institute

Professor of Physiology

University of Pennsylvania

- 9:30 – 10:15am **Andrew P. Somlyo Honorary Lecture**
Jennifer Lippincott-Schwartz, PhD
 Senior Group Leader and Head of Janelia's 4D Cellular Physiology,
 HHMI Janelia Research Campus
*“How the cytoskeleton controls the structure and dynamics of the
 endoplasmic reticulum”*
- 10:15 – 10:30am **Adam Fenton (Holzbaur and Jongens Labs)**
 University of Pennsylvania
*“FMRP-associated protein synthesis locally determines mitochondrial
 organization in neurons”*
- 10:30 – 11:00am **Coffee Break, Posters**
- 11:00 – 11:45am **Andrew P. Somlyo Honorary Lecture**
Andrew P. Carter, PhD
 Investigator, MRC Laboratory of Molecular Biology
“Cargo transport by dynein/dynactin”
- 11:45am – 12:15pm **Roberto Dominguez, PhD**
 William Maul Measey Presidential Professor of Physiology,
 University of Pennsylvania
*“Structural-Functional Mechanisms Controlling Actin Filament Barbed
 and Pointed End Dynamics”*
- 12:30 – 1:30pm **Lunch, Posters**
 Location: BRB Lobby*
**Table seating available in BRB 14th Floor Lounge*
- 1:30 – 1:45pm **Xingyuan Fang (Svitkina Lab)**
 University of Pennsylvania
*“Mechanism of branched actin assembly in microtubule- and APC-
 dependent manner”*
- 1:45 – 2:00pm **Qing Tang, PhD (Lakadamyali Lab)**
 University of Pennsylvania
“Insight into cytoskeleton sorting from microtubule detyrosination”
- 2:00 – 2:30pm **Hansell H. Stedman, MD**
 Professor of Surgery, University of Pennsylvania
*“Gene Therapy for Inherited Muscle Disease: A Glimpse of the Summit
 Ridge from Everest Base Camp”*
- 2:30 – 3:00pm **Coffee Break, Posters**
- 3:00 – 3:15pm **Jennifer Petrosino, PhD (Prosser Lab)**
 University of Pennsylvania
*“The Hitchhiker’s Guide to the Myocyte: Active transport of tRNAs
 facilitates distributed protein synthesis”*

- 3:15 – 3:45pm **Sharlene M. Day, MD**
Presidential Associate Professor of Medicine & Director, Translational
Research, Division of Cardiovascular Medicine
University of Pennsylvania
*“Mechanisms of Myosin Binding Protein C Mutations in Hypertrophic
Cardiomyopathy”*
- 3:45 – 4:00pm ***Introduction: Jean and Joseph Sanger Lecture in Muscle Biology***
E. Michael Ostap, PhD
- 4:00 – 4:45pm ***Jean and Joseph Sanger Lecture in Muscle Biology***
James A. Spudich, PhD
Douglass M. and Nola Leishman Professor of Cardiovascular Disease,
Stanford University
*“Myosin, the exquisite nanomachine: From basic science to biotech to
medicines”*
- 4:45 – 5:45pm **Reception, Posters**
Location: BRB Lobby
- 5:45 – 6:00pm **Farewell, Posters Take-down**
Location: BRB Lobby



Pennsylvania Muscle Institute

Perelman School of Medicine

University of Pennsylvania

The Pennsylvania Muscle Institute (PMI) is an internationally renowned center for muscle and motility research supported by Penn Medicine with a mission to:

- Discover the mechanisms of muscle function, muscle disease and motile biological systems through innovative and cross-disciplinary research, and to apply these discoveries to new therapies,
- Develop state-of-the-art technologies for the study of muscle and motile systems,
- Provide education and training in muscle biology and motility to scientists, physicians, and students.

Research is conducted by its more than 60 laboratories using biophysics, biochemistry, genetics, physiology and ultrastructure to understand cell migration and intracellular transport, molecular motors, cell division, muscle contraction and development, muscle pathologies and therapies targeted to muscle disease. We are prominent in technological and methodological development for these investigations especially in advanced light microscopy, structural spectroscopy, nanotechnology, biochemical kinetics, image processing, molecular biology, and viral gene targeting. Extramural grants, seminars, symposia, and journal clubs are uniquely initiated and supported by the PMI. Additionally, the PMI sponsors vigorous graduate and post-doctoral training activities, including a NIAMS-supported training program in “Muscle Biology and Muscle Disease.”

For questions or inquiries about PMI membership, please contact:

E. Michael Ostap, Ph.D.

Director, PMI
Professor of Physiology
Email: ostap@pennmedicine.upenn.edu

Benjamin L. Prosser, Ph.D.

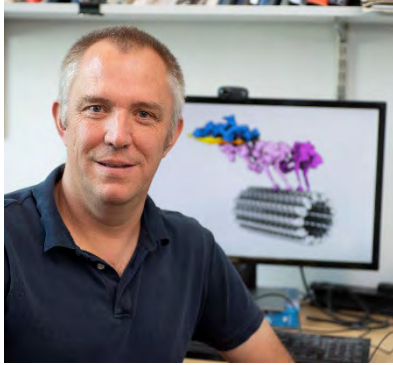
Associate Director, PMI
Associate Professor of Physiology
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Pennsylvania Muscle Institute (PMI)
Perelman School of Medicine at the University of Pennsylvania
700A Clinical Research Building
415 Curie Blvd. Philadelphia, PA 19104

Please visit our website: <http://www.med.upenn.edu/pmi/>

Guest Speaker Biographies

Andrew P. Somlyo Honorary Lectures



Andrew P. Carter, PhD

Investigator, MRC Laboratory of Molecular Biology

Dr. Andrew Carter studied Biochemistry at Oxford University. He obtained his PhD with Dr. Venki Ramakrishnan at the MRC Lab of Molecular Biology (LMB), working on how antibiotics bind the ribosome. He was part of the team which contributed to Venki's 2009 Nobel Prize. In 2003, Dr. Carter joined the lab of Professor Ron Vale at UCSF to investigate the structural mechanism for dynein binding to the microtubule. He set up his own lab, in the LMB

Structural Studies division in 2010, where he and his team have used X-ray crystallography, cryo-EM and many other approaches to understand how cytoplasmic dynein and its cofactor dynactin select and transport cargos. Dr. Carter is a fellow of Clare College, a Wellcome Investigator, and a member of EMBO. Dr. Carter was recently awarded the British Society of Cell Biology (BSCB) Hooke Medal award for 2023.



Jennifer Lippincott-Schwartz, PhD

Senior Group Leader and Head of Janelia's 4D Cellular Physiology, HHMI Janelia Research Campus

Dr. Jennifer Lippincott-Schwartz is a Senior Group Leader at the Howard Hughes Medical Institute's Janelia Research Campus. She has pioneered the use of green fluorescent protein technology for quantitative analysis and modelling of intracellular protein traffic and organelle dynamics in live cells and embryos. Her innovative techniques to label, image, quantify and model specific live cell protein populations and track their fate have provided vital tools used throughout the research community. Her own findings using these techniques have reshaped thinking about the biogenesis, function, targeting, and maintenance of various subcellular organelles and macromolecular complexes and their crosstalk with regulators of the cell cycle, metabolism, aging, and cell fate determination. She is an elected member of the National Academy of Sciences, the National Academy of Medicine, the American Society of Arts and Sciences and the European Molecular Biology Organization. She is also a Fellow of The Biophysical Society, The Royal Microscopical Society and The American Society of Cell Biology. Her awards include the E.B. Wilson Medal of the American Society of Cell Biology, the Newcomb Cleveland Prize of the American Association for the Advancement of Science, the Van Deenen Medal, the Keith Porter Award of the American Society of Cell Biology, the Feodor Lynen Medal, and the Feulgen Prize of the Society of Histochemistry. She co-authored of the textbook "Cell Biology" with Tom Pollard and Bill Earnshaw and was President of the American Society of Cell Biology. Dr. Lippincott-Schwartz attended Swarthmore College, received her MS from Stanford University, and obtained her PhD in Biochemistry from Johns Hopkins University in 1986.

Jean and Joseph Sanger Lecture in Muscle Biology**James A. Spudich, PhD**

Douglass M. and Nola Leishman Professor of Cardiovascular Disease, Stanford University

Dr. James Spudich, Douglass M. and Nola Leishman Professor of Cardiovascular Disease, is in the Department of Biochemistry at Stanford University School of Medicine. He received his B.S. in chemistry from the University of Illinois in 1963 and his Ph.D. in biochemistry from Stanford in 1968. He did postdoctoral work in genetics at Stanford and in structural biology at the MRC Laboratory in Cambridge, England. From 1971 to 1977, he was Assistant, Associate, and Full Professor in the Department of Biochemistry and Biophysics, University of California, San Francisco. In 1977, he was appointed Professor in the Department of Structural Biology at Stanford University. Dr. Spudich served as Chairman of the Department of Structural Biology from 1979-1984. Since 1992 he has been Professor in the Department of Biochemistry, where he served as Chairman from 1994-1998. From 1998 to 2002, he was Co-Founder and first Director of the Stanford Interdisciplinary Program in Bioengineering, Biomedicine and Biosciences called Bio-X. He is also an Adjunct Professor at the National Center for Biological Sciences, Tata Institute of Fundamental Research and InStem in Bangalore, India. Dr. Spudich is the Founder of four biotech companies: 1998 Cytokinetics, focused on treatments for diseases characterized by compromised muscle function like amyotrophic lateral sclerosis and heart failure, with several small molecule modulators in late stage clinical trials; 2012 MyoKardia, focused on developing targeted therapies for the treatment of rare genetically-based cardiovascular diseases such as hypertrophic and dilated cardiomyopathy, resulting in a \$13.1B buyout by Bristol Myers Squibb and an FDA approved drug Camzyos (mavacamten); 2019 Kainomyx, focused on targeting cytoskeletal components of Plasmodium parasites for treatment of malaria; 2022 Cyntegron Therapeutics, focused on targeting cytoskeletal components for the treatment of cancers.

Dr. Spudich has given more than 50 named lectureships and keynote addresses, and has received many honors, including election to the National Academy of Sciences in 1991, and recipient of the Albert Lasker Basic Medical Research Award in 2012.

Over the last five decades, the Spudich laboratory studied the structure and function of the myosin family of molecular motors in vitro and in vivo, and they developed multiple new tools, including in vitro motility assays taken to the single molecule level using laser traps. That work led them to their current focus at Stanford on the human cardiac sarcomere and the molecular basis of hypertrophic and dilated cardiomyopathy. Spudich postulated in 2015 that a majority of hypertrophic cardiomyopathy mutations are likely to be shifting beta-cardiac myosin heads from a sequestered off-state to an active on-state for interaction with actin, resulting in the hyper-contractility seen clinically in HCM patients. This unifying hypothesis is different from earlier prevailing views, and this viewing an old disease in a new light has become the favored view in the field of the molecular basis of hypercontractility caused by HCM mutations. While maintaining his lab at Stanford, Spudich serves as CEO and President of both Kainomyx and Cyntegron Therapeutics.

Andrew P. Somlyo Honorary Lectures



Andrew P. Somlyo, M.D.
(1930 – 2004)

Professor of Physiology and Pathology and founding Director of the Pennsylvania Muscle Institute, Dr. Somlyo was a luminary in the field of smooth muscle physiology. His research (in collaboration with Dr. Avril Somlyo) played a key role in showing that actin-myosin interactions are responsible for force generation in smooth muscle. With colleagues at the University of Pennsylvania, Dr. Somlyo developed electron probe microanalysis to determine local ion concentrations in tissues at nanometer resolution. Additionally, his pioneering work in signaling revealed the mechanisms that regulate contraction of smooth muscle independently of the membrane potential – a process he termed pharmacomechanical coupling. Dr. Somlyo had a passion for science that is evident in the remarkable imprint that he left on the field of muscle physiology and on his students and colleagues. He was also a noted collector of Asian art. Dr. Somlyo left Penn Medicine in 1988 to chair the Department of Molecular Physiology and Biological Physics at the University of Virginia School of Medicine.

Jean and Joseph Sanger Lecture in Muscle Biology



Jean M. Sanger, PhD

Professor, Department of Cell and Developmental Biology
SUNY Upstate Medical University

Joseph W. Sanger, PhD

Professor, Department of Cell and Developmental Biology
SUNY Upstate Medical University

Drs. Jean and Joseph Sanger are pioneers in the development and use of fluorescently labeled proteins to examine the architecture and dynamics of a range of biological processes in developing and mature cells. As former members of the Department of Cell and Developmental Biology, they were founding members of the Pennsylvania Muscle Institute. The Sangers were among the first cell biologists to take advantage of probes to follow the assembly and changing localizations of cytoskeletal components in living cells. Their research led to impactful new discoveries about cell division, actin based bacterial infections, and assembly and maintenance of myofibrils in muscle cells. Importantly, the Sangers were the first scientists to visualize and quantify the kinetics of sarcomeric proteins

entering newly developing and mature myofibrils. In real time, they followed key components of the contractile machinery during myofibrillogenesis. The revolutionary models they formulated for how Z-bands, thick and thin filaments, and other sarcomeric components are templated during development are still the standards in the field. More recently, the Sangers were the first to determine the role of the ubiquitin–proteasome system in the progression of nascent myofibrils to maturity, and possible mechanisms for the off-target effects on hearts by chemotherapeutics. In addition to their scientific achievements, the Sangers have been leaders and role models in the Cell Biology community as educators, mentors to trainees and faculty, editors, reviewers, conference organizers, and administrators. Dr. Joseph Sanger served as interim chair of PSOM’s Department of Cell and Developmental Biology. The Sangers left Penn in 2006 for SUNY Upstate Medical University, where Dr. Jean Sanger became Professor and Dr. Joseph Sanger became Professor and Chair of Cell and Developmental Biology. They were and are parts of the soul of the Pennsylvania Muscle Institute.

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