



Department of

Biochemistry and Molecular Biophysics

Spring 2014

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Message from the Department Head

Dear Colleagues and Friends:

Welcome to the second annual newsletter from the Department of Biochemistry and Molecular Biophysics. I am pleased to continue to have the opportunity to lead the department as interim head of the department. I am grateful for the enthusiastic support of the department, including the faculty, staff and students, along with the support of the Dean and the university central administration.

The department continues to move forward with active and exciting research programs and with vital contributions to the teaching of graduate and medical students. While extramural funding for research is a challenge for everyone, I am very proud of our success and in our efforts to improve efficiency and work together.

Our most exciting accomplishment this year was the successful recruitment of a new faculty member, Greg Bowman. Greg is a world-class expert in molecular dynamics, a computational approach that will be a vital part of collaborative research in developing new therapies. Greg is particularly excited to apply his highly sophisticated and modern approaches to important medical and biological problems, working together with a wide array of individuals on campus. Greg comes to us from the University of California at Berkeley, where he holds a distinguished position as a Miller Research Fellow. He also has the distinction of receiving a Burroughs Wellcome Fund Career Award at the Scientific Interface. We welcome Greg and his spouse, Angela Bowman, who will have a vital role in leading new efforts in regenerative medicine on campus.

Another accomplishment is our ongoing effort to consolidate high-throughput screening efforts on campus. With the assistance and cooperation of numerous individuals and departments, we are improving the opportunities for translational science in the form of screening for novel pharmacological and biological agents. I am grateful to Dr. Scott Wildman, a faculty member in our department, for his leadership in this effort. Our capabilities in screening will complement our efforts in computational biology and medicinal chemistry, helping us to move forward in the field of chemical biology.

The department maintains its key role as an intellectual core of research in using quantitative approaches to understand the structure and function of biological molecules at a detailed level. We maintain our focus and strength in the study of a range of processes of fundamental importance to biology and medicine, including protein folding, DNA replication, RNA function, membrane protein function, and cell signaling, among others.

Leading Together, the capital campaign of the university, is providing faculty and staff with opportunities to contribute directly to efforts that are focused on topics of special interest to individual departments and centers of excellence on campus. Our department has created several such opportunities, and I ask you to join me in the support of these critical endeavors.

We continue to have a tremendous sense of momentum and excitement as we approach the challenges of biomedical research in the 21st century. Please be in touch, keep us informed of your activities, and feel free to drop in and visit.

With warmest regards,

John Cooper, MD, PhD
Interim Head, Department of Biochemistry and Molecular Biophysics



 **Washington**
University in St. Louis
SCHOOL OF MEDICINE

Mission Statement

Members of the Department of Biochemistry and Molecular Biophysics are dedicated to investigating the complex relationships and mechanisms that control biological processes. These processes are defined by interactions among proteins, nucleic acids (DNA and RNA) and between proteins or nucleic acids with small metabolites.

Our investigators use experimental structural, thermodynamic, kinetic and single molecule methods as well as computational approaches to understand and quantify structural and dynamic aspects of macromolecular interactions. Our research provides fundamental knowledge that enables advances in medicine and improvements in the quality of life.

Graduate Students Spotlight



Josh Brettmann is a fourth year graduate student in the laboratory of Dr. Katie Henzler-Wildman. Josh is a great asset for the Biochemistry and Computational and Molecular Biophysics graduate programs; he is full of enthusiasm for good science and good community. Striking a great balance

between lab and outside life, when he is not purifying proteins in the lab to gear up for cutting-edge NMR experiments on ion channels, he finds the time to engage in numerous other activities.

Josh is actively involved in the Central West End community. He keeps track of the local restaurants and bars, is involved in his local church, and plays every sport with everyone as much as he can--including being an integral member of the departmental softball team. He also finds the time to garden with his wife, brew beer, and even make a surprise appearance as Santa at the Holiday party.

As the chair of the student liaison committee and the organizer for BMB Science Fridays, Josh plays an active role in the department. His contribution to the laboratory is equally strong. He has bravely embarked on a new project, expanding the laboratory's horizons beyond EmrE to use solution NMR to study a new system--ion channel. Despite the inevitable challenges of developing a new project, he encourages everyone in the lab to keep an optimistic attitude and fosters team spirit by organizing lab trips to tea time and bringing surprise treats to lab meetings.



"Santa" with Eric Galburt's two oldest sons.

Cori Lecture - Remembering a Legacy

In celebration of the scientific legacy and accomplishments of Carl and Gerty Cori, the department was honored to have Dr. James A. Spudich present the 2013 Cori Lecture on May 8th, in the Eric P. Newman Auditorium.

Dr. Spudich presented his talk on “The underlying molecular basis of human hypertrophic and dilated cardiomyopathies.” Dr. Spudich is the Douglass M. and Nola Leishman Professor of Cardiovascular Disease, 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 his 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 at the 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, and served as Chairman from 1994-1998. He has held a joint appointment as Professor in the Department of Developmental Biology since 1989. From 1998 to 2002, he was Co-Founder and first Director of the Stanford Interdisciplinary Program in Bioengineering, Biomedicine and Biosciences called Bio-X. At present 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's research focuses on the structure and function of molecular motors *in vitro* and *in vivo*. His major areas of specific interest are the molecular basis of energy transduction that leads to ATP-driven myosin movement on actin, the roles of the myosin family of molecular motors in eukaryotic cells, the regulation of actin and myosin interaction and their assembly states, and the biochemistry and regulation of the attachment of molecular motors to their corresponding cargo.

In 2012 Dr. Spudich, along with Michael Sheetz and Ron Vale, received the Albert Lasker Basic Medical Research Award for “discoveries concerning cytoskeletal motor proteins, machines that move cargoes within cells, contract muscles, and enable cell movements.” In addition to the Lasker award, Dr. Spudich received the E.B. Wilson Medal from The American Society for Cell Biology in 2011, the Arthur Kornberg and Paul Berg Lifetime Achievement Award in Biomedical Sciences in 2012 and the Wiley Prize in Biomedical Sciences also in 2012.

An additional treat this year was the publication of the book “Crucible of Science, The Story of the Cori Laboratory” written by Dr. John H. Exton. This book details the life and work of the Cori's during their time at Washington University. A special lunch was held in Dr. Exton's honor and he was on hand to give the opening remarks prior to Dr. Spudich's presentation. Distinguished guests such as Dr. Tom Cori, son of the late Carl and Gerty Cori and Dr. Bill Danforth II who was a postdoctoral fellow with Carl Cori and Chancellor of Washington University from 1971 to 1995 were in attendance.

Immediately following the seminar, a reception was held for all of the attendees. In the evening the faculty in the Department of Biochemistry and Molecular Biophysics, and their spouses, enjoyed a dinner at Herbie's with both seminar speakers.

History of the Cori Lectureship:

The Cori's came to Washington University in 1931 and during the ensuing years, they elucidated the pathway for glycogen degradation. They also discovered that protein phosphorylation represented a mechanism for regulating the activity of enzymes. For their discoveries, Carl and Gerty Cori were awarded the Nobel Prize in 1947. Gerty died in 1957. Upon Carl's death in 1984, the department established the Carl and Gerty Cori Lecture to celebrate the life and work of this remarkable couple. The couple's lasting legacy included the training of successive generations of scientists – six other future Nobel Laureates worked with Carl and Gerty Cori in their laboratory at Washington University: Christian de Duve, Arthur Kornberg, Edwin G. Krebs, Luis F. Leloir, Severo Ochoa, and Earl W. Sutherland. Previous Cori Lecturers include Gobind Khorana, Arthur Kornberg, and Jim Wells.

Annual Graduate Program Retreat



Shankar Parajuli, graduate student, presenting his poster to Admire Munanairi.

*Keynote Speaker
Gaya Amarasinghe, PhD*



*Keynote Speaker
Hani Zaher, PhD*



Siyao Xing, graduate student, presenting one of the student talks.



Keep Calm and Research On! Apurwa Sharma, Lin Hao, Alex Holehouse and Mariah Lawler modeling the retreat t-shirt.

Once again, the Department sponsored and participated in the annual retreat of the Biochemistry and Computational and Molecular Biophysics graduate programs on October 25-26th. The retreat was held at the Cedar Creek Conference Center, which is located in New Haven, MO near the Missouri river. For this year's retreat, the organizers, Weikai Li and Tom Brett, invited two outstanding scientists within our very own Washington University Community to give the keynote lectures on Friday night. The first keynote address was from Gaya Amarasinghe, Assistant Professor in the Department of Pathology and Immunology. Dr. Amarasinghe's research focuses on characterizing microbial immune evasion mechanisms using structural and biochemical methods in order to develop a framework to understand how intracellular signaling is altered during microbial infections. The title of his talk was "Self/non-self Recognition of RNA: Lesson from Structure". The second keynote speaker was Hani Zaher, Assistant Professor of Biology. Dr. Zaher's research focuses on understanding the mechanisms that govern translational fidelity as well as their impact on cellular fitness and codon evolution. The title of his talk was "Mechanism and Implications of Proofreading on the Ribosome".

The retreat started on Friday afternoon with six high-quality talks by selected graduate students and postdocs. After dinner and the keynote talks, it was time for the poster session, with wine, beer, light snacks, and s'mores to enjoy by the campfire. Anne Georges, a second-year graduate student, brought her powerful telescope so we could once again enjoy the starry night out in the country. The students also enjoyed inventing new games by the camp fire.

The next morning, we heard five more excellent talks by students and postdocs. Most of the talks were given by graduate students in the two programs, but a few were given by students with biochemical/biophysical interests who are in other programs (Chemistry, Biology, Biomedical Engineering, and Molecular Cell Biology). The interdepartmental participation of students and faculty lent strength to the program, the talks and the follow-up discussions. Out of the 95 retreat participants, 24 of them were from outside of the department and the two graduate programs.

Best student poster prizes went to Mark Zaydman, from Jianmin Cui's lab, and Joseph Stodola, from Peter Burgers' lab. Sunjoo Lee, from Colin Nichols's lab, and Chris Brosey, from Tom Ellenberger's lab, were presented with the best postdoc poster prizes. At the end of the retreat, Yang Li from Jianmin Cui's lab was awarded best talk.

Thanks for a successful retreat goes especially to Melissa Torres, coordinator for the Biochemistry and Biophysics programs, who perfectly organized every logistic aspect of the retreat. Additional thanks go to the scientific organizers, Weikai Li and Tom Brett, and to the many Departments and Divisions that provided financial contributions.

Faculty Spotlight: Elliot Elson, PhD

Stepping into Elliot Elson's lab is like falling into the rabbit hole in Alice in Wonderland. There are movable amplifiers perched precariously on a sled of steel runners, lasers in black boxes, pieces of salvaged equipment, cords and cables spewing like spaghetti from another machine, and a huge black tent that looks like it was inspired by Darth Vader. This is a workshop for scientific invention. The tunnel burrows deeper into the natural world's mysteries. The elusive White Rabbit entices us to follow and to probe the enigmas of life. Elliot Elson seeks to

understand and characterize cells and tissues as physical entities. His "white rabbit" has led him to adventures and discoveries that have yielded new insights into the inner workings of life itself—in several different key fields.



Elliott Elson, PhD

Education:

- AB, Biochemistry, Harvard University, 1959
- PhD, Stanford University, 1964
- Postdoctoral Training, U. of California-San Diego, 1964-1968

Titles:

- The Alumni Endowed Professor of Biochemistry and Molecular Biophysics
- Professor of Physics
- Professor of Biomedical Engineering

Family:

Wife, Frances Tietov, who is a retired principal harpist at the Saint Louis Symphony Orchestra; sons Louis Woodhams, 35, graduated from the University of Miami with a degree in philosophy, and Julian Elson, 30, graduated from the University of Chicago with a degree in economics. Both sons live in St. Louis.

Honors:

- Fellow, American Association for the Advancement of Science, 2004
- Gregorio Weber Award for Excellence in Fluorescence Theory and Applications, Biophysical Society, 2007
- Fellow, American Academy of Arts and Sciences, 2013

Publications:

- Over 160 peer-reviewed journal articles
- Over 11,000 citations

Books:

Fluorescence Correlation Spectroscopy, R. Rigler and E. Elson, editors, 2001

Dynamic Molecular Processes. As a new assistant professor at Cornell, Elliot and graduate student Robert Clegg collaborated with physics professor Bruce Maxfield to develop a rapid pressure perturbation kinetics instrument, which made it possible to look at chemical reactions in solution on a very fast time scale. This technology was later used to study how the protein cytochrome c folds to acquire its tertiary structure. During this time, in collaboration with Watt Webb and Doug Magde of the Cornell Applied Physics Department, he also initiated studies of spontaneous concentration fluctuations and developed an elegant method for detecting molecular motion by passing a laser beam through a solution containing fluorescent molecules. When a molecule enters the beam, it fluoresces. A mathematical analysis of the resulting intensity record makes it possible to determine how many molecules are in the beam and how fast the molecules diffuse under specific conditions. This method, which they dubbed fluorescence correlation spectroscopy (FCS), was first used to study the physical chemistry of DNA. With enhancements in laser excitation, more sensitive photon detectors, and confocal microscope optics, FCS has become a widely-used method for studying the diffusion and reactions of molecules in solution and in living cells. Elliot and his colleagues went on to devise a related method, now called fluorescence recovery after photobleaching (FRAP), for studying the dynamics of proteins on cell membranes and measuring diffusion of molecules on cell surfaces.

Mechanical Properties and Functions of Cells and Tissues. Elliot has also been fascinated by cellular mechanics—the mechanical properties of cells and the role of mechanical and other cellular forces on cell biological processes. To assess the stiffness and elasticity of single cells, he and colleagues Bill McConnaughey and Nils Petersen created the cell pocker, which uses a tiny probe to indent living cells and measure the resisting force of the cell. To study the contraction of cells, for example cells that restore tissue integrity during wound healing, he and his team created an apparatus to sense the tension in a band of artificial tissue. In collaboration with Greg Goldberg (Medicine-Dermatology), he showed that the interstitial collagenase MMP-1 moves along collagen fibrils and thus serves as a novel molecular motor.

Tissue Engineering/Regenerative Biology. Elliot and his team are currently using stem cells to manufacture cardiac tissues. Working with Guy Genin from Mechanical Engineering and Materials Science, they have been putting heart muscle cells into a collagen substrate and studying their properties. The cells are either from chicken embryo hearts or from human induced pluripotent stem cells that have been differentiated into a cardiac lineage. During the first 2-3 days the heart cells make connections to each other and start beating synchronously.

How has Elliot accomplished these scientific advancements? "It's from that incredible brain," says Tony Pryse, who started out as Elliot's graduate student at Cornell and has been collaborating with him as a key member of his lab for more than three decades. "Few people have the breadth of knowledge and insight he has. He can talk to physicists who do the statistical physics of polymers. He can turn around and talk to cell biologists about biochemistry and the biology of cells. And he can talk to mechanical engineers about the constitutive equations of tissues. Personally, he just couldn't be a better person to work for." This thought is echoed by many of his colleagues and collaborators.

Faculty Spotlight: Elliott Elson, PhD (cont.)

Phil Bayly, head of Mechanical Engineering and Materials Science and a long-time collaborator, shared this tribute: “I hate to use a cliché, but Elliot epitomizes the term ‘a scholar and a gentleman.’ He is a brilliant biophysicist who has contributed unique technical innovations, such as the cell pocker, and fluorescence correlation spectroscopy, and used them to solve important problems involving the mechanics of cells and the extracellular environment. He is also a generous collaborator and mentor, who has advanced the careers of dozens of colleagues and students. He’s one of my favorite people at Washington University—and there are many others who feel the same way.”

Carl Frieden summarized his thoughts in his inimitably sage style:

How lucky can I be to have Elliot’s lab next door to mine.

Always available,

Always willing to help,

Always thoughtful,

Always insightful.

What a pleasure.

But in fact, it’s not just me,

All of Washington University is lucky to have Elliot here.

Thank you, Dr. Elson! We await your next scientific adventures.

In celebration of Elliot’s many contributions to science and his birthday, the Department of Biochemistry and Molecular Biophysics held a symposium on September 22 and 23, 2013. The symposium started off with a reception and dinner which included the current Elson research group, Biochemistry faculty, staff and spouses, Elliot’s immediate family (including his brother from Chicago) a couple of cousins, and a number of current and former colleagues, students and postdocs. The next day the symposium started out with Dr. Carl Frieden giving a talk on “*ApoE3 vs. ApoE4 and Alzheimer’s Disease: An Enigma Wrapped in a Mystery Wrapped in a Riddle*”. Other presenters included, Drs. Barbara Baird from Cornell University, Hong Qian from the University of Washington, Enrico Gratton from the University of California in Irvine, Patrick Jay from Washington University, Joseph Schlessinger from Yale University, Tetsuro Wakatsuki from InvivoSciences, and Saveez Saffarian from the University of Utah. Dr. Joseph (Yossie) Schlessinger, current chair of Pharmacology at Yale, and a postdoc of Elliot’s at Cornell in the early ‘70’s, gave a great talk honoring Elliot and reminiscing about their long collaboration and friendship. Elliot spoke briefly thanking all for their attendance and friendship.



Reception and Dinner for the Elson Symposium.



Dr. Barbara Baird from the Dept. of Chemistry, Cornell University.



Faculty and guests at the Elson Symposium.



Students and Faculty enjoying the reception after the symposium.

Special thanks go to the symposium organizers Drs. Tony Pryse, Pat Jay, and Guy Genin, and to the Biochemistry staff for their help with the symposium. Organizers and guest speakers were presented with their very own Elliott Elson bobblehead dolls. Bobbleheads also were given to both Drs. John Cooper and Phil Bayly as heads of the sponsoring departments, and to Frances and Elliot. Additional thanks goes to the Departments of Biochemistry and Molecular Biophysics and to Mechanical Engineering & Materials Science for their financial contributions toward the symposium. Last, but certainly not least, we would like to thank the 100 people who were in attendance throughout the symposium coming from as far as Israel, Canada, Taiwan, and from different parts of the country. Your attendance made this a very successful symposium.

Departmental Student Fellowships

The Sigma Chemical Company Predoctoral Fellowship in Biological Chemistry in Memory of Gerty T. Cori

The Sigma Fellowship was created in 1958 with an annual donation from the Sigma Chemical Company. Currently, the donation is used to attract the best and the brightest graduate students into the Biochemistry and Computational and Molecular Biophysics graduate programs. Each year, the Sigma Fellowship is awarded to two incoming graduate students. During the first year of graduate school, recipients receive funds to cover first-year educational and research expenses. In their second year of study, the funds are used to cover part of the student's stipend. Every summer, a luncheon is scheduled to honor the current Sigma Fellows. Last year, our current Sigma Fellows, Kirk Hou (2009), Jay Rammohan (2010), John Robinson (2011) and Mariah Lawler (2012), participated in the luncheon by giving an update on their current research projects. Also in attendance were Dr. Rakesh Sachdev, Sigma-Aldrich President and CEO; a number of other Sigma officials, Dean Larry Shapiro and a number of WUSM faculty. Congratulations to the 2014 Sigma Fellows: Melanie Sparks and Josh Rackers.



Sigma Luncheon on July, 2013

*Front Row: Mariah Lawler, Ms. Jan A. Bertsch, Dr. Rakesh Sachdev, Dean Larry Shapiro
Back Row: John Robinson, Kirk Hou, Jay Rammohan, Mr. Eric M. Green, Mr. George L. Miller*

David F. Silbert Fellowship



Kara Ramsey, Mrs. Shirley Silbert and Qi Xiao

The David F. Silbert Fellowship was established in 1997 by contributions in memorium of Dr. David Silbert. Each year one or two medical students receive support from this fellowship to perform short-term research on projects related to Dr. Silbert's area of interest.

David Silbert was born in 1936 in Cambridge, Massachusetts and received a degree in medicine from Harvard Medical School in 1962. He completed his internship and residency at Barnes Hospital then worked as a research associate in the Laboratory of Molecular Biology at the National Institutes of Health (NIH). Dr. Silbert returned to St. Louis as a postdoctoral fellow in 1966 and joined the faculty of the Department of Biochemistry and Molecular Biophysics in 1968. His research focused on the role of macromolecular interactions in cell function. The 2013 Silbert award was given to Kara Ramsey and Qi Xiao.

Kara worked with Dr. Randall Bateman, the Charles F and Joanne Knight Distinguished Professor, in the Department of Neurology. Dr. Bateman's research interest focuses on Alzheimer disease pathophysiology. Kara's summer research project focused on the detection of AB in the Blood.

Qi worked with Dr. Michael Gross, Professor in the Departments of Chemistry, Pathology and Immunology, and Internal Medicine. Dr. Gross's research focuses on the development and application of mass spectrometry in biophysics, biochemistry, and medicine. Qi's research project focused on the fast photochemical oxidation of protein footprinting of intrinsically disordered proteins.

In January the Silbert fellows, along with their research mentors, were invited to a luncheon with Dr. Silbert's wife, Mrs. Shirley Silbert, Drs. Koong-Nah Chung, John Cooper, and Linda Pike. At this time the fellows gave a brief description of their summer research projects and talked about how their summer research experience impacted their future scientific careers.

Meet the Brennecke Endowed Professors

Marvin A. Brennecke, M.D.

Marvin A. Brennecke grew up in Jackson, a small town in southeastern Missouri., whose residents donated \$5,000 to send Brennecke to medical school. After two years of medical school at the University of Missouri, Columbia, Brennecke transferred to Washington University and graduated in 1930. He served an internship at Missouri Baptist Medical Center before moving to Hawaii where he stayed until his death in 1994. Brennecke realized the importance of basic science research, and through a living trust, donated funds to support three endowed professorships: the Marvin A. Brennecke Chair in Molecular Microbiology, the Marvin A. Brennecke Chair in Biological Chemistry and the Brennecke Chair in Biophysics.

Professorship in Biological Chemistry



The Marvin A. Brennecke Chair in Biological Chemistry is currently held by Professor Peter Burgers. Professor Burgers received his B.Sc. in biochemistry in 1969, his M.S. in organic chemistry in 1972 and his Ph.D. in organic chemistry in 1977, all from the State University of Leiden in The Netherlands. He completed two postdoctoral fellowships: one at the Max-Planck Institute for Experimental Medicine from 1977-80 and another at Stanford University from 1980-82. Dr. Burgers joined the Department of Biochemistry and Molecular Biophysics at Washington University in 1982 as an assistant professor, was promoted to associate professor in 1989 and to professor in 1995. His research interests include DNA replication and DNA damage response mechanisms in yeast and in human cells. Specifically, his lab is attempting to understand the functions of nuclear DNA polymerases at the replication fork under normal replication conditions, and how these functions are altered during replication stress or in response to DNA damage. He is the author of more than 150 journal articles. In 2010, he received an honorary Doctorate in Medicine from the University of Umea in Sweden and also became a fellow of the American Association for the Advancement of Science.

Professorship in Biophysics



In 2010, Timothy M. Lohman, Ph.D., was named the Brennecke Professor of Biophysics. Professor Lohman earned his A.B. in chemistry from Cornell University in 1973 and a Ph.D. in physical chemistry from the University of Wisconsin-Madison in 1977. He did postdoctoral work at the University of California, San Diego and the University of Oregon's Institute of Molecular Biology. He was a faculty member at Texas A&M University from 1981 to 1990, after which he came to Washington University School of Medicine and was appointed professor of biochemistry and molecular biophysics. Professor Lohman studies the unwinding of DNA by proteins called helicases. As cells divide, they must unwind the double helix of DNA to replicate the two strands. Unwinding also must occur before damage from chemicals or irradiation can be repaired. Dr. Lohman investigates how the helicases are assembled and how they use the energy supply of cells to unwind the DNA while translocating along the DNA filament. His lab also studies the SSB protein, a helix-destabilizing protein that facilitates the unwinding of DNA. Dr. Lohman is the author of more than 150 journal articles and sits on several editorial boards. He is a member of the Biophysical Society, the American Association for the Advancement of Science, and the American Society of Biochemistry and Molecular Biology. He received an American Cancer Society Faculty Research Award in 1986 and was named a fellow of the American Association for the Advancement of Science in 2004. He was named the Marvin A. Brennecke Professor in Biological Chemistry in 2000 and held that professorship until 2010 when he relinquished it to Dr. Peter Burgers to become the Brennecke Professor of Biophysics.

High-Throughput Screening Core

The High-Throughput Screening Core (HTSC) is now operating in the recently remodeled 2nd floor of the Cancer Research Building. The HTSC is the combination of two former screening cores: the CGSC and the HTC, and represents a collaboration between the Siteman Cancer Center and the Department of Biochemistry and Molecular Biophysics. This resource is available to the entire Washington University community.

The Core is under the direction of Dr. John Cooper, with Dr. Scott Wildman as the Scientific Director. Dr. Maxene Ilagan has been hired to manage the day-to-day operations.

We provide plate-based assay services, screening resources, expertise, automation and libraries for both siRNA and small-molecule compound libraries suitable for cell-based and biochemical assays. Users may take advantage of stand-alone plate readers, high content imagers and liquid handlers, or may employ our newly refurbished screening robot for fully automated HTS. For more information, please visit our website: htsc.wustl.edu.

For a detailed description of services and prices, researchers interested in high content imaging and high-throughput screening of any kind should contact Maxene Ilagan: ilaganmg@wustl.edu.

Grants, Fellowships & Awards

Recent Faculty Grants

Peter M. Burgers, PhD, received a four year renewal grant award from the National Institute of General Medical Sciences for his research entitled “*Kinase Activation in the DNA Damage Checkpoints*”.

Carl Frieden, PhD and Scott Hultgren, PhD, received a new five year, MPI grant award from the National Institute of Allergy and Infectious Diseases for their research entitled “*Biogenesis and Inhibition of Biofilm-Associated Bacterial Amyloid*”.

Eric Galburt, PhD, received a new five year grant award from the National Science Foundation for his research entitled “*Mechanism of Eukaryotic Transcription Initiation*”.

Eric Galburt, PhD and Christina Stallings, PhD, received a new five year MPI grant award from the National Institute of General Medical Sciences for their research entitled “*Investigating Novel Mechanisms of Transcription Initiation Regulation in Mycobacteria*”.

William A. Frazier, PhD, received a one year subcontract with Vasculox, Inc. from the National Cancer Institute for his research entitled “*Tumor-toxic CD47 mAb therapy for leukemia: a proof of concept study*”.

Weikai Li, PhD, was selected to receive a three year award from the American Society of Hematology (ASH) Scholar Award for his research entitled “*Understanding the interplay between VKOR supported blood coagulation and disulfide formation*”.

Weikai Li, PhD, also received a new five year grant award from the National Heart, Lung, and Blood Institute for his research entitled “*Structural and Functional Basis of the Vitamin K Cycle*”.

Garland Marshall, PhD, received a new four year grant award from the National Institute of General Medical Sciences for his research entitled “*Discovery of New Therapeutics for Drug-Free Remission of HIV*”.

Linda Pike, PhD, received a new four year grant award from the National Institute of General Medical Sciences for her research entitled “*Signal Transduction by ErbB2/ErbB3 Oligomers*”.

Awards

Peter Burgers, PhD was chosen to receive the WUSM 2014 Distinguished Investigator Award.

Elliot Elson, PhD was installed as an Honorary University Professor at Xi’an Jiaotong University in December.

Recent Fellowships and Career Awards

Congratulations to the following doctoral students and postdoctoral fellows who have garnered several highly competitive fellowships:

Chris A. Brosey, PhD in the laboratory of Dr. Tom Ellenberger, received a two year fellowship grant award from the National Institute of General Medical Sciences for her research entitled “*Structural mechanisms of AIF release during poly (ADP-ribose)-induced cell death*”.

Wei Cheng, PhD in the laboratory of Dr. Weikai Li, has been selected as the 2014 Judith Graham Pool Postdoctoral Fellowship award recipient. The two year fellowship award is from the National Hemophilia Foundation for his research entitled “*Understanding the interplay between electron transfer and VKOR supported blood coagulation*”.

Sarem Hailemariam, graduate student in the laboratory of Dr. Peter Burgers, received a three-year predoctoral fellowship from the National Science Foundation, for her proposed studies of cell cycle checkpoint regulation in response to DNA double-stranded breaks.

Marie Laury, PhD in the laboratory of Dr. Garland Marshall, received the W.M. Keck fellowship from Washington University for postdoctoral training.

Justin Sparks, graduate student in the laboratory of Dr. Peter Burgers, received the Olin Biomedical Science Fellowship in April. The Olin Fellowships are presented to Ph.D. and M.D./Ph.D. students conducting research in the biomedical sciences in any Washington University graduate program who have made significant contributions, and demonstrated the potential to become outstanding research scientists.

Paulina Wanrooij, PhD, in the laboratory of Dr. Peter Burgers, received the Svenska Kultur Fellowship from the Swedish Cultural Foundation in Finland for her research entitled “*The Mechanisms of Checkpoint Activation in Eukaryotic Cells*”.

Selected Faculty Publications

Galburt EA, Tomko EJ, Stump WT, Ruiz Manzano A. Force-dependent melting of supercoiled DNA at thermophilic temperatures. *Biophys Chem.* 2014 Mar-Apr;187-188:23-8. doi: 10.1016/j.bpc.2014.01.001. Epub 2014 Jan 17. *We show that negatively supercoiled DNA denatures at 0.5 pN lower tension at thermophilic vs. mesophilic temperatures. This work demonstrates the ability to monitor DNA supercoiling at high temperature and opens the possibility to perform magnetic tweezers assays on thermophilic systems. The data allow for an estimation of the relative energies of base-pairing and DNA bending as a function of temperature and support speculation as to different general mechanisms of DNA opening in different environments.*

Garai, K and Frieden, C. Quantitative analysis of the time course of A β oligomerization and subsequent growth steps using tetramethylrhodamine-labeled A β . *Proc Natl Acad Sci (USA)* 110 3321-3326 (2013). *A β is a peptide derived from a large protein called the amyloid precursor protein. Aggregates of A β are found in structures called plaques and it is generally believed that the presence these plaques in the brain is directly related to the development of Alzheimer's disease. Oddly, there are several different A β peptides that range in length from 37-43 amino acids but the one that appears most deleterious is that of 42 amino acids. Recently, attention has turned to oligomers, rather than aggregates, of A β as the toxic factor. In this paper we show, for the first time, a simple way to measure*

the formation of oligomers during the process of A β aggregation.

Kumar, S and Burgers, P. Lagging strand maturation factor Dna2 is a component of the replication checkpoint initiation machinery. *Genes Dev* 27 (2013) 313-321. *The initiation of cell cycle checkpoints requires that the Mec1/ATR protein kinase is activated by an activator protein. This study shows that the different phases of the cell cycle employ different activator proteins for checkpoint initiation. Interestingly, Dna2, a nuclease-helicase that is essential for Okazaki fragment maturation, also senses the stalling of DNA replication forks during S phase and stimulates Mec1 kinase to initiate the replication checkpoint.*

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The 2013 season was another fun and successful season for the Lab Rats. Welcoming a few new members to the team, we saw our size swell to the highest number in recent history. Success on the field was there too, as Manager Paul Buske led the team to a 9-2 record in his final year on the team, finishing tied for 1st in the division. The Lab Rat's lost painfully in the playoffs to rivals The Biohitters. We look forward to welcoming new members this year and seeing off old members with a championship effort.



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