2013

Boston Taiwanese Biotechnology Symposium

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Boston Taiwanese Biotechnology Association

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Welcome Message

Welcome to the Boston Taiwanese Biotechnology Symposium 2013!

This is the first event held by Boston Taiwanese Biotechnology Association (BTBA). BTBA is a group of bio-related graduate students and postdoctoral researchers who care about things both inside and outside of the ivory tower. The global trend of over-production of Ph.D. graduates inspires us to ask the following questions.

What is the connection between our own research to other bio-related fields?
What are the possibilities of our next step, and how can we achieve it?
What is the future of biotechnology and how can we contribute?

To this end, we are creating different platforms of communication such as symposiums and seminars that would facilitate interdisciplinary crosstalk, experience sharing, and possibilities of collaborations. Hopefully, through our synergistic efforts and brainstorming, some creative answers will emerge.

We thank all the participants for contributing to the Boston Taiwanese Biotechnology Symposium 2013; we thank the Organizing Committee for their time and dedication; we thank kind help from our co-organizers: National Science Council, Taiwan (中華民國行政院國家科學委員會), Science and Technology Division, Taipei Economic and Cultural Representative Office in the U.S. (駐美國台北經濟文化代表處科技組) and Harvard GSAS Taiwan (ROC) Student Club. Finally, we thank our sponsors: Education Division, Taipei Economic and Cultural Office in Boston (駐波士頓台北經濟文化辦事處教育組), Quintara Biosciences, Formosa Marketplace, PosterSmith, ORT Patent Law, Taiwanese American Foundation and generous friends for supporting the symposium financially.

We believe that this is going to be an exciting event and look forward to seeing you in a couple days!

Sincerely,

Sheng-hong Chen
Organizing Committee Chair,
Boston Taiwanese Biotechnology Association

Content

Organizing Committee

Chair

Sheng-hong Chen, 陳昇宏, Ph.D., Postdoctoral Fellow,
Department of Systems Biology, Harvard Medical School

Administration

Ying-Ja Chen, 陳映嘉, Ph.D., Scientist,
Pronutria
Huei-Mei Chen, 陳慧美, Ph.D., Postdoctoral Fellow,
Department of Molecular and Cellular Biology, Harvard University
Grace Lin, 林瑞治, Project Manager,
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Whitehead Institute & Massachusetts Institute of Technology
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Tzu-Ming Liu, 劉子銘, Ph.D., Assistant Professor,
Institute of Biomedical Engineering, National Taiwan University
Shau-Kwaun Chen, 陳紹寬, Ph.D., Postdoctoral Fellow,
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Department of Health Sciences, Boston University
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University of Utah

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Ho-Chou Tu, 杜荷洲, Ph.D., Postdoctoral Fellow,
Children's Hospital Boston/Harvard Medical School
Ruei-Jr Wu, 吳瑞智, Graduate student,
Photonics Center, Boston University
Ruei-Zeng Lin, 林叡增, Ph.D., Postdoctoral Fellow,
Children's Hospital Boston/Harvard Medical School
Chih-Chi Yuan, Ph.D., Research Fellow,
Massachusetts General Hospital

Organizer

Boston Taiwanese Biotechnology Association

Co-organizer

National Science Council, Taiwan (中華民國行政院國家科學委員會)
Science and Technology Division, Taipei Economic and Cultural Representative Office in the U.S.(駐美國台北經濟文化代表處科技組)
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Direction

Wong Auditorium

Wong Auditorim is located in Tang Center, Massachusetts Institute of Technology, 70 Memorial Dr, Cambridge, MA 02142

Directions to Tang Center

By public transportation

Subway: Take the Red Line to Kendall Square stop. You'll be on Main Street and head south. Turn right at the Bank of America corner onto Wadsworth Street. Continue on Wadsworth Street one block (about 100 yards). The Tang Center entrance is just across Amherst Street.

Bus: Take the Bus #1 to Massachusetts Ave. @ Memorial Dr. stop. Head south on Massachusetts Ave. and turn left at Memorial Dr. Continue on Memorial Dr. about 0.5 miles. The Tang Center is on your left hand side.

By Car

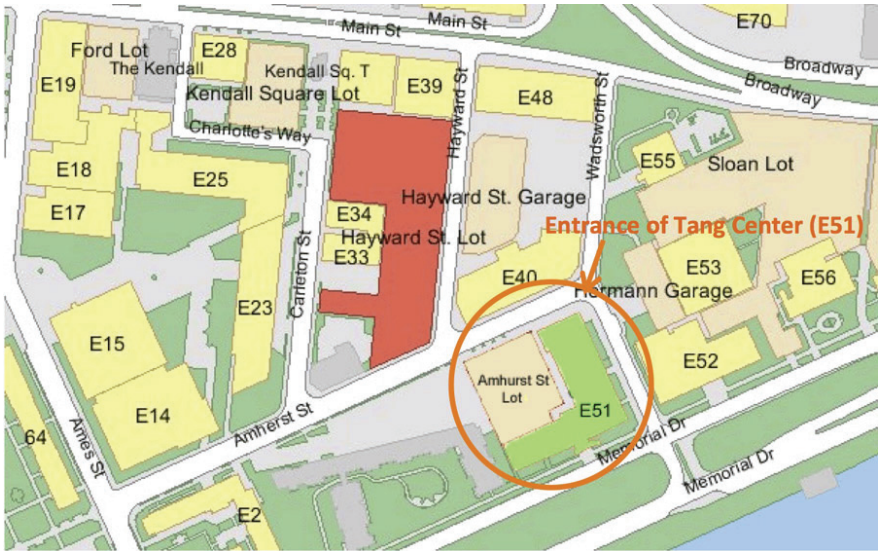
From the North (via I-93): Heading south on I-93, take exit 26 and follow the signs to Massachusetts 28 S/Storrow Dr. On the Storrow Dr., take exit MA-3N and follow the signs to Government Center/Kendall Square. Then follow the signs to Cambridge/Memorial Dr., cross the Longfellow Bridge and turn right at Edwin H Land Blvd. Continue on Edwin H Land Blvd. and turn right at Memorial Dr. The Tang Center is on your right hand side.

From the South (via I-93): Heading north on I-93, take exit 26 and follow the signs to Storrow Dr. Then follow the same direction as from the North.

From the West (via I-90, the Mass Turnpike): Follow I-90 east to the Cambridge/Brighton exit 18. Follow the signs to Cambridge, cross the River Street Bridge and turn right at Memorial Dr. Continue on Memorial Dr. about 2 miles. The Tang Center is on your left hand side.

Parking

Parking in Cambridge is generally not an enjoyable experience. Hayward Lot is affiliated to MIT and free in the weekend. One Memorial Drive Garage near the Tang Center (617-621-1238, Entrance is on Memorial Drive) is a public parking lot and $10 in the weekends. There are also several commercial lots are located at Vassar Street & Broadway. 2hr-limit meter slots are on Ames, Amherst & Main Street.



Agenda

8:30-9:00	**Registration and Poster Setup**
9:00-9:10	**Opening Remarks** Sheng-hong Chen, Harvard Medical School
9:10-10:00	**Keynote:** Chi-Huey Wong, President, Academia Sinica *"From Discovery Research to Translational Innovation: Interface of Chemistry and Biology"*
10:00-10:30	**Coffee Break**
10:30-11:10	**Disease Model** Session chair: Leslie Wu, Boston University Yueh-Chiang Hu, Whitehead Institute *"TALEN-mediated editing of the Mouse Y Chromosome"* Jieru Lin, Thomas Jefferson University *"Preventing systemic genotoxic tumorigenesis and colitis by suppressing AKT-dependent intestinal barrier dysfunction"* Shau Kwaun Chen, University of Utah *"Autoimmunity developed in Hoxb8 knockout mice"* Jimmy Yen, Indiana University School of Medicine *"IFNβ promotes the conversion of pro-inflammatory M1-like into anti-inflammatory M2-like microglia"* Ho-Chou Tu, Boston Children's Hospital *"*The *LIN28/let-7 axis regulates colorectal cancer development in vivo"*
11:10-12:10	**Panel: How to start a successful academic career** Moderator: Sherry Lee, Whitehead Institute Panelists: Chia-Ying Chu, Assistant Professor, Life Sciences, National Taiwan University Hwai-Chen Guo, Professor and Chair, Biological Sciences, University of Massachusetts, Lowell Tien Hsu, Professor, Medicine, Boston University Yi-Hsiang Hsu, Assistant Professor, Hebrew Rehabilitation Center, Harvard University Ronglih Liao, Associate Professor, Brigham and Women's Hospital, Harvard University Tsyr-Yan Yu, Postdoctoral Fellow, Harvard/Assistant Professor, Academia Sinica
12:10-13:30	**Lunch**
13:30-14:20	**Keynote:** Li-Huei Tsai, Director, Picower Institute for Learning & Memory, MIT *"Targeting epigenetic mechanisms for treating memory disorders"*
14:20-15:00	**Molecular Mechanisms** Session chair: Ho-Chou Tu, Boston Children's Hospital Yi-Ying Lee, University of Maryland *"flagellar basal body protein fliL is a key factor for bacterial swarming and surface sensing"* Heng-Chi Lee, University of Massachusetts, Worcester *"RNA detection and memories: Function of small RNAs in defense against foreign nucleic acids"* Chun-Hao Huang, Memorial Sloan-Kettering Cancer Center *"RNAi screen identifies therapeutic targets in hepatocellular carcinoma"* Tsai-Yi Lu, University of Massachusetts, Worcester *"Brain responses to traumatic injury require glial DRK-SOS signaling"* Sherry Lee, Whitehead Institute *"Genetically engineered red blood cells"*
15:00-15:30	**Coffee Break**
15:30-16:10	**Modeling and Technology** Session chair: Yung-Chih Cheng, Boston Children's Hospital Yen-Tsung Huang, Brown University *"Integrative modeling of multi-platform genomics data"* Wei-Lun Hsu, Indiana University *"Mechanisms of binding diversity and partner selection in protein disorder: Molecular recognition features mediating protein interaction networks "* Hua-Sheng Chiu, Columbia University *"ceRNA interactions cooperate with genomic variability to modulate drivers of tumorigenesis"* Tsung-Han Tsai, Massachusetts Institute of Technology *"Endoscopic optical coherence tomography"* Pao Lin, Massachusetts Institute of Technology *"Mid-infrared chemical sensors on-a-chip using air-clad pedestal silicon waveguides"*
16:10-17:10	**Panel: Career opportunities outside of academics** Moderator: Ying-Ja Chen, Pronutria Panelists: Alex Shih-Min Huang, Drug Discovery Program Leader, Sanofi Oncology Jeng-Shin Lee, Co-founder, AB Biosciences Ruei-Che Ray Liu, Biostatistician, Millenium, The Takeda Oncology Company Hsiao-Lan Sun, Senior Applications Scientist, Agilent Technologies. Miao-Chih Tsai, Scientific Editor, Molecular Cell, Elsevier. Jeannie Wu, Associate, ORT Patent Law
17:10-18:30	**Poster Session and Reception**

Keynote Speaker

Chi-Huey Wong,
9th & 10th President of Academia Sinica

Dr. Chi-Huey Wong is the 9th and 10th President of Academia Sinica and a Distinguished Research Fellow at the Genomics Research Center, Academia Sinica.

Born in Taiwan, Dr. Wong received his B.S. and M.S. degrees from National Taiwan University, and Ph.D. in Chemistry (with George M. Whitesides) from Massachusetts Institute of Technology in 1982. He then moved with Professor Whitesides to Harvard University as a postdoctoral fellow for another year. He started his independent career as Assistant Professor of Chemistry at Texas A&M University in 1983, became Associate Professor in 1986 and Professor in 1987. He was Professor and Ernest W. Hahn Chair in Chemistry at the Scripps Research Institute (1989-2006) and Director of the Genomics Research Center at Academia Sinica, Taipei (2003-2006). He became President of Academia Sinica in 2006 with joint appointment as professor of chemistry at National Taiwan University and The Scripps Research Institute.

His research interests are in the areas of bioorganic and synthetic chemistry and biocatalysis, including synthesis of complex carbohydrates, glycoproteins and small-molecule probes for the study of carbohydrate-mediated biological recognition. He has trained more than 300 Ph.D. students and postdoctoral fellows in the past 30 years and is the author and co-author of over 650 publications (H-index 94), 100 patents, and four books in the field of chemical biology.

Dr. Wong is a recipient of The Searle Scholar Award in Biomedical Sciences (1985), the Presidential Young Investigator Award in Chemistry (1986), the American Chemical Society A. C. Cope Scholar Award (1993), the Roy Whistler Award of the International Carbohydrate Organization (1994), the American Chemical Society Harrison Howe Award in Chemistry (1998), the American Chemical Society Claude S. Hudson Award in Carbohydrate Chemistry (1999), the International Enzyme Engineering Award (1999), the U.S. Presidential Green Chemistry Challenge Award (2000), The American Chemical Society Award for Creative Work in Synthetic Organic Chemistry (2005), the F.A. Cotton Medal (2008) for Excellence in Chemical Research, the American Chemical Society Arthur C. Cope Award (2012), and the Nikkei Asia Prize for Science, Technology and Innovation (2012).

He is a member of Academia Sinica, Taipei, the American Academy of Arts and Sciences, the US National Academy of Sciences, and the World Academy of Sciences (TWAS). He was Chairman of the Executive Board of Editors of the Tetrahedron Publications (2006-2008), Editor-in-Chief of Bioorganic and Medicinal Chemistry (1993-2010), a board member of the US National Research Council on Chemical Sciences and Technology (2000–2003), a scientific advisor of the Max-Planck Institute (2000–2008), and the Chief Science Advisor of the Executive Yuan, Taiwan (2008-2011). He is currently an Editorial Advisory Board member for the Journal of American Chemical Society, Angewandte Chemie, Advanced Synthesis and Catalysis, and Current Opinion in Chemical Biology. He is also a member of Board of Scientific Governors of the Scripps Research Institute, the Steering Committee of the Lilly TB Drug Discovery Initiative, and the Chief Science Advisor of the Ministry of Science, Taiwan.

Keynote Speaker

Li-Huei Tsai

http://www.lihueitsai.org/li-huei-tsai/

Director, The Picower Institute for Learning and Memory,
Picower Professor of Neuroscience, Department of Brain and Cognitive Sciences,
Investigator, Howard Hughes Medical Institute.

Li-Huei Tsai received her D.V.M from National Chung Hsing University, M.S. from University of Wisconsin, Madison, and Ph.D from the University of Texas Southwestern Medical Center at Dallas. After completing her postdoctoral work with Ed Harlow's laboratory at Cold Spring Harbor laboratory and Massachusetts General Hospital, Dr. Tsai joined the faculty in the Department of Pathology at Harvard Medical School in 1994 and was named an investigator of Howard Hughes Medical Institute in 1997. In 2006, she was appointed Professor in the Department of Brain and Cognitive Sciences, and joined the Picower Institute for Learning and Memory at MIT. She is currently the Director of the Picower Institute for Learning and Memory.

Dr. Tsai is the recipient of numerous awards including Outstanding Contributor Award from the Alzheimer Research Forum, Alzheimer's Research Consortium, Simons Foundation Autism Research Initiative Award, NIH Cantoni Lecture Award, and Glenn Award For Research in Biological Mechanisms of Aging. She is an Academician of Academia Sinica of Taiwan, a Fellow of American Association for the Advancement of Science (AAAS), and an Elected Member of Institute of Medicine (IOM) of the US.

Academic Panelists

Chia-Ying Chu

Assistant Professor, Department of Life Science/ Institute of Zoology/ Center for Systems Biology, National Taiwan University

台灣大學生命科學系/動物學研究所/系統生物學研究中心助理教授

Dr. Chia-Ying Chu is now an assistant professor of College of Life Science at National Taiwan University, Taiwan. She received her BS and MA degrees from the Department of Zoology at National Taiwan University, and earned the Ph.D. in Biochemistry and Molecular Pharmacology from University of Massachusetts Medical School. After completing her Ph.D., Dr. Chu received the post-doctoral training at Sanford-Burnham Medical Research Institute. She joined the College of Life Science at National Taiwan University as a faculty member in 2009. Her research focuses on understanding mechanisms of small RNA-mediated gene silencing in mammalian cells, particularly the RISC-induced translational repression and the RNA processing in cytoplasm.

Hwai-Chen Guo 郭懷誠

Professor and Acting Department Chair, Biological Sciences, University of Massachusetts, Lowell
麻州大學洛威爾分校生物系教授及代系主任

Dr. Hwai-Chen Guo is a Professor with tenure of Biological Sciences at UMass Lowell. He received his Ph.D. in Molecular Biology with a minor concentration in Chemical Engineering from Cornell University, and post-doctoral training as a Cancer Research Institute Fellow in Structural Biology at Harvard University. Dr. Guo joined the Department of Biophysics at Boston University School of Medicine as an Assistant Professor in 1994, was appointed Associate Professor in 2001, and subsequently promoted to Full Professor in 2010. In the 2011, Dr. Guo joined UMass Lowell and is now the Acting Chair of the Biological Sciences Department. Dr. Guo's research focuses on understanding the relationship of macromolecule three-dimensional structures to biochemical functions by employing X-ray crystallography, molecular biology, and protein chemistry.

Yi-Hsiang Hsu 許益祥

Assistant Professor of Medicine, Hebrew SeniorLife Institute for Aging Research, and Co-Director, GeriOmics (Geriatric+Omics) Center, Harvard Medical School

Dr. Yi-Hsiang Hsu is the Co-Director of the GeriOMICS Center, Hebrew SeniorLife Institute for Aging Research. He is also an Assistant Professor at Harvard Medical School and at Program for Quantitative Genomics, Program of Molecular and Integrative Physiological Sciences, Harvard School of Public Health, Boston, MA. Dr. Hsu is a Statistical Geneticist and his research focuses on (1) genetic contribution of common aging relevant disorders (such as osteoporosis, sarcopenic obesity, metabolic syndrome,

type 2 diabetes and hypertension) using population-based next generation whole genome sequencing, exome-sequencing and GWAS approaches; (2) statistical method development on multiple-phenotype association analyses; (3) integrative omics dataset using system genetics and bioinfomatic approaches and (4) identifying biomarkers of osteoporosis using metabolomics.

Tien Hsu 徐泗

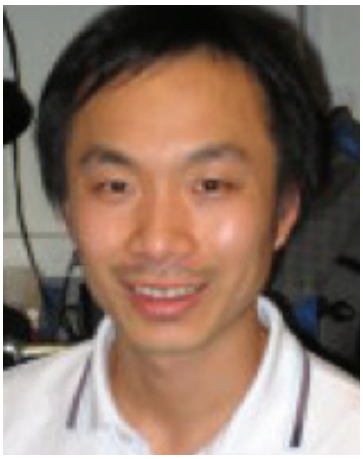
Professor of Medicine at the Boston University School of Medicine, and Director of the Stromal Biology and Cancer Program

Dr. Tien Hsu (徐泗）graduated from the Department of Agricultural Chemistry, National Taiwan University, in 1981. He received the PhD degree in Molecular Biology from the Medical University of South Carolina in 1988, and postdoctoral training in the Biological Laboratory at Harvard University until 1993. He obtained his first faculty appointment as an Assistant Professor in December 1993 and is now the Professor of Medicine at the Boston University School of Medicine, and Director of the Stromal Biology and Cancer Program. Dr. Hsu has served on several NIH study sections and is a member on the Scientific Advisory Board of VHL Family Alliance, a patient advocacy group. His research interest is in the developmental and pathological functions of tumor-related genes.

Ronglih Liao

Associate Professor, Brigham and Women's Hospital, Harvard Medical School

http://dms.hms.harvard.edu/BBS/fac/Liao.php



Tsyr-Yan Yu

Postdoc in Harvard Medical School/Assistant Professor, Academia Sinica

I got my PhD in 2008 from Washington University in St. Louis. I am still a postdoc at Harvard medical school but going to be an assistant researcher at Institute of atomic and molecular sciences, Academia Sinica in November 2013. My research interests are physical chemistry and structural biology.

Industry Panelists

Alex Shih-Min Huang

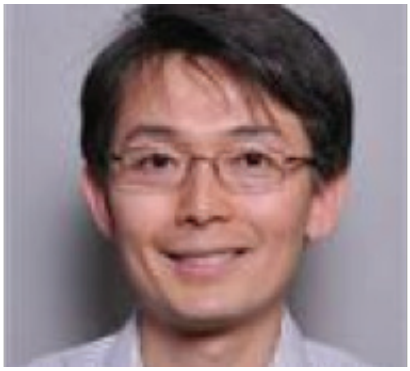
Principal Research Investigator, Project Team Leader at Sanofi Oncology

Alex (Shih-Min) Huang obtained his bachelor degree from National Taiwan University and his doctoral degree in Microbiology and Immunology from University of Rochester. He later joined Genomics Institute of the Novartis Research Foundation (GNF) in San Diego for his post-doctoral training and experienced first-hand the innovation in genome-wide pathways interrogation technology. In 2006, Alex joined the initiative to target oncogenic signaling pathways at Novartis Institutes for Biomedical Research in Cambridge. Subsequently, he and the team identified Tankyrase as a novel druggable target in Wnt pathway. This accomplishment was published and featured in Nature in 2009. Later, Alex expanded his scope. He led a multi-disciplinary team and successfully identified cellular active, specific, and potent inhibitors against an ubiquitin modifying enzyme that is previously believed to be "undruggable". In 2010, Alex joined the newly formed Sanofi Oncology in Cambridge to lead and shepherd highly matrixed project team to advance drug discovery programs into early development phase. In this role, he not only direct and streamline drug discovery activities globally, but also spearhead translational research and establish patient stratification strategies through in-depth mechanistic studies, biomarker, and responder signature discoveries to enable design of diverse clinical paths. Furthermore, Alex is the research lead for Sanofi JAK2 inhibitor program currently in Phase III trial. In this role, he is responsible for establishing and executing internal research initiatives and external collaborations to address clinical relevant opportunities and enable market differentiation for Sanofi JAK2 inhibitor.

Jeng-Shin Lee

Chief Scientific Officer, AB Biosciences, Inc.

Dr. Jeng-Shin Lee is the Chief Scientific Officer at AB Biosciences, Inc. Founded in 2007, AB Biosciences Inc. (ABB) is a development stage biotechnology company, striving to create the best niche antibody-based biologics in order to fulfill the research and development needs of the biomedical and biopharmaceutical communities. The long range goal is to develop therapeutic and diagnostic entities. Before joining ABB in March 2011, Dr. served as the Deputy Director of Harvard Gene Therapy Initiative, an organization founded in 1998 within Harvard Medical School with the objective of promoting the use of gene transfer technology in both research and therapeutic applications. Over the last decade, his group has been primarily responsible for the development of three cell based products intended for cancer immunotherapy, processes for both research and clinical grade production of adeno-associated viral vectors targeting neuromuscular systems, as well as newer generation lentiviral vector systems. The work has supported four approved investigational new drug (IND) applications in the United States and Europe, in collaboration with physician scientists at Dana Farber Cancer Institute and elsewhere. Dr. Lee received post-doctoral training at Whitehead Institute, MIT, and Children's Hospital, Boston. Prior to that, he received his PhD in Virology from Harvard University in 1995 and MD from National Taiwan University in 1990.



Ruei-Che (Ray) Liu

Biostatistician, Millenium, The Takeda Oncology Company

Dr. Ray Liu is the head of non-clinical and translational statistics group at Millennium, the global oncology arm of Takeda Pharmaceutical Company, headquartered in Cambridge, Massachusetts. His group provides statistical support to various functional areas in R&D, including Discovery, DMPK, pharmaceutical science, drug safety, Translational Medicine, Health Economics Outcome Research, Pharmacovigilance, and Regulatory Affairs.

Ray is an active contributor in the statistical community. He has organized and presented at multiple statistical conferences sponsored by national organizations such as ASA, MBSW, and ICSA. He is the author of more than 20 statistical and scientific publications, and is a member of Non-Clinical Biostatistics Leaders' Forum. He is also the leading statistician of Cardiac Hypertrophy Working Group of PSTC, the FDA-industry consortium under Critical Path Institute with aims at qualifying new safety biomarkers.
Dr. Ray Liu received his bachelor and master degrees from National Taiwan University and PhD degree from Columbia University. He worked for Pfizer Inc prior to his current position.

Hsiao-Lan Sun

Senior Application Scientist, Agilent Technologies

Patty Sun is currently a Senior Field Applications Scientist at Agilent Technologies. She received her M.S. in Environmental Engineering from National Taiwan University and Ph.D. in Biological Engineering from Massachusetts Institute Technologies. Shortly after graduating from MIT in 2006, she joined the Metabolomics group at BG Medicine. In 2007, she joined the ADME Biology department at Pfizer Inc., and transferred to Formulation and Delivery Chemistry department in 2010. She has more than seven years in practice of analytical biochemistry in the biotech and pharmaceutical industries, particularly with liquid chromatography and mass spectrometry. Her training at MIT focused on molecular toxicology and enzymology.

Miao-Chih Tsai 蔡妙智

Scientific Editor, Molecular Cell, Elsevier

I was born and raised in a traditional Buddhist family in a small town of south Taiwan. My heart still belongs to this sunny place where people would know whom my grandfather is when I am walking on the street.
During my Masters I worked on ced-12, a gene involved in programmed cell death in C. elegans, with Yi-Chun Wu at National Taiwan University. I then decided to move to C. elegans' home town (Cambridge, UK) for my PhD. I investigated how embryonic cell polarity is set up in the one cell stage in Dr. Julie Ahringer's lab at Gurdon Institute, Cambridge, UK. I then crossed another ocean to work with Dr. Howard Chang at Stanford for my posdoc research from 2007-2010. I studied how a long noncoding RNA may function as a scaffold for different protein complexes. I became a scientific editor at Molecular Cell since 2011.

Jeannie Wu

Ph.D., J.D., Associate, ORT Patent Law

Jeannie's practice emphasizes U.S. and foreign patent prosecution, opinion work, and client counseling in the areas of biotechnology and other biological and medical sciences. She has worked on projects related to gene and cell-based therapies, small inhibitory RNAs, DNA vaccines, peptide display technologies, diagnosis and treatment for various disorders (including autoimmune disorders, diabetes, asthma, achondroplasia, cancer, and cardiovascular diseases), immunodiagnostics and therapeutics, drug discovery, and prosthetic and other medical devices.

Professional Experience

Prior to joining Occhiuti Rohlicek & Tsao, Jeannie was a clerk/associate with Fish & Richardson P.C. (2006-2010), an intern at a pharmaceutical company working on patent matters relating to biotechnology, and an intern at the United States Attorney's Office in Boston.

Education

J.D., Northeastern University School of Law
Ph.D., Molecular Biology, Princeton University
B.S., Biology, Massachusetts Institute of Technology

Bar Admissions

Registered to practice before the United States Patent and Trademark Office
Admitted to the bar in Massachusetts

Languages

Jeannie is fluent in Mandarin Chinese

Selected Publications and Presentations

Wu J, Tolstykh T, Lee J, Boyd K, Stock JB, Broach JR. Carboxyl methylation of the phosphoprotein phosphatase 2A catalytic subunit promotes its functional association with regulatory subunits in vivo. EMBO J. 2000 Nov 1;19(21):5672-81.

Abstracts of Oral Presentation

TALEN-mediated editing of the Mouse Y chromosome

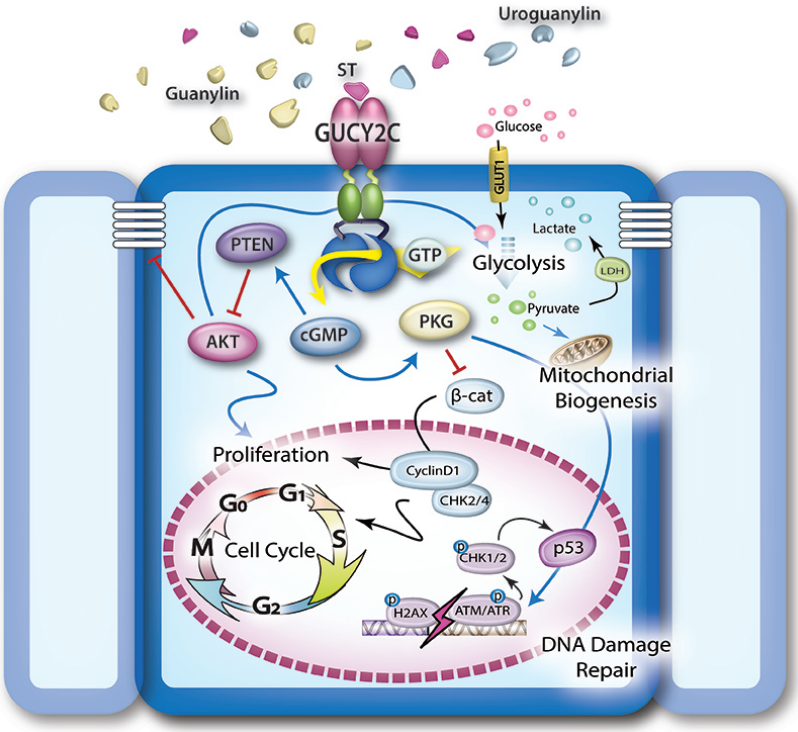
Yueh-Chiang Hu[1, 2, 7], Haoyi Wang[1, 7], Styliani Markoulaki[1], G. Grant Welstead[1], Albert W. Cheng[1, 3], Chikdu S. Shivalila[1, 4], Tatyana Pyntikova[1], Daniel B. Dadon[1, 4], Daniel F. Voytas[5], Adam J. Bogdanove[6], Rudolf Jaenisch[1, 4] and David C. Page[1, 2, 4]
[1]Whitehead Institute for Biomedical Research, Cambridge, Massachusetts, USA [2]Howard Hughes Medical Institute [3]Computational and Systems Biology Program, Massachusetts Institute of Technology, Cambridge, Massachusetts, USA [4]Department of Biology, Massachusetts Institute of Technology, Cambridge, Massachusetts, USA [5]Department of Genetics, Cell Biology and Development, University of Minnesota, Saint Paul, Minnesota, USA [6]Department of Plant Pathology and Plant-Microbe Biology, Cornell University, Ithaca, New York, USA
[7]These authors contributed equally to this work.

The Y chromosome has unique structure and gene content and has evolved into a chromosome that is highly specialized for male sex differentiation and fertility. A comprehensive approach to study the function of Y-linked genes in mice is needed to unravel the biology of the Y chromosome. Perhaps due to the unique structural features of the Y chromosome, conventional gene targeting strategies in mESCs to generate mutations in Y-linked genes have been unsuccessful. Therefore, our understanding of the functions of murine Y-linked genes is limited to insights gained from studies of mice that carry spontaneous deletions, random gene trap insertions or autosomal transgenes. Although two Y-linked knockout mESC clones and one transgenic mouse line have been generated using an insertional targeting strategy (an unconventional method causing DNA duplications around the targeting site), no mouse with a targeted gene knockout and knockin on the Y chromosome has ever been reported. Here we report using TALEN-mediated gene editing to efficiently manipulate genes on the mouse Y chromosome and produce mice with targeted gene disruptions and insertions in two Y-linked genes – Sry and Uty.

Preventing systemic genotoxic tumorigenesis and colitis by suppressing AKT-dependent intestinal barrier dysfunction

Jieru E. Lin, Scott A. Waldman
Thomas Jefferson University

The intestine epithelium represents the largest surface of the human body that is continually exposed to commensal and pathogenic microbes, and environmental toxic or carcinogenic substances. However, our understanding of protection provided by the intestine barrier was limited to against microbe invasion and local inflammation-induced colorectal tumorigenesis. Here, we demonstrated that GUCY2C, an intestinal tumor suppressor that maintains crypt-villus homeostasis, guardians barrier integrity opposing colitis and systemic tumorigenesis through AKT1-dependent regulation of tight junction integral proteins. Gucy2c$^{-/-}$ mice exhibited disrupted tight junctions, associated with reduced junctional proteins and barrier hyperpermeability. Conversely, ligand activation of GUCY2C in mice through genetic expression or oral ligand supplementation increased junctional proteins and reduced barrier permeability. Further, eliminating GUCY2C exacerbated, while activation reduced, DSS-induced barrier disruption and colitis. Moreover, eliminating GUCY2C amplified, while activation reduced, systemic oxidative DNA damage. Genotoxicity was associated with increased spontaneous and carcinogen-induced systemic tumorigenesis in Gucy2c$^{-/-}$ mice. GUCY2C regulated barrier integrity by repressing AKT1 which increased the junction proteins occludin and claudin 4 in mice and Caco2 cells. The pathophysiological significance of GUCY2C-dependent barrier protection is highlighted by its impact on colitis and systemic genotoxicity and tumorigenesis. Its translational potential is underscored by the clinical development of GUCY2C ligands, which can be used for chemoprophylaxis in inflammatory bowel disease and cancer.



Autoimmunity developed in Hoxb8 knockout mice

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Hoxb8 belongs to the homeobox transcription factor family. Hoxb8 knocked out (KO) mice exhibit a compulsive grooming, similar to trichotillomania (an impulse control disease) in humans. Hoxb8 is expressed in multiple hematopoietic cells. Bone marrow (BM) cells from Hoxb8 KO are less competitive than wildtype (wt) BM cells in granulocyte/monocyte and T cell lineages, yet more competitive in B cell lineage. How these changes affect development and functions of lymphocytes remain unknown. Here we report that autoimmunity was developed in Hoxb8 KO. Hoxb8 KO sera contain autoantibody against several self-tissues, including brain, kidney and liver. Splenomegaly was found with a higher frequency in KO mice, associating with increased B and T cell numbers. The percentages of surface IgG^+ B and activated T cells were significantly increased as well. Moreover, serum IgG levels showed an age-dependent increase: there were trends of increased IgG levels in 3 and 6 month old KO, compared to aged matched wt mice, but all IgG isotypes, except IgG3, were significantly increased in the 9-month-old KO mice. Finally, we showed that autoimmunity developed in Hoxb8 KO mice may not be the major cause of the excessive grooming behavior since compulsivegrooming remains in Hoxb8/RAG2 double KO mice. This observation suggests that defects of Hoxb8 in the immune system may play a supportive but not a major role in the pathogenesis of compulsive behavior, which agrees with our microglia hypothesis.

IFNβ promotes the conversion of pro-inflammatory M1-like into anti-inflammatory M2-like microglia

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IFNβ is an approved therapeutic option for the treatment of certain autoimmune diseases such as MS/EAE. However, the molecular mechanisms underlying the effects of IFNβ in MS/EAE are not fully understood. In this study, we identified a novel mechanism for the beneficial effect of IFNβ in MS/EAE through the conversion of microglia (MG) from pro-inflammatory M1-like (MG1) to anti-inflammatory M2-like (MG2). Our results show that IFNβ inhibited expression and production of proinflammatory M1-type cytokines, such as IL-12p40, IL-23 and TNFα and promotes the anti-inflammatory M2 cytokine IL-10 in LPS-stimulated primary MG. In addition, IFNβ treatment also enhanced the expression of specific M2 makers, such as arginase and YM-1. Through this phenotype switch, IFNβ-treated MG suppressed Th1 and Th17 activation leading to the downregulation of IFNγ and IL-17. *In vivo*, IFNβ-treated EAE mice exhibit lower clinical scores, reduced Iba-1 expression, and increased expression of the M2 markers, arginase, YM-1 and IL-10 in the CNS. Taken altogether, our results demonstrate that IFNβ favors the generation of MG2 leading to the secretion of the anti-inflammatory cytokine IL-10 and reduced expression of the pro-inflammatory cytokines, IL-12, IL-23, IFNγ and IL-17. AHA 12SDG8170005

The LIN28/let-7 axis regulates colorectal cancer development *in vivo*

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Lin28 is an evolutionarily conserved RNA binding protein that orchestrates the developmental timing in early C. elegans larvae. In mammals, LIN28A and its paralog LIN28B are highly expressed in embryonic stem cells (ESC) and in early developing tissues. Through blocking the terminal processing of let-7 miRNAs and/or by regulating the translation of its direct binding mRNAs targets, LIN28 post-transcriptionally controls the expression of an array of proteins that mediate proliferation, pluripotency, differentiation and metabolism. Although LIN28A/B are undetected in most normal adult tissues, aberrant overexpression of these two paralogs is reported in a variety of human cancers, including germ cell tumors, neuroblastoma, breast, lung, cervical and colorectal adenocarcinoma. Mechanisms typically at play during early embryonic development and stem cell self-renewal are often aberrantly activated in cancer. Indeed, impaired differentiation is a common feature of advanced forms of malignancy in humans in which many display an ESC-like gene expression profile. In this study, we hypothesize that the reactivation of molecular machineries utilized during early embryonic development, such as the maintenance of high levels of LIN28, is essential for tumorigenesis We specifically focused on the role of LIN28 in colorectal cancer (CRC). Despite a rich history of investigation describing a number of critical gene mutations associated with CRC initiation and progression, CRC remains one of the major contributors to cancer-related mortality. Therefore, identification of novel players contributing to CRC development becomes critical, because these potential players could be the next attractive targets for more effective therapeutics. To explore how aberrantly high level of LIN28 effects CRC development and progression, we generated an inducible LIN28 transgenic animal models, such that Lin28a or LIN28B is specifically expressed in the epithelia of the small intestine and colon. Interestingly, overexpression of Lin28a leads to hyperplastic over-growth of the intestinal epithelia, with abnormal enlarged proliferative crypts and a near complete loss of terminally differentiated cells in the villi. Nevertheless, no malignant tumors are observed in Lin28a transgenic animals. In contrast, transgenic animals with LIN28B overexpression in the intestinal epithelia developed aggressive intestinal adenocarcinoma with a latency of 6-7 months post induction. These results indicate that Lin28A/B play different roles that effect the homeostasis of intestinal epithelia, and eventually leads to CRC formation through distinct pathways. In summary, here we report the generation of novel animal models for human colorectal cancer. These animals provide excellent pre-clinical platforms for us to further dissect the mechanistic interplay between LIN28A/B and let-7 in contributing to CRC development. Exploration of specific molecules targeting this pathway could provide novel insights into potential therapeutics for treatment of CRC or other cancers overexpressing LIN28.

Flagellar basal body protein FliL is a key factor for bacterial swarming and surface sensing

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Swarming is a bacterial motile behavior driven by flagella rotation allowing bacterial cells moving over surfaces or in viscous liquid. Proteus mirabilis, a Gram-negative enterobacterium and opportunistic urinary tract pathogen, is well-known for its ability of swarming and dimorphic cell differentiation. Swarming motility of P. mirabilis is associated with the pathogenicity and progresses in a cyclic nature resulting in the 'bull eye' colony pattern on a nutrient agar (Fig. 1). In liquid culture, P. mirabilis cells are uniformly 1.5-2.0 μm rods with 4-6 flagella, called swimmer cells. When P. mirabilis encounters a highly viscous environment or a solid surface, swimmer cells differentiate into elongated (10-80 μm), highly flagellated swarmer cells that lack of septa and contain multiple nucleoids. The bacteria detect a surface by monitoring the rotation of their flagellar motors. This process involves an enigmatic flagellar protein called FliL, the first gene in an operon (fliLMNOPQR) that encodes proteins of the flagellar rotor switch complex and flagellar export apparatus. We used a fliL knock out mutant to gain further insight into the function of FliL. Loss of FliL results in cells that cannot swarm (Swr-), but do swim (Swm+), and produce cells that look like wild-type swarmer cells, "pseudoswarmer cells", that are elongated, contain multiple, evenly spaced nucleoids, and lack septa. Unlike swarmer cells, pseudoswarmer cells are not hyperflagellated due to reduced expression of flaA (the gene encoding flagellin), despite an increased transcription of both flhD and fliA, two positive regulators of flagellar gene expression. We found that defects in fliL prevent viscosity-dependent sensing of a surface and viscosity-dependent induction of flaA transcription. The data support a dual role for FliL, as a critical link in sensing a surface and in the maintenance of flagellar rod integrity.

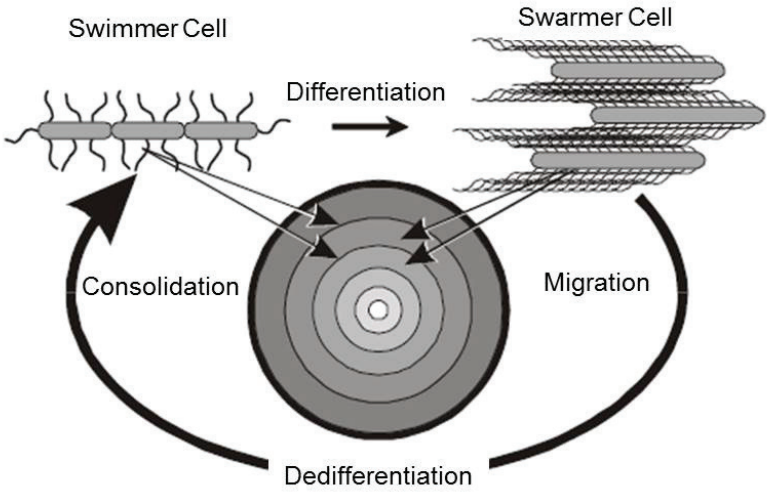

Figure 1. The cyclic nature of swarmer cell differentiation and colony migration.

RNA detection and memories: function of small RNAs in defense against foreign nucleic acids

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Failure to control invading nucleic acids of transposon and viruses can lead to genome instability and diseases, including infertility and cancers. In nematode C. elegans, foreign DNAs (transgenes) are often silenced in the germline, but not somatic cells. Our research focuses on understanding the functions of non-coding RNAs in transgene silencing using C. elegans as a model organism. Small non-coding RNAs, whose sizes range from 21-29 nucleotides, play important roles in regulating gene expression in various biological processes. Members of the conserved Argonaute (AGO) protein family interact with and utilize these small RNA sequences as guides in the recognition of target sequences. A class of small RNAs named piRNAs interacts with members of the PIWI-Argonaute sub-family, and promotes fertility in all animals tested to date. One amazing feature of piRNAs in animals is that they are remarkably diverse. For instance, C. elegans genome encodes over 25,000 distinct piRNAs. We have recently demonstrated that piRNAs are required to initiate the silencing against transgenes. However, once silenced, transgene can remain silent without PIWI/piRNA for multiple generations. Instead, genetic analysis demonstrates that the maintenance of transgene silencing requires another Argonaute family, WAGO argonautes. By engineering piRNA reporters that contain piRNA complimentary sequences, we have shown piRNAs can initiate sequence-specific gene silencing of their targets. Additionally, some degree of mismatch in base pairing between the piRNAs and their targets appears to be tolerated, which greatly increases the targeting capacity of piRNAs. As most of the endogenous genes are likely to have piRNA target sites, a mechanism should exist to protect them from piRNA targeting, which may involve Arognaute CSR-1. Together, our current results support a model that C. elegans piRNAs utilize their enormous sequence targeting capacity to scan the transcriptome for foreign sequences, while memory of "self" or "non-self" transcripts is established by endogenous small RNAs that associate with CSR-1 or WAGO Argonautes, respectively.

References:

Lee HC, Gu W, Shirayama M, Youngman E, Conte DJ, Mello CC. 2012 "*C. elegans* piRNAs mediate the genome-wide surveillance of germline transcripts", ***Cell.*** 150 (1): 78-87.

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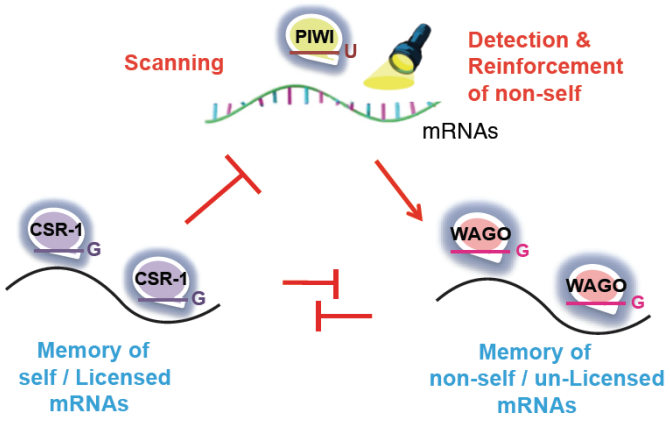

RNAi screen identifies therapeutic targets in hepatocellular carcinoma

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Liver cancer is the third leading cause of cancer related mortality worldwide. Hepatocellular carcinoma (HCC), the most common type of primary liver cancer, is a very aggressive type of cancer that lacks effective treatment, in part, due to the undruggable nature of its main genetic drivers, such as oncogene MYC amplification or loss of tumor suppressor TP53. The introduction of the multikinase inhibitor Sorafenib represents the biggest therapeutic advance in the past decade, extending life expectancy from 8 to 11 months. However, its reduced therapeutic efficacy emphasizes the urgent need for improved targeted therapies. In this regard, RNA interference (RNAi) screen is an ideal method to identify potential drug targets as knockdown by small hairpin RNAs (shRNAs) can mimic target inhibition by small molecule inhibitors. Recently, our lab has developed a pipeline for rationally designed libraries of shRNAs and pinpointed an epigenetic regulator BRD4 as a novel drug target for acute myeloid leukemia.The current study combines our shRNAs pipeline with a recently developed inducible RNAi vector optimized for *in vitro* negative selection screens to identify potential drug targets in a mosaic HCC mouse model (c-Myc; $p53^{-/-}$) that recapitulates human HCC. To systematically probe genetic vulnerabilities required for HCC maintenance, we have designed a library that contains 2,245 shRNAs targeting 442 "drugged" genes, including genes targeted by FDA-approved drugs, small molecules in clinical trials and pre-clinical lead compounds. Pharmacological or shRNA-mediated inhibition of candidate genes led to robust antitumor effects, both *in vitro* and *in vivo*. Our results highlight the utility of RNAi screening for studying cancer vulnerabilities that can be exploited for direct pharmacological intervention.

Brain responses to traumatic injury require glial DRK-SOS signaling

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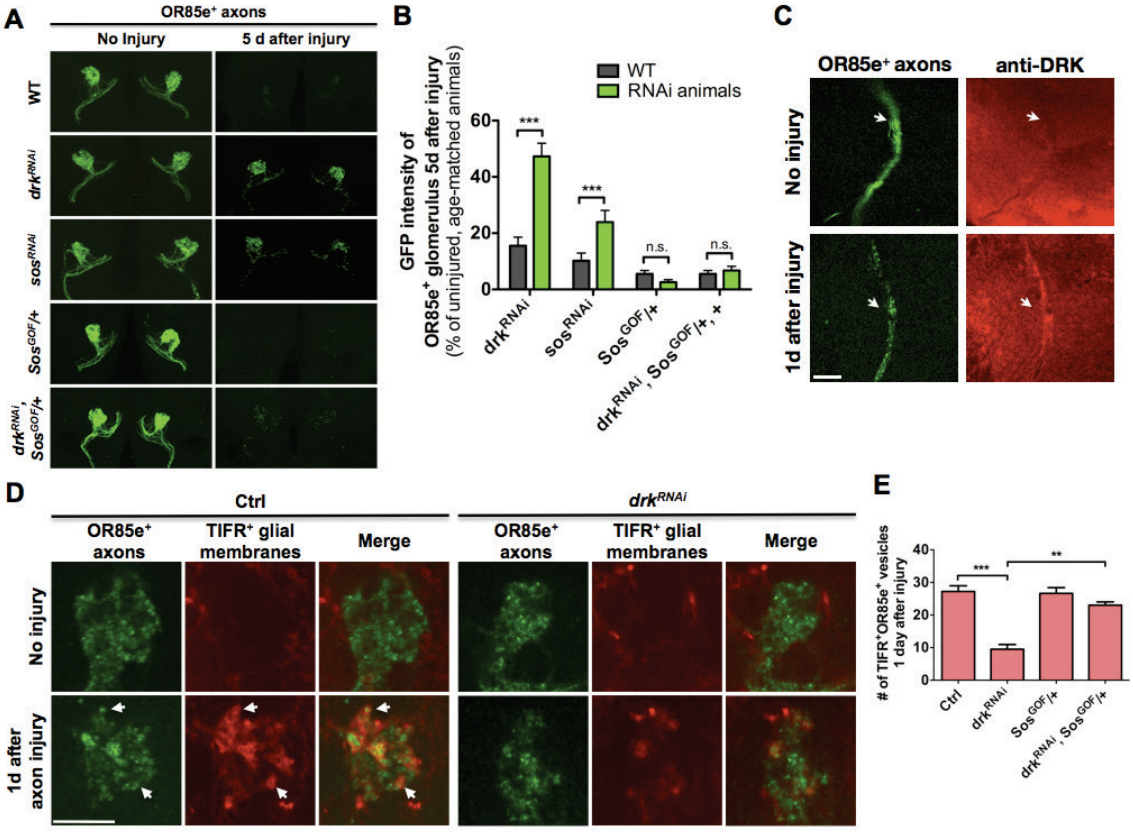
Glia are the primary cells that sense neuronal injury and clear axonal/dendritic debris in the brain. To identify new genes required for glia to properly clear degenerating axons, we performed an *in vivo* RNAi screen in Drosophila melanogaster (fruit fly), where candidate genes were specifically knocked down in glia using GAL4-UAS system, and evaluated the efficiency of glial clearance of degenerating axons ("OR85e+ axons", below). We found knocking down DRK or SOS (mammalian orthologs of Grb2 and mSos1, respectively) resulted in a significant delay of axonal debris clearance from the brain, as shown by lingering GFP-labeled axon debris 5 days after injury (Fig. A and quantified in B). Consistent with a role for DRK in glial phagocytic function we observed DRK protein accumulation specifically around injured axons 1 day after injury (Fig. C). Moreover, by quantifying the internalization of axonal debris by glial cells we found that knockdown of glial DRK suppressed glial phagocytosis of axon material (Fig. D and quantified in E). Increasing SOS activity by introducing a gain-of-function sos allele was sufficient to rescue the lack of DRK activity in glia during engulfment of axonal debris suggesting that SOS is a downstream effector of DRK (Fig. A and E). Together these data indicate DRK-SOS signaling plays an important role *in vivo* to help glia to engulf axonal debris. Since DRK and SOS are both highly conserved between fruit fly and mammals, we suspect mammalian glia use similar mechanism to clear degenerating axons, perhaps in many neurodegenerative diseases.



Genetically engineered multi-purpose red blood cells

Sherry Lee[1], Xiaofei Gao[1], Jiahai Shi[1], Lenka Kundrat[1], Hidde Ploegh[1, 2] and Harvey Lodish[1, 2, 3]
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Red cells could be useful diagnostic and therapeutic tools, since they have large surface area, good biocompatibility and long life span in circulation. We have developed an ex vivo culture system to produce large numbers of enucleated human red cells using human CD34+ hematopoietic progenitors. The four-stage culture system yields 30,000-fold expansion after a 20-day culture. The cells were highly synchronized during the culture process. At the end of the culture, the cells went through enucleation efficiently, and the enucleated cells resemble normal human reticulocytes or red blood cells. We have applied “sortagging” technique, which refers to the process in which sortase catalyzes a transpeptidation reaction between a target protein and the substrates, to engineered red blood cells. Since enucleated red cells do not possess remnants of foreign DNA, we have generated genetically-modified red cells expressing glycophorin A fused with a sortagging motif. Upon sortagging reaction, we are able to equip red cells with payloads of interest. These engineered red blood cells could potentially serve as therapeutic devices, immune modulators, and imaging modalities.

Integrative modeling of multi-platform genomics data

Yen-Tsung Huang
Brown University

Genome-wide association studies (GWAS), expression- and methylation- quantitative trait loci (eQTL and mQTL) studies constitute popular approaches for investigating the association of single nucleotide polymorphisms (SNPs) with disease, mRNA expression and DNA methylation, respectively. Here we propose to integrate epigenetic methylation and gene expression to investigate the SNP effect on disease. We propose a joint model for a biological process from genetics (SNPs) to epigenetics (DNA methylation) and gene expression and then to disease. We characterize all possible causal relations among SNPs, DNA methylation and mRNA expression and study three path-specific effects: 1) from SNPs to disease, 2) from SNPs to mRNA expression to disease, and 3) from SNPs to epigenetic methylation to disease. We develop a statistical procedure to evaluate the overall genetic effect and path-specific effects. We illustrate the utility of the proposed method in numerical simulation studies and an asthma GWAS data. From both simulation and asthma data, the proposed integrative approach outperforms conventional SNP-only analyses.

Mechanisms of binding diversity and partner selection in protein disorder: molecular recognition features mediating protein interaction networks

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Intrinsically disordered proteins are proteins characterized by lack of stable tertiary structures under physiological conditions. Evidence shows that disordered proteins are not only highly involved in protein interactions, but also have the capability to associate with more than one partner. Short disordered protein fragments, called “molecular recognition features” (MoRFs), were hypothesized to facilitate the binding diversity of highly-connected proteins termed “hubs”. MoRFs often couple folding with binding while forming interaction complexes. Two protein disorder mechanisms were proposed to facilitate multiple partner binding and enable hub proteins to bind to multiple partners: 1. One region of disorder could bind to many different partners (one-to-many binding), so the hub protein itself uses disorder for multiple partner binding; and 2. Many different regions of disorder could bind to a single partner (many-to-one binding), so the hub protein is structured but binds to many disordered partners via interaction with disorder. Thousands of MoRF-partner protein complexes were collected from Protein Data Bank in this study, including 321 one-to-many binding examples and 514 many-to-one binding examples. The conformational flexibility of MoRFs was observed at atomic resolution to help the MoRFs to adapt themselves to various binding surfaces of partners or to enable different MoRFs with non-identical sequences to associate with one specific binding pocket. Strikingly, in one-to-many binding, post-translational modification, alternative splicing and partner topology were revealed to play key roles for partner selection of these fuzzy complexes. On the other hand, three distinct binding profiles were identified in the collected many-to-one dataset: similar, intersecting and independent. For the similar binding profile, the distinct MoRFs interact with almost identical binding sites on the same partner. The MoRFs can also interact with a partially the same but partially different binding site, giving the intersecting binding profile. Finally, the MoRFs can interact with completely different binding sites, thus giving the independent binding profile. In conclusion, we suggest that protein disorder with post-translational modifications and alternative splicing are all working together to rewire the protein interaction networks.

ceRNA interactions cooperate with genomic variability to modulate drivers of tumorigenesis

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Recent evidence suggests that RNAs compete for binding and regulation by a finite pool of microRNAs (miRNAs), thus regulating each other through a competitive endogenous RNA (ceRNA) mechanism. Using a kinetic model, we show that pathophysiologically relevant regulation occurs when ceRNA interactions are mediated by multiple miRNAs, while interactions mediated by a single miRNA may have negligible magnitude. Furthermore, our model predicts that ceRNA interactions mediated by multiple miRNAs are largely independent of the individual miRNA's expression and thus highly conserved across distinct cellular states. Indeed, we predict and validate an ultra-conserved network that includes >160,000 ceRNA interactions which are conserved across tumor and non-tumor related cellular contexts. We show that this network integrates genetic and epigenetic alterations of cognate ceRNA regulators to dysregulate established oncogenes and tumor suppressors, accounting for a large fraction of the missing genomic variability in tumors.

Oral Presentation, Modeling and Technology, Abstract ID: O14

Endoscopic optical coherence tomography

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Optical coherence tomography (OCT) is a real-time optical imaging technique that is similar to ultrasonography in principle, but employs lasers instead of sound waves and allows depth-resolved images with near-microscopic resolution. Endoscopic OCT uniquely allows evaluation of broad and subsurface areas and can be used ancillary to standard endoscopy, narrow band imaging, chromoendoscopy, magnification endoscopy, and confocal microendoscopy. This presentation will provide an overview of the clinical utility of endoscopic OCT in the gastrointestinal tract and of recent achievements using state-of-the-art endoscopic 3D-OCT imaging systems.

Mid-infrared chemical sensors on-a-chip using air-clad pedestal silicon waveguides

Pao Tai Lin, Lionel C. Kimerling, and Anu Agarwal
Microphotonics, MIT

Towards a future lab-on-a-chip spectrometer, we demonstrate a compact chip-scale air-clad silicon pedestal waveguide as a Mid-Infrared (Mid-IR) sensor capable of in-situ monitoring of organic solvents. The sensor is a planar crystalline silicon waveguide which is highly transparent between λ=2.5 μm and 6.5 μm, so that its operational spectral range covers most characteristic chemical absorption bands due to bonds such as C-H, N-H, O-H, C-C, N-O, C=O, and C≡N, as opposed to conventional UV, Vis, Near-IR sensors which use weaker overtones of these fundamental bands. To extend light transmission beyond λ=3.7 μm, a spectral region where a typical silicon dioxide under-clad is absorbing, we fabricate a unique air-clad silicon pedestal waveguide. The sensing mechanism of our Mid-IR waveguide sensor is based on evanescent wave absorption by functional groups of the surrounding chemical molecules which selectively absorb specific wavelengths in the Mid-IR, depending on the nature of their chemical bonds. From a measurement of the waveguide mode intensities, we demonstrate in-situ identification of chemical compositions and concentrations of organic solvents. For instance, we show that when testing at λ = 3.55 μm, the Mid-IR sensor can distinguish hexane from the rest of the tested analytes (methanol, toluene, carbon tetrachloride, ethanol and acetone) since hexane has a strong absorption from the aliphatic C-H stretch at λ=3.55 μm. Analogously, applying the same technique at λ=3.3 μm, the Mid-IR sensor is able to determine the concentration of toluene dissolved in carbon tetrachloride, because toluene has a strong absorption at λ=3.3 μm from the aromatic C-H stretch. With our demonstration of an air-clad silicon pedestal waveguide sensor, we move closer towards the ultimate goal of an ultra-compact portable spectrometer-on-a-chip.

Poster List and Abstracts

#	Author and Affiliation	Title
P01	Leo Chan, Nexcelom Bioscience LLC	Accurate measurement of peripheral blood mononuclear cell concentration using image cytometry to eliminate RBC-induced counting error
P02	Yu-Fang Chang, Cornell University	Yeast as a model organism to study lipid metabolism
P03	Chien-Fu Chen, Columbia University	Neuronal connections from piriform cortex to prefrontal cortical areas of mice
P04	Hsiao-Rong Chen, Boston University School of Medicine	Unfolded protein response in the progression of clear cell renal cell carcinoma
P05	Hsing-Yu Chen, University of Rochester Medical Center	Inhibition of redox/fyn/c-cbl pathway function by cdc42 controls tumor initiation capacity and tamoxifen sensitivity in basal-like breast cancer cells
P06	Po-Hao Chen, Robert Wood Johnson Medical School	mTORC2 modulates receptor processing and surface expression during thymocyte development
P07	Sheng-Hong Chen, HMS	Systems approach to decision-making dynamics
P08	Wei-Yu Chen, Brigham and Women's Hospital, Harvard Medical School	Common genetic variation at the IL1RL1 locus regulates IL-33/ST2 signaling
P09	Ying-Ja Chen, MIT	Characterization and modeling of natural and synthetic bacterial terminators
P10	Chieh-Yang Cheng, Cornell University	Crucial role of neuropeptides in promoting prostate carcinogenesis
P11	Yung-Chih Cheng, Boston Children's Hospital	ATF3 induction and axon regeneration in DRG neurons
P12	Wei-Yin Chiang, Brigham & Women's Hospital	Fractal activity regulation: disturbed by lesions of dorsomedial hypothalamic and suprachiasmatic nuclei, and partially rescued by food restriction
P13	Po-Lin Chiu, Harvard Medical School	Structural studies of the interactions of raft lipids with AQP0
P14	Hui-Ting Chou, Harvard Medical School	Molecular organization of the GARP tethering complex
P15	Wen-Chi Chou, Hebrew SeniorLife/Havard Medical School	Copy number variations are associated with bone mineral density: a large-scale genome-wide analysis in the framingham study
P16	Daisy Dai, University of Colorado Anschutz Medical Campus	TAp63α promotes the transition of hair follicle stem cells to interfollicular keratinocytes during wound re-epithelialization
P17	Fu-Kai Hsieh, UMDNJ/Rutgers	Histone chaperone fact action during transcription through chromatin by RNA polymerase II
P18	Kai-Yin Hsu, New England School of Acupuncture	Who uses a teaching acupuncture clinic: demographic and MYMOP symptom results
P19	Fei Huang, Cornell University	ITK tunes the development of antigen specific CD8+ T cell memory during listeria monocytogenes infection
P20	Hsuan-Ting Huang, Boston Children's Hospital	A screen for epigenetic regulators of hematopoiesis reveals chd7 is a cell autonomous regulator of hematopoietic stem cells
P21	John Huang, BWH	Floating cultured melanoma cells are a distinct subpopulation enriched for cancer stem cell biomarkers
P22	Kuo-Chan Hung, New England Biolabs	Developing peptide and antibody-mimetic ligands for the cell surface receptor β2AR and DC-sign
P23	Chih-Fei Kao, UMass Medical School	Decoding the neurogenesis in the drosophila brain

P24	Amy Ku, Baylor College of medicine	Tcf3 promotes cell migration and wound repair through regulation of lipocalin 2
P25	Chih-Jung Kuo, Cornell University	Elastin, a novel extracellular matrix protein adhering to mycobacterial antigen 85 complex
P26	I-Hsin Kuo, University of Rochester Medical Center	Activation of epidermal toll-like receptor 2 enhances tight junction function: implications for atopic dermatitis and skin barrier repair
P27	Tsung-Yi Lin, University of Massachusetts-Amherst	Fluvirucin biosynthesis: an alternative view of polyketide engineering
P28	Tzi-Hsuan Lin, Univ. of Massachusetts-Amherst	Heavy metal, black smokers, high pressure. A resilient archaeon: Roane.
P29	Yi-Dong Lin, Academia Sinica, Taiwan	A nanopatterned cell-seeded cardiac patch prevents electro-uncoupling and improves the therapeutic efficacy of cardiac repair
P30	Chieh-Lun Liu, University of Maryland Center for Environmental Science	eIF2α expression and phosphorylation in response to nutritional status and stressors in zfl cells
P31	Shin-Wu Liu, National Institutes of Health	The decapping activity of vaccinia virus D10 protein enhances viral replication and virulence in mice
P32	Hao-Wei Su, Massachusetts Institute of Technology	Electrical characterization of cells using DEP spring
P33	Pin-Chih Su, Center for Pharmaceutical Biotechnology	Structure activity relationship (SAR), crystallography and computational binding free energy prediction of a new class *F. tularensis* enoyl reductase (FABI) inhibitors
P34	Ming-Shian Tsai, National Taiwan Univeristy	Impaired ability of inhibitory interneurons links with eplieptogenesis using a Dravet mouse model
P35	Tsung-Yuan Tsai, Massachusetts General Hospital	A novel dual fluoroscopy imaging for determination of THA kinematics: *in vitro* and *in vivo* study
P36	Yane-Shih Wang, Yale University	Expanding genetic codes for protein modifications
P37	Teng-Sing (Sean) Wei, Harvard University	3D printing of interdigitated Li-ion microbattery architectures (3D-IMA)
P38	Chia-Ling Wu, Boston University	Genome-wide identification of Bcl-3 and p50 target genes in disuse muscle atrophy
P39	Xiaobin Xu, Boston University	Identification of direct binding proteins of Synphilin-1 using chemical cross-linking and mass spectrometry
P40	Yi-Cheun Yeh, University of Massachusetts Amherst	Dendronized gold nanoparticle for siRNA delivery
P41	C.C. Yuan, Harvard Medical School/Mass General Hospital	H3R2me2s modulates effector protein binding to H3K4me3

Accurate measurement of peripheral blood mononuclear cell concentration using image cytometry to eliminate RBC-induced counting error

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Peripheral blood mononuclear cells (PBMCs) have been widely researched in the fields of immunology, infectious disease, oncology, transplantation, hematological malignancy, and vaccine development. Specifically, in immunology research, PBMCs have been utilized to monitor concentration, viability, proliferation, and cytokine production from immune cells, which are critical for both clinical trials and biomedical research. The viability and concentration of isolated PBMCs are traditionally measured by manual counting with trypan blue using a hemacytometer. One of the common issues of PBMC isolation is red blood cell (RBC) contamination. The RBC contamination can be dependent on the donor sample and/or technical skill level of the operator. RBC contamination in a PBMC sample can introduce error to the measured concentration, which can pass down to future experimental assays performed on these cells. To resolve this issue, RBC lysing protocol can be used to eliminate potential error caused by RBC contamination. In the recent years, a rapid fluorescence-based image cytometry system has been utilized for bright-field and fluorescence imaging analysis of cellular characteristics (Nexcelom Bioscience LLC, Lawrence, MA). The Cellometer image cytometry system has demonstrated the capability of automated concentration and viability detection in disposable counting chambers of unpurified mouse splenocytes and PBMCs stained with acridine orange and propidium iodide under fluorescence detection. In this work, we demonstrate the ability of Cellometer image cytometry system to accurately measure PBMC concentration, despite RBC contamination, by comparison of five different total PBMC counting methods: (1) manual counting of trypan blue-stained PBMCs in hemacytometer, (2) manual counting of PBMCs in bright-field images, (3) manual counting of acetic acid lysing of RBCs with TB-stained PBMCs, (4) automated counting of acetic acid lysing of RBCs with PI-stained PBMCs, and (5) AO/PI dual staining method. The results show comparable total PBMC counting among all five methods, which validate the AO/PI staining method for PBMC measurement in the image cytometry method.

Poster Presentation, Abstract ID P02

Yeast as a model organism to study lipid metabolism

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The baker's yeast, Saccharomyces cerevisiae, is a unicellular eukaryote and its genome shares about 50 % homology with human. It is easy to grow yeast to large quantities for biochemical and genetic analyses, and the entire yeast genome has been sequenced. In my research, I use yeast as a model organism to study lipid metabolism, which helps to define regulatory networks and factors underlying major human diseases such as obesity, diabetes and atherosclerosis. Phosphatidic acid (PA), the simplest form of phospholipids, plays important roles in various cellular processes such as serving as a major precursor for phospholipids and triacylglycerol synthesis, involving in vesicular trafficking, endocytosis and signal transduction. Yet, the map of PA pools in subcellular compartments remains elusive due to the lack of specific PA probes. My goal is to apply a PA-binding protein, Opi1p, which is a repressor in phospholipid biosynthesis in yeast, to delineate a possible PA pool that involves in lipid droplet biogenesis when the cells are starved with inositol, another precursor for phospholipid biosynthesis. This study will help to shed insights on the mechanism of lipid droplet biogenesis and a pool of PA involved in this biogenesis. Supported by NIH grant GM019629.

Neuronal connections from piriform cortex to prefrontal cortical areas of mice

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Piriform cortex, the main olfactory processing area, has been shown to have projections to prefrontal cortex providing olfactory input and receive projections from prefrontal cortex as a potential downstream modulatory pathway. While recent data establish the projections from the prefrontal areas to piriform, the projections from piriform to prefrontal areas remain less understood. To investigate these connections, we utilized retrograde tracing and confocal microscopy. We injected the retrograde tracer, cholera toxin subunit b (CTb), via iontophoretic injection in the prefrontal areas of lateral orbitofrontal cortex (LO) or agranular insular cortex (AI). The C57BL/6 mice were perfused seven days after CTb injection. The CTb iontophoretic injection created very confined injection sites of a diameter of 150 to 200 μm. Our preliminary data reveal that for mice injected in the LO, CTb positive cells were found in endopiriform nucleus and the ventral-medial area of layer II/III of the anterior piriform cortex. Furthermore, in the LO injected mouse, we found labeled cells in agranular insular and mediodorsal nucleus of thalamus. In the AI injected mice, a similar labeling pattern was seen in endopiriform nucleus with sparsely labeled cells in ventral medial anterior piriform cortex. In both experiments, we found no labeled cells in the dorsal anterior piriform cortex or posterior piriform cortex. Together the data suggest that piriform cortex may be composed of finer anatomical subdivisions that project to prefrontal areas. Whether these subdivisions perform specific functional roles remains to be determined.

Unfolded protein response in the progression of clear cell renal cell carcinoma

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von Hippel–Lindau disease is an autosomal dominantly inherited familial syndrome characterized by the development of vascular tumors (hemangioblastomas) in the retina and central nervous system, clear-cell renal cell carcinoma (ccRCC), pheochromocytoma, pancreatic endocrine tumors and occasional epididymal adenoma [1]. The disease is invariably linked to mutations in the tumor suppressor gene *VHL*. Biallelic loss of *VHL* is also correlated with up to 70% of sporadic ccRCC. Restoration of *VHL* function in $VHL^{-/-}$ ccRCC results in significant inhibition of tumor formation in nude mice, demonstrating the tumor suppressor function of *VHL* [2].

Our laboratory recently observed a highly interesting phenotype of inflammation and hyperplasia in mouse knocked out for *Vhl* in specific kidney tubule segments. This represents a unique model that directly links inflammation to tumor formation. *VHL* mutant cells are known to elicit a pseudo-hypoxic response because of increased expression of hypoxia-induced factor α (HIF-α). Since hypoxia is a known inducer of unfolded protein response (UPR)[3], we hypothesize that the cause of the precancerous inflammation is the dysregulated UPR that results from chronic ER stress induction in *VHL* mutants. Upon accumulation of unfolded/misfolded proteins in the endoplasmic reticulum (ER), ER stress is elicited and leads to UPR. Three ER transmembrane protein sensors initiate UPR: inositol requiring enzyme 1 alpha (IRE1α), PKR-like ER kinase (PERK) that activates the ATF4-CHOP apoptotic pathway, and activating transcription factor 6 alpha (ATF6α). IRE-1α can also induce inflammatory response via activation of JNK and NFκB. Thus, UPR is essential for normal cellular and organismal physiology and also contributes to the etiology of many diseases when dysregulated, including cancer.

In this report, we present data linking elevated IRE-1a and ATF4 signaling to the precancerous inflammation and apoptosis phenotype, and show that modulation of the ATF4 level may be an important switch during ccRCC development that enable the cancer cells to escape ER stress-induced cell death.

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Inhibition of redox/Fyn/c-Cbl pathway function by Cdc42 controls tumor initiation capacity and tamoxifen sensitivity in basal-like breast cancer cells

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One of the substantial challenges for cancer research is to identify means by which we are able to overcome resistance of malignant cells to existing therapies and to eliminate the unique small population within bulk tumors, named tumor initiating cells or cancer stem cells which have been proposed to regenerate resistant relapsed tumors. In this study, we offer a novel therapeutic target for both aspects on basal-like (triple-negative) breast cancer cells, one of the most challenging cancers to treat with current regimens.Our present findings emerged from examining the puzzling differences in regulation of activation of the E3 ubiqutin ligase c-Cbl in normal cells and in cancer cells. While low microM tamoxifen exposure is sufficient to induce oxidative changes in cancer cells, we find Fyn (a member of the Src-family of kinases) is activated, but not its downstream counterpart c-Cbl. Basal-like breast cancer cells which express high levels of epidermal growth factor receptor (EGFR) exposed to tamoxifen, without any surprise, fail to show degradation of EGFR due to this inactivation of c-Cbl when such sequential activation of the redox/Fyn/c-Cbl pathway has been demonstrated in normal progenitors to cause reductions in levels of multiple tyrosine kinase receptors, including EGFR.We now have found that tamoxifen-induced activation of c-Cbl in basal-like breast cancer cells is inhibited due to expression of Cdc42. Cdc42 sequestered c-Cbl, prevented its activation and prevented EGFR from being degraded. Restoration of c-Cbl function, by inhibiting activation of Cdc42, reduced EGFR levels in these cells. More critically, restoring c-Cbl function sensitized these cells to tamoxifen both in vitro and in vivo. Analysis of tumor growth and formation in vivo showed that reducing the levels of Cdc42 both reduced the size of tumors, increased sensitivity to tamoxifen and decreased tumor forming capacity.The results provide a novel defense mechanism that basal-like breast cancer cells utilize to prevent EGFR degradation which may have high relevance to treatment of these tumors. Of particular importance is the ability of cdc42 to confer TMX sensitivity on these otherwise resistant tumor cells.

Poster Presentation, Abstract ID P06

mTORC2 modulates receptor processing and surface expression during thymocyte development

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An efficient immune response relies on the presence of T-cells expressing a functional T-cell receptor (TCR). While the mechanisms generating TCR diversity for antigenic recognition are well defined, what controls its surface expression is less known. Here we found that mTOR complex 2 (mTORC2) modulates T-cell ontogeny by controlling the quantity of TCR that reaches the cell surface. Deletion of the mTORC2 component rictor at early stages of T-cell development led to aberrant maturation and increased proteasomal degradation of nascent TCR polypeptides. Consequently, the levels of TCR as well as other receptors, including CD4, CD8 and CD147 were significantly attenuated on the surface of rictor-deficient thymocytes. Since CD147 was also defectively glycosylated and expressed in SIN1-deficient fibroblasts, our findings suggest that mTORC2 is involved in the co/post-translational processing of membrane receptors. Thus, we uncover a novel function for mTORC2 that provides rationale to target this complex in disorders caused by deregulated expression of surface receptors.

Systems approach to decision-making dynamics

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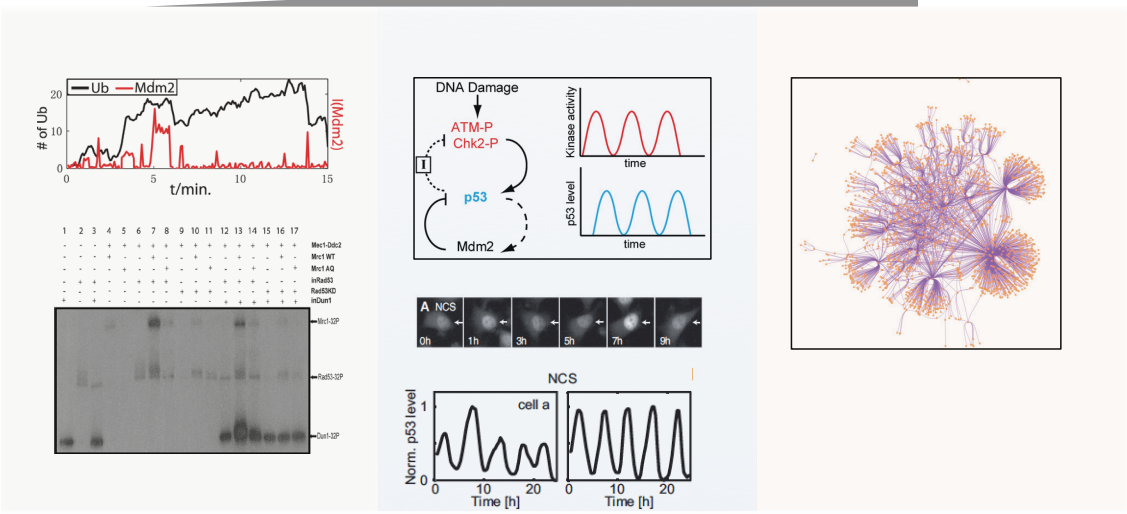
Lives are dynamic systems. A cell in our body contains trillions of molecules. Many of them adjust their interacting partners to form signaling networks for specific functions, sometimes to generate energy for growth; sometimes to stall cell cycle in order to repair damaged parts; sometimes to commit to cell death when catastrophic events happen. All these signaling networks function as dynamic systems for proper integration and interpretation of environmental- and intra-cellular information for decision-making. Therefore, to be able to precisely characterize the behavior of signaling networks over time will shed lights on how cells make decisions. p53-signaling network is identified to be mutated in the majority of the cancer patients, and is important for cell to commit to proliferation, growth arrest, or cell death. Thus, I am taking multi-faceted approach to investigate the p53-signaling network from three levels: molecular mechanism; signal dynamics; and pathway identification. At the molecule level, I am developing a single-molecule ubiquitination assay coupled to cell-free p53-ubiquitination system to characterize the kinetics of p53 ubiquitination. At the systems level, I am using single-cell time-lapse imaging to monitor p53 dynamics after a variety of perturbations including candidate cancer therapeutic drugs. Using these time-series of p53 abundance from imaging analysis, I am constructing a mathematical model for hypothesis generation and system behavior predication. Finally, adopting proteomic approach and synthetic biology approach, I would like to construct a more comprehensive picture of p53- signaling networks.

In Vitro Complexity In Vivo



Molecule Mechanism
Biochemical reconstitute
Single-molecule kinetics

Systems dynamics
Single-cell imagine
Mathematical modeling

Pathway Identification
Proteomics
Synthetic Biology

Common genetic variation at the IL1RL1 locus regulates IL-33/ST2 signaling

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Experimental studies suggest that the ST2-interleukin (IL)-33 pathway plays an important role in immune and inflammatory disease. We investigated the genetic determinants of soluble ST2 (sST2) concentrations in 2,991 Framingham Offspring Cohort participants. Clinical and environmental factors explained only 14% of the variation in sST2, whereas genetic factors accounted for nearly half of the remaining variation (h^2=0.45, P=8.2 x 10^{-16}). In a genome-wide association study (GWAS), multiple SNPs within the *IL1RL1* gene cluster on chromosome 2q12 (the gene encoding ST2) demonstrated significant associations with sST2 (lowest P=7.1 x 10^{-94} for rs950880). Five missense variants (A433T, T549I, Q501K, Q501R and L551S) were associated with higher sST2 levels in the GWAS, and mapped to the intracellular domain of ST2, which is not present in sST2.

To confirm the clinical GWAS result, we generated stable lines expressing the *IL1RL1* variants for the in vitro functional studies. Intracellular domain variants (A433T, T549I, Q501K, Q501R, and L551S), but not the extracellular domain variant (A78E), were associated with increased basal sST2 expression when compared with WT expression (P<0.05). The effect of IL-33-induced sST2 was further enhanced by A433T and Q501R variants, suggesting increased IL-33 responsiveness specifically by the A433T and Q501R variants. Pre-incubation of the cells with anti-IL-1β mAb eliminated the enhanced IL-33-induced sST2 protein in A433T and Q501R variants (P<0.05), indicating that the elevated IL-1β may mediate the enhanced IL-33 responsiveness in A433T and Q501R variants.

The *IL1RL1* intracellular missense variants (A433T, T549I, Q501K, Q501R, and L551S) were associated with higher basal phospho-NF-κB p65 and phospho-c-Jun levels). Consistent with enhanced IL-33 responsiveness in A433T and Q501R cells, levels of IL-33-induced NF-κB and c-Jun phosphorylation were further enhanced in these two variants. In contrast to the levels of phosphorylated NF-κB and c-Jun, A433T and Q501R variants showed lower basal phospho-AKT levels.

Binding of Mal to ST2L was increased by the intracellular variants. Only A433T and Q501R interact with PI3K-p85 subunit, indicating that these two *IL1RL1* variants may regulate the PI3K-AKT signaling pathway through the interaction of the ST2L intracellular domain with the PI3K-p85 subunit. Knockdown of Mal and MYD88 by siRNA completely inhibited sST2 induction by intracellular *IL1RL1* variants, indicating that Mal and MYD88 are necessary for ST2L-mediated sST2 induction. Knockdown of PI3K-p85 had no effect on IL-33-induced sST2, whereas knockdown of PI3K-p85 blocked A433T and Q501R-enhanced IL-33 responsiveness. These results suggested that the increased binding of Mal to ST2L intracellular domain mediated the intracellular *IL1RL1* variants induced sST2 expression. Furthermore, the recruitment of PI3K-p85 to *IL1RL1* variants A433T and Q501R mediated the enhanced IL-33 responsiveness.

In summary, our experiments demonstrate that IL-33 induces sST2 expression through NF-κB and AP-1, and that the *IL1RL1* intracellular domain variants regulate IL-33-induced sST2 expression via two mechanisms: 1) Enhanced induction of IL-33 via enhanced NF-κB and AP-1 signaling; 2) Enhanced IL-33 responsiveness via increasing ST2L expression (Figure 1). Thus, genetic variants that change intracellular signaling of the transmembrane ST2 receptor can induce human sST2, revealing a new pathway in immune and inflammatory regulation.

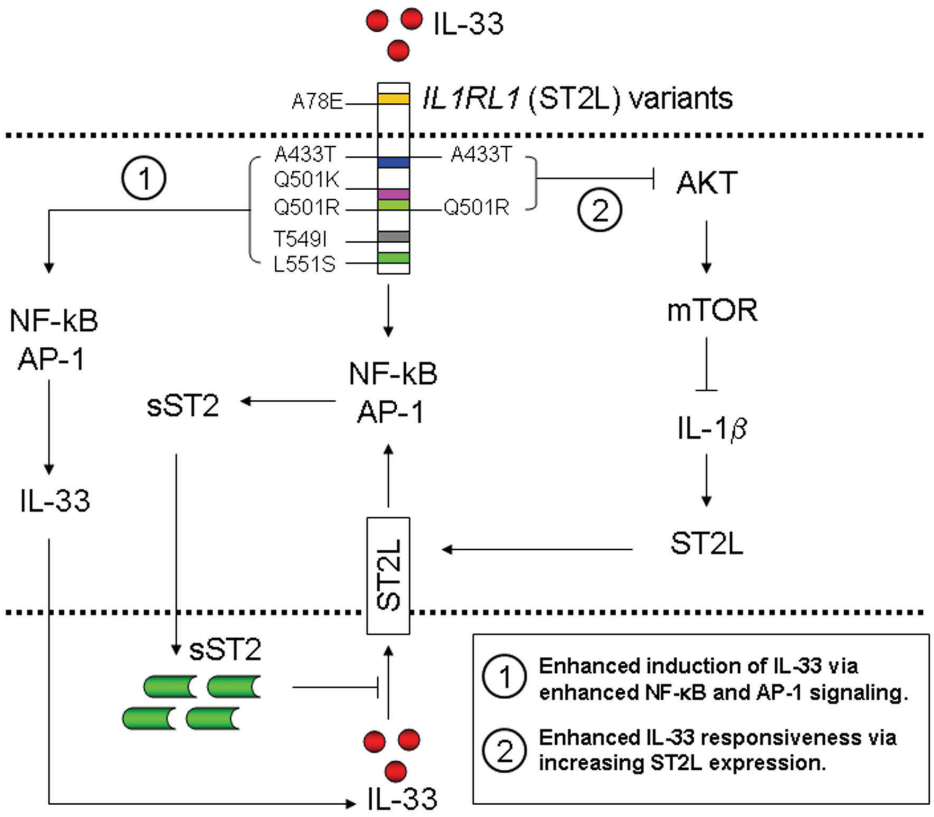

Figure 1. Schematic showing of the regulation of sST2 expression by *IL1RL1* variants through via intracellular signaling.

Poster Presentation, Abstract ID P09

Characterization and modeling of natural and synthetic bacterial terminators

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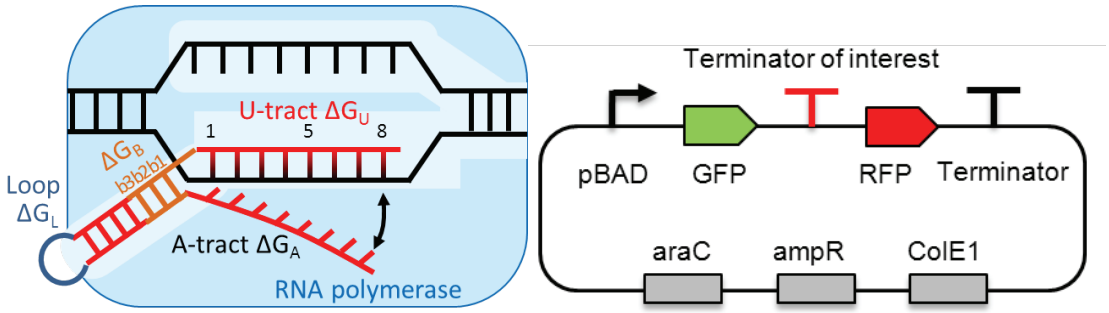
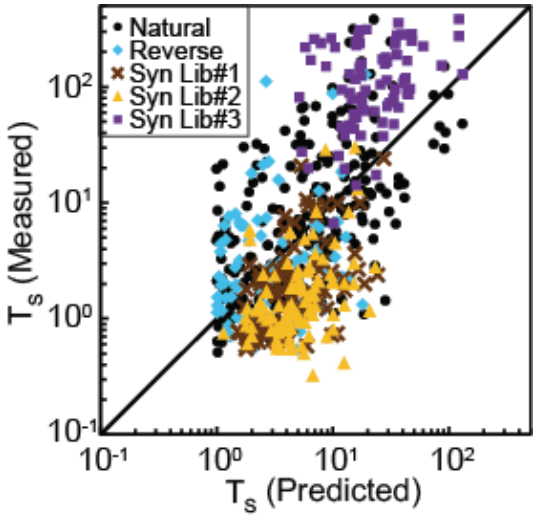
Large genetic engineering projects require more cistrons and consequently more strong and reliable transcriptional terminators. We have measured the strengths of a library of terminators, including 227 that are annotated in Escherichia coli—90 of which we also tested in the reverse orientation—and 265 synthetic terminators. Within this library we found 39 strong terminators, yielding >50-fold reduction in downstream expression, that have sufficient sequence diversity to reduce homologous recombination when used together in a design. We used these data to determine how the terminator sequence contributes to its strength. The dominant parameters were incorporated into a biophysical model that considers the role of the hairpin in the displacement of the U-tract from the DNDNA. The availability of many terminators of varying strength, as well as an understanding of the sequence dependence of their properties, will extend their usability in the forward design of synthetic cistrons.





Crucial role of neuropeptides in promoting prostate carcinogenesis

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Increased amounts of neuropeptides in prostate neoplasms are positively correlated with prostate cancer progression, castrate-resistance, and poor prognosis. However, specific mechanisms of neuropeptides' effects on prostate cancer pathogenesis are not well understood. To address this question we have studied prostates of mice lacking neutral endopeptidase ($NEP^{-/-}$), Pten ($PtenPE^{-/-}$) or both genes. By 18 months of age $NEP^{-/-}$ mice do not develop any detectable prostate epithelium lesions, while $PtenPE^{-/-}$mice develop prostatic intraepithelial neoplasms (PIN) in the distal region of prostatic ducts. Notably $PtenPE^{-/-}NEP^{-/-}$ compound mice develop prostate neoplasms not only in the distal region of prostatic ducts as $PtenPE^{-/-}$ mice, but also in proximal region of prostatic ducts, the known niche for prostatic stem cells. Such lesions had higher cell proliferation rate and decreased senescence, as compared to PINs of $PtenPE^{-/-}$ mice. Since one of the main NEP substrates is bombesin, we have tested its effects on the prostate stem cell pool. Addition of bombesin increased sphere-forming capacity of mouse prostate epithelium cells and human prostate cancer cells, in parallel with increased fraction of ALDH positive cancer propagating cells. Bombesin also increased motility and invasion of human prostate cancer cells. All these effects have been negated by addition of bombesin receptor antagonist, [Tyr4, D-Phe12]-Bombesin. Taken together, our results provide the first in vivo evidence of the cooperative effect between NEP and Pten deficiency on prostate carcinogenesis and show that elevated amount of neuropeptides may play an important role in promoting prostate carcinogenesis by increasing cell proliferation, rescuing cellular senescence, expansion of cancer propagating cells, and stimulating cell motility and invasion. Addition of bombesin receptor antagonist may enhance current therapeutic approaches.

ATF3 induction and axon regeneration in DRG neurons

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Activating transcriptional factor 3 (ATF3) is highly up-regulated in all injured adult primary sensory neurons. Over-expression of ATF3 in adult cultured DRG neurons enhances neurite outgrowth and increases neuronal survival in neonatal cultured neurons after NGF withdrawal. Furthermore, forced ATF3 expression in transgenic mice enhances peripheral nerve regeneration by increasing the intrinsic growth state of injured sensory neurons. In order to find compounds that can enhance ATF3 expression and thereby promote sensory neuron regeneration after nerve injury, we generated hATF3-pro/GLuc stable clones in B104 neuroblastoma cells and mATF3-pro/RmGFP reporter mice for high throughput drug screening. We applied compounds reported in the literature to induce ATF3 expression to the stable clones, measuring Gaussia luciferase intensity in a 384 well format using Hamamatsu FFS7000 dynamic plate reader and found several compounds that increase ATF3 reporter activity. . To confirm if these induce ATF3 in primary neuron cells, we applied the compounds to pre-conditiontioned and naive mATF3-pro/RmGFP DRG cells, then measured GFP intensity. After 24 hours, we found the GFP intensity was indeed enhanced by those compounds that activated the hATF3-pro/GLuc stable clone. To examine if the compounds has the potential to promote regeneration in neuron cells, wild-type DRG cells were stimulated with those compounds by different doses for 24 hours. After fixing, immunostaining with GFP-βIII tubulin, calculation of neurite length by ImagExpressmicro high content screening system, we found these compounds induced a 25% increase in neurite length in wild-type DRG neurons. Taken together, we developed a screening strategy suitable for identifying compounds that have the ability to induce ATF3 and promote neurite ourgrowth in peripheral DRG neuron cells. We will now survey chemical libraries for ATF3-inducing compounds using the B104 hATF3-pro/GLuc stable clone as primary screen, and then identify and confirm these using mATF3-pro/RmGFP reporter DRG cells as a secondary screen followed by a tertiary screen in an injured peripheral nerve mouse model.

Fractal activity regulation: disturbed by lesions of dorsomedial hypothalamic and suprachiasmatic nuclei, and partially rescued by food restriction

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Introduction: Motor activity exhibits robust fractal fluctuations with similar temporal structure and statistical properties at different time scales. This multiscale regulation persists during light-dark and constant dark conditions but is disrupted in animals after the lesion of suprachiasmatic nucleus (SCN). Here we tested whether the SCN's impact on fractal activity regulation occurs via dorsomedial hypothalamic (DMH) nucleus, an important neural node influencing motor activity and likely being involved in food anticipation. Furthermore, we explore how 24-hour rhythm of food availability affects fractal activity regulation.

Methods: We studied locomotor activity of 6 Wistar rats that underwent a 29-day food restriction (FR) protocol twice, one after DMH lesion (DMHx) and the other one after DMH and SCN lesion (DMHSCNx). The FR protocol contains: a 13-day baseline without FR; and a 16-day FR period (food only available at Zeitgeber time 6-7 hour). Detrended fluctuation analysis (DFA) was used to quantify fractal correlations in activity fluctuations across time scales from 1-20 hours.

Results: Baseline activity fluctuations possessed different fractal correlations in two time scale regions (Region I: < ~4 hours; and Region II: >4 hours), indicating altered fractal regulation. Compared to Region I, activity fluctuations in Region II became more random as characterized by the decrease in a DFA-derived exponent that quantifies the correlation property in activity fluctuations, i.e., α_1 (Region I) > α_2 (Region II). The difference was much smaller after DMHx (mean±SE: 0.25±0.07; $p=0.011$) than the difference after DMHSCNx (0.53±0.04; $p<0.0001$). With FR, the difference between α_1 and α_2 became not significant for DMHx (0.12±0.09; $p>0.26$) and smaller but still significant for DMHSCNx (0.22±0.05; $p=0.007$).

Conclusion: Both DMH and SCN impart fractal activity regulation with much stronger influence from the SCN. 24-hour rhythm of food availability can compensate, at least partially, for the multiscale influences of the DMH and SCN lesion on activity regulation.

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Structural studies of the interactions of raft lipids with AQP0

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Lipid raft, mostly consisted of sphingomyelin and cholesterol, is a specialized lipid microdomain in liquid-order phase. It is proposed to influence membrane protein sorting and functioning. Aquaporin-0 (AQP0) natively forms two-dimensional (2D) arrays in lens membranes, which are mostly composed of raft lipids. However, based upon the prior knowledge, it is still unclear how lens lipids help AQP0 tetramerization and arrange AQP0 into membrane arrays. Here we determined the AQP0 structures associated with raft lipids, which could improve our understanding of how this lipid-protein interaction occurs in native environments. At different sphingomyelin-to-cholesterol ratios, the two different membrane crystals were reconstituted, and the electron diffraction patterns of untilted and tilted specimens were collected by cryo-electron microscopy. The final models were calculated and refined at about 2.4 Å using conventional crystallographic method with electron scattering constants. Our preliminary models showed that compared to our previous structures of AQP0 in DMPC and E. coli lipid polar extract, the interaction surface between AQP0 and raft lipids is similar. At least one specific cholesterol-binding site could be identified by comparing the models of different cholesterol ratios. Further structural analysis is needed to characterize as if the specific binding sites of raft lipids contribute the stabilization of the membrane arrays.

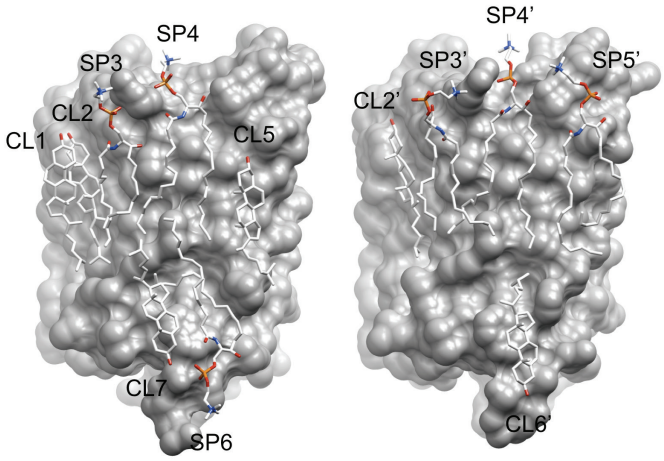

Figure 1. The atomic coordinates of AQP0 with sphingomyelin and cholesterol at the ratios of 2:1 and 1:2, respectively.

Molecular organization of the GARP tethering complex

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The steps in intracellular trafficking include vesicle budding, movement, tethering and fusion with the target membrane. The first physical interaction between a transport vesicle and its target membrane is mediated by tethering factors, which are recruited to the membrane by Rab GTPases and facilitate the assembly of SNARE complexes. These three components determine the specificity and efficiency of vesicle fusion. Here, we focus on GARP (Golgi- associated retrograde protein), the multisubunit tethering complexes (MTCs) on the trans-Golgi membrane tethering the vesicles derived from endosomes. GARP contains 4 subunits (Vps51, Vps52, Vps53 and Vps54) and its association with the Golgi apparatus is mediated by the Rab GTPase Ypt6. GARP is a member of the CATCHR subfamily of MTCs, which also includes the Dsl1, COG and Exocyst complexes. GARP mutants/deletions are lethal in mice and plants. In mice, the point mutant L967Q in Vps54 can cause degeneration of motor neurons, resulting in progressive muscle weakness, atrophy and contractures similar to the human disease amyotrophic lateral sclerosis (also known as Lou Gehrig's disease). Crystal structures show that the C-terminal domains of Vps53 (residue 554-822) and Vps54 (residue 836-974) form elongated alpha-helical bundles, similar to those seen in subunits of Dsl1, COG and exocyst. We are using single-particle electron microscopy to study the structure and molecular organization of GARP in an effort to understand how each subunit contributes to tethering, GTPase binding and SNARE complex assembly. The results show GARP and the Cog1-4 core complex share similar overall structure and subunit organization although the sequence similarity between their subunits is very weak. We are now localizing the binding sites for the two GTPases, Ypt6 and Arl1, on GARP to understand how GARP links Rab GTPases to SNARE complexes.

Copy number variations are associated with bone mineral density: a large-scale genome-wide analysis in the Framingham Study

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Bone mineral density (BMD) is a complex phenotype with high heritability. Our previous genome-wide SNP association study identified more than 56 BMD loci in Caucasian populations, explaining < 6% of BMD variation. Copy number variation (CNV), a type of genomic structural variation, accounts for > 20% variation of the human genomic structure between individuals. CNVs may explain the missing heritability of BMD. Thus, we conducted a genome-wide CNV association analysis with BMD in Framingham Study participants.This study included 7,451 adult Caucasians (4,126 men and 3,325 women) with mean age of 55 years. BMD at lumbar spine (LS) and femur neck (FN) was measured by dual energy X-ray absorptiometry. CNVs were estimated using Affymetrix 500K genotyping array and PennCNV package. A CNV was defined as a DNA segment longer than 1 kbp and composed of at least three consecutive genotyping probes. Under an additive genetic model, we employed a linear mixed effects model to account for family relatedness, and also adjusted for age, sex, estrogen usage, menopause status, cohorts within the Framingham Study and principal components for population stratification. To correct for multiple-testing, a genome-wide significant cutoff ($p < 4 \times 10^{-6}$) was defined by a false-discovery rate as less than one false-positive result among the genome-wide significant findings. Up to 6,398 individuals had valid CNV calls and information on covariates.Two CNVs (at chrom 2q14.2 and 6q25.3) and four (at chrom 5q23.1, 15q22.31, 17p13.1 and 17q21.2) were significantly associated with LS BMD and FN BMD, respectively. The length of the CNVs ranged from 133 kbp to 1,025 kbp. The most significantly associated CNV with $p = 1.9 \times 10^{-20}$ was located at chromosome 15q22.31 (SMAD6). The Smad6 protein inhibits signaling of bone morphogenetic proteins. Among 6,398 individuals included in the association analysis of the CNV, 5 had this CNV. Individuals with deleted CNVs had lower FN BMD. In addition, we identified three genome-wide suggestive CNVs associated with BMD at $p < 2.7 \times 10^{-6}$. In summary, we identified six genome-wide significant CNVs and three genome-wide suggestive CNVs associated with FN BMD or LS BMD in the Framingham Study. To replicate the CNV-BMD associations, we are performing analyses in independent samples. The newly identified CNVs in this study may provide additional biological information regarding the genetic determinants of BMD and may explain some of the missing heritability.

Poster Presentation, Abstract ID P16

TAp63α promotes the transition of hair follicle stem cells to interfollicular keratinocytes during wound re-epithelialization

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p63 is an essential transcription factor expressed as isoforms that either contain (TA) or lack (ΔN) a transactivation domain. The ΔNp63 isoforms are constitutively expressed in the basal layer of the murine epidermis, and have been shown to orchestrate the stratification and differentiation of simple epithelia to stratified epithelia. This contrasts with the TAp63 isoforms, which are not required for epidermal development, but are instead induced upon wounding. Consistent with its expression during wounding, TAp63α-null mice exhibit a marked delay in epidermal wound healing. In order to understand the role of TAp63α during the wound response, we have generated an inducible mouse model that expresses the TAp63α isoform in the epidermis when crossed to a K5 activator and treated with doxycycline (dox). Unexpectedly, continual treatment with dox from birth resulted in the failure of TAp63α-expressing mice to develop a coat of hair. Histological analyses of TAp63α-expressing skin revealed a progressive transformation of hair follicles into cyst-like structures that appeared to contain stratified epidermis. In order to confirm that ectopic differentiation was occurring in the TAp63α-expressing mice, we examined the differentiation markers keratin 1, involucrin, and filaggrin via IF and found that each of these markers were ectopically expressed in the follicular cysts. In order to determine if this transition occurred in the hair follicle stem cells (HFSCs), we performed immunofluoresence and real-time qPCR on HFSC markers keratin 15, lgr5 and CD34. Consistent with the absence of hair follicles, we saw a significant reduction in each of these HFSC markers in TAp63α-expressing mice, suggesting that TAp63α promotes the conversion of HFSCs to interfollicular keratinocytes. Previous studies have shown that HFSCs can convert to interfollicular keratinocytes that migrate and contribute to a wound *in vivo*, providing an additional reservoir of cells to help in re-epithelialization. Combining what is known about the role of HFSCs during wound healing with the effect of TAp63α on HFSCs, we preemptively activated TAp63α before wounding to determine if we can accelerate the wound healing process. Collectively, we found that priming the epithelia with TAp63α before wounding consistently accelerated the wound healing process by 3 days as evidenced by migration, re-epithelialization, and keratin 6 expression. Thus, TAp63α activation provides a mechanism by which hair follicle stem cells convert to interfollicular keratinocytes to assist in the wound healing process.

Histone chaperone FACT action during transcription through chromatin by RNA polymerase II

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FACT (facilitates chromatin transcription) is a histone chaperone that promotes chromatin recovery during transcription, with additional roles in cell differentiation. Although several models of the action of FACT during transcription have been proposed, they remain to be experimentally evaluated. Here we show that human FACT (hFACT) facilitates transcription through chromatin and promotes nucleosome recovery *in vitro*. FACT action depends on the presence of histone H2A/H2B dimers in the nucleosome. Kinetic analysis suggests that hFACT decreases the lifetime of nonproductive Pol II–nucleosome complexes and facilitates the formation of productive complexes containing nucleosomal DNA partially uncoiled from the octamer. Taken together, our data suggest that hFACT interacts with DNA-binding surfaces of H2A/H2B dimers, facilitating uncoiling of DNA from the histone octamer. Thus, hFACT–H2A/H2B interactions play a key role in overcoming the nucleosomal barrier by Pol II and promoting nucleosome survival during transcription.

Poster Presentation, Abstract ID P18

Who uses a teaching acupuncture clinic: demographic and MYMOP symptom results

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While Acupuncture is becoming become more widely accepted by the American public as well as federal policy makers, relatively little data has been obtained to date of acupuncture users' demographic characteristics and reasons for using acupuncture teaching clinics in the U.S. It is important to understand patients' sociodemographics as well as their symptoms in order to better serve acupuncture consumers and provide information to health care providers and investigators.

DESIGN: This retrospective chart review reports on the 678 patients using one of the student clinics at the New England School of Acupuncture (NESA) in Massachusetts, USA in 2011. Annually, NESA interns administer over 27,000 treatments for a variety of conditions across all of its clinics. The NESA teaching clinics are learning environments where student interns treat patients under the direct supervision of experienced and licensed acupuncturists.

METHODS: A retrospective chart review was used to look at all patients who visited the NESA main clinic site in 2011. This report focuses on patient demographics and "Measure Your Medical Outcome Profile" (MYMOP) results.

RESULTS: Patients were mostly female (69%) and White (82%) with 87% having at least a college education. Common activities that subjects sought help for are improvements in their ability to exercise, and work.Pain, fatigue, and anxiety were the most common symptoms for which treatment was sought.

ITK tunes the development of antigen specific CD8+ T cell memory during Listeria monocytogenes infection

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ITK is important for T cell signaling and development. Here we have examined whether ITK plays a role in development of antigen-specific CD8+ T cell memory after primary response to Listeria monocytogenes (LM)-OVA infection. We transferred naïve OTI Rag1-/- T cells or OTI Itk-/-/Rag1-/- T cells into WT mice and found no difference in their memory T cell differentiation in response to low dose LM infection (5X104). In contrast, during higher dose LM infection (5X105), WT OTI T cells fail to differentiate into memory cells while formation of memory Itk-/- OTI T cells remain robust. The resultant Itk-/- T cells produced significantly less IFN-γ and TNF-α in both doses of LM infection during effector and memory T cell formation phases. Expression of IL-7Rα (CD127) was significantly higher on Itk-/- OTI T cells compared to WT counterparts in higher dose LM infection, suggesting that survival signals via IL-7Rα is deficient in WT T cells. The expression of eomesodermin, a positive regulator of memory T cell differentiation, is also significantly higher in Itk-/- OTI T cells in high dose LM infection. Further, by co-transfer of both WT and Itk-/- OTI T cells to the same hosts, we found the kinetics of Itk-/- OTI T cells became the same as WT OTI T cells in high dose LM infection, indicating WT OTI can compromise the survival of Itk-/- OTI T cells by influencing the microenvironment of T cell differentiation. Taken together, our data suggest that signals of ITK limit the development of memory cells in response to higher dose LM infection by regulating the expression of IL-7Rα and eomesodermin. The signals of ITK may also contribute to a strong inflammatory microenvironment that impairs the development of memory T cells through robust cytokine secretion. Our findings suggest that ITK may be a target for modulating the extent of T cell responses during vaccination to maximize the quantity and the quality of memory T cells.

Poster Presentation, Abstract ID P20

A screen for epigenetic regulators of hematopoiesis reveals chd7 is a cell autonomous regulator of hematopoietic stem cells

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Hematopoietic stem cells (HSC) are specified during embryogenesis, and the induction process involves not only transcription factors but also epigenetic factors that modulate chromatin to regulate the hematopoietic transcriptional programs. To identify the epigenetic regulators, we performed a reverse genetic screen to identify all the chromatin factors that are required for HSC induction in zebrafish. The zebrafish homologs of 425 human chromatin factors were identified by reciprocal BLAST and knocked down by injecting morpholinos designed against each homolog into the single cell embryo. Morphants were then analyzed for changes in blood formation by in situ hybridization for β-globin e3 expression in primitive erythrocytes at 17 hours post-fertilization (hpf) and for c-myb and runx1 in definitive stem cells at 36 hpf. chd7, a member of the chromodomain helicase DNA-binding gene family, was identified from the screen, increasing c-myb+ and runx1+ cells in the AGM region when knocked down. Additional lineage markers such as pu.1, gata1, and ikaros were also upregulated. Transplants of chd7 deficient Tg(c-myb:GFP) blastomeres into Tg(lmo2:DsRed) blastulas resulted in higher chimerism of c-myb+ blood cells compared to control transplants, demonstrating a cell autonomous effect. Our studies indicate a new role for chd7 in hematopoiesis in which it functions to repress HSC formation during embryogenesis.

Poster Presentation, Abstract ID P21

Floating cultured melanoma cells are a distinct subpopulation enriched for cancer stem cell biomarkers

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Among the heterogeneous cancer cell subpopulations, slowcycling and drug- resistant cancer stem cells are characterized by self-renewal, tumorigenic growth *in vivo*, and spherogenic growth *in vitro*. Melanoma cells in culture grow either as adherent, or as non-adherent, 'floating' cells. We have determined that the subpopulation of viable floating cells express a slow-cycling phenotype, and thus reasoned that cancer stem cells may be enriched in this fraction. Melanoma floating cells were found to be more capable than adherent cells of spherogenic growth *in vitro*($p<0.05$). Moreover, they were selectively resistant to the cytotoxic effects of dacarbazine treatment ($p<0.01$). Additionally, floating cells were capable of generating both cells with adherent and floating phenotypes, in keeping with stem cell capacity both for self-renewal and for giving rise to non-stem cell progeny. To characterize further the differences between floating and adherent cells, mRNA expression of cancer stem cell markers was analyzed. Floating cells exhibited distinctive profiles for ABCB5, SOX10, PAX3, FOXD3, and MITF. However, SOX2, CD20, and CD133 were not differentially expressed. Accordingly, floating melanoma cells express a distinctive phenotype in which certain properties shared by cancer stem cells preferentially reside, and thus may represent a novel subpopulation for study of melanoma stem cell biology. Funded by NIH NCI R01CA138231.

Poster Presentation, Abstract ID P22

Developing peptide and antibody-mimetic ligands for the cell surface receptor β_2AR and DC-SIGN

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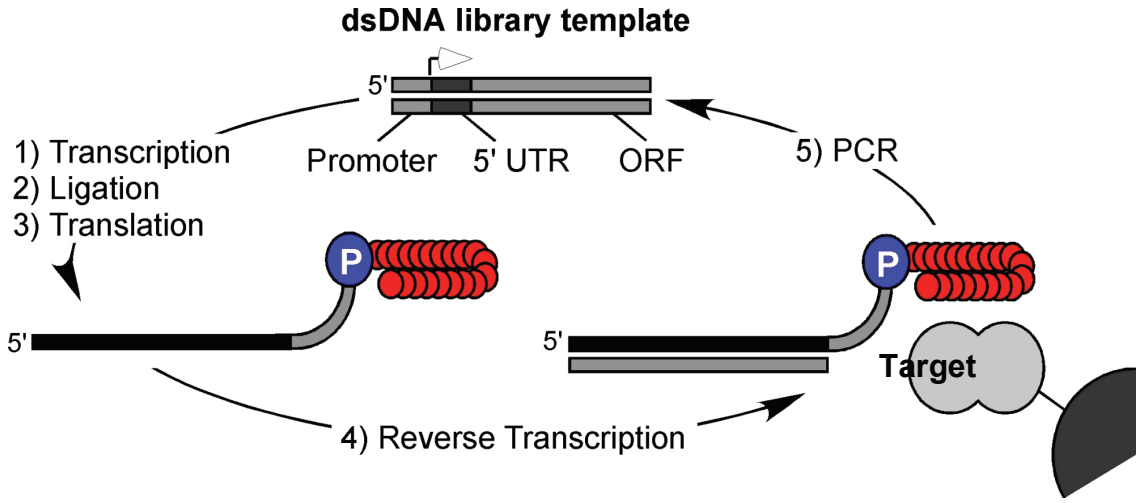
mRNA display is an *in vitro* selection technique that can evolve novel ligands to modulating protein-protein interactions and regulate crucial biological functions. Previous efforts have focused on soluble protein targets. However, here we use mRNA display to target cell surface receptors that represent 60% of drug targets but remain the most challenging targets. Two cell surface receptors, beta-2 adrenergic receptor (β_2AR) and Dendritic Cell-Specific ICAM-3-Grabbing Non-integrin (DC-SIGN), were chosen as our targets in order to develop novel ligands for structural studies, drug development, or vaccine design. mRNA display using a doped Gαs C-terminal peptide library was capable of targeting the active state of β_2AR, resulting in active state-specific peptide ligands with function similar to Gs protein. Selections against both mouse and human DC-SIGN by mRNA display using an antibody-mimetic library resulted in ligands with dual specificity to both mouse and human DC-SIGN. One selected DC-SIGN specific ligand could induce antigen-specific immune responses in human dendritic cells and has the potential for developing DC-based cancer vaccines. In these proof of concept studies, we demonstrated a general approach for the development of novel functional ligands capable of targeting cell surface receptor.



Decoding the neurogenesis in the drosophila brain

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Numerous neuron types are derived from a limited number of neural stem cells along the development of central nervous system. Earlier studies have observed an intriguing phenotype that distinct neuron types are sequentially generated from a given progenitor cell. Importantly, the temporally stereotypic behavior of neural stem cells can be found in various model systems, including vertebrate and insect nervous systems. To better understand the temporal behaviors of neural stem cells and elucidate their underlying mechanisms, it demands the technical capacity that can faithfully identify and label individual neuron types, retrieve the birth sequence of distinct neuron types, and perform mutant analyses to uncover the involved molecular machinery. The genetic mosaic labeling techniques we have designed in the Drosophila system give us the very opportunity to conduct such kind of comprehensive neuron typing analyses efficiently, as well as to precisely determine the alterations of neural stem cell behavior elicited by mutant genes. By decoding the temporal compositions of neuron types produced from individual neural stem cells, we will ultimately resolve a complete cellular and developmental blueprint of the Drosophila brain. Moreover, learning the molecular mechanisms that govern the temporal changes of neural stem cell behavior will also help us better understand how neuronal diversification is achieved.

Poster Presentation, Abstract ID P24

Tcf3 promotes cell migration and wound repair through regulation of Lipocalin 2

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Cell migration is an integral part of re-epithelialization during the skin wound healing, a complex process involving molecular controls that are still largely unknown. Here we identify a novel role for Tcf3, an essential transcription factor regulating embryonic and adult skin stem cell functions, as a key downstream effector of epidermal wound repair. We show that Tcf3 is upregulated in skin wounds and demonstrate that Tcf3 overexpression accelerates keratinocyte migration and skin wound healing. Promoter analysis and binding studies reveal Stat3 as upstream regulator of Tcf3, which in turn rescues defective cell migration in Stat3-null cells. Mechanistically, we show that pro-migration effects are non-cell autonomous and independent of Tcf3/β-catenin interactions of Wnt signaling. Finally, we identify Lipocalin-2 downstream of Tcf3 as the key secreted factor that promotes cell migration *in vitro* and wound healing *in vivo*. Our findings provide new insights into the molecular controls of wound-associated cell migration and identify potential therapeutic targets for the treatment of defective wound repair.

Elastin, a novel extracellular matrix protein adhering to mycobacterial antigen 85 complex

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The antigen 85 complex (Ag85) consists of three predominantly secreted proteins (Ag85A, Ag85B, and Ag85C), which play a key role in the mycobacterial pathogenesis and also possess enzymatic mycolyltransferase activity involved in cell wall synthesis. Ag85 is not only considered to be a virulence factor because its expression is essential for intracellular survival within macrophages, but also because it contributes to adherence, invasion, and dissemination of Mycobacteria in host cells. In the present study, we report that the extracellular matrix (ECM) components, elastin and its precursor (tropoelastin) derived from human aorta, lung, and skin, serve as binding partners of Ag85 from mycobacterium tuberculosis (MTB). The binding affinity of MTB Ag85 to human tropoelastin (HTE) was characterized (KD = 0.13±0.006 μM) and a novel Ag85-binding motif, AAAKAA(K/Q)(Y/F), on multiple tropoelastin modules was identified. In addition, the negatively charged E258 of Ag85 was demonstrated to participate in an electrostatic interaction with HTE. Moreover, binding of Ag85 on elastin siRNA transfected Caco-2 cells was significantly reduced (34.3%), implying that elastin acts as an important ligand contributing to mycobacterial invasion.

Activation of epidermal toll-like receptor 2 enhances tight junction function: implications for atopic dermatitis and skin barrier repair

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Atopic dermatitis (AD) is a Th2-skewed, allergen-driven skin disease characterized by epidermal tight junction (TJ) defects and a propensity for Staphylococcus aureus (S. aureus) skin infections. One widely held hypothesis is that the leaky epithelial barrier promotes immunologic responsiveness to allergens through the skin. Toll-like receptor (TLR) 2, a key innate receptor responsive to S. aureus, was originally recognized for its antimicrobial actions, but recently it has been shown to regulate intestinal epithelial barrier. We hypothesized that an effective cutaneous innate immune response might also include skin barrier repair. Furthermore, this barrier repair response may be impaired in AD patients. To determine the importance of TLR2 in epidermal barrier function, we used primary human keratinocytes (PHK), discarded human skins and Tlr2-/- mice. The TLR2 agonist increased TJ protein expression and function in PHK and enhanced TJ barrier repair in a murine wound model that mimics the itch-scratch cycle observed in AD patients. Since AD is a Th2-polarized inflammatory disorder, we hypothesized that Th2 cytokines might impair this TLR2-mediated barrier repair function. Th2 cytokines decreased TLR2 protein expression and attenuated TLR2's barrier repair function in PHK and human epidermis. STAT6VT mice with a hyper-Th2 immune profile had reduced epidermal TLR2 protein expression and impaired TJ barrier recovery in response to TLR2 agonist. Bringing this observation back to human AD, we observed that epidermal TLR2 protein immunoreactivity was significantly reduced in nonlesional and lesional AD skin as compared to nonatopic controls (NA). The intensity of the TLR2 staining inversely correlated with skin barrier integrity and two Th2 biomarkers (serum total IgE levels and circulating eosinophil counts).In summary, TLR2 activation enhances TJ barrier in murine and human epidermis and is an important part of an epidermal wound repair response. Th2 cytokines commonly found in AD skin reduce epidermal TLR2 expression and barrier repair function. Our findings strongly suggest that antagonizing Th2 cytokines in AD patients may restore TLR2-mediated innate immune responses, which will help repair epidermal barrier defects and possibly also eliminate unwanted cutaneous pathogens.

Fluvirucin biosynthesis: an alternative view of polyketide engineering

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Fluvirucin B1, an antiviral antibiotic produced by Actinomodura vulgaris, contains polyketide-derived, 14-membered macrolactam core. We have identified the polyketide synthase gene cluster responsible for its production from A. vulgaris genome analysis. The synthase consists of 5 modules, 4 of which contain the full set of tailoring domains (ketoreductase, dehydratase, and enoyl reductase) similar to mammalian fatty acid synthase. The remaining module harbors a single ketoreductase domain and is responsible for generation of the lone hydroxyl group on the macrolactam core. To facilitate future engineering efforts, we are now attempting to reconstitute the biosynthetic pathway in E. coli. Ultimately, we plan to exploit the unique fatty acid synthase-like module composition for generating chemically diverse macrolactam structures without the need for introducing heterologous enzymes or modules.

Heavy metal, black smokers, high pressure. A resilient archaeon: Roane.

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Introduction: Dissimilatory iron reduction is the microbial respiration of Fe^{3+} to Fe^{2+} and is an important biogeochemical process in the anoxic subsurface [1], [2]. It may have been an important process on the early Earth, and could be a metabolism for life beyond Earth. Hyperthermophiles are organisms that grow optimally above 80°C, and represent life forms found early in life history. Our study sought to determine the biogenic minerals that form due to hyperthermophile-mineral interactions and the potential this has to be a biosignature. Iron reduction in deep-sea hydrothermal vents has been largely overlooked due to the reduced nature of most minerals present and the insolubility of Fe^{3+} in circumneutral fluids. However, iron oxide minerals in the form of ferrihydrite [$Fe(OH)_3$] are common in mildly reducing hydrothermal systems due to seawater oxidation of iron sulfide minerals and could serve as an oxidizing agent for microbial respiration [3]. Indeed, hyperthermophilic iron reducers were ubiquitous in hydrothermal sulfide deposits collected from the Endeavour Segment hydrothermal vents [4].
Here, we examine the mineralogy of hyperthermophile reduction of ferrihydrite by two novel archaea, *Hyperthermus* sp. Ro04 and *Pyrodictium* sp. Su06 isolated from actively venting hydrothermal sulfide chimneys from the Endeavour Segment.

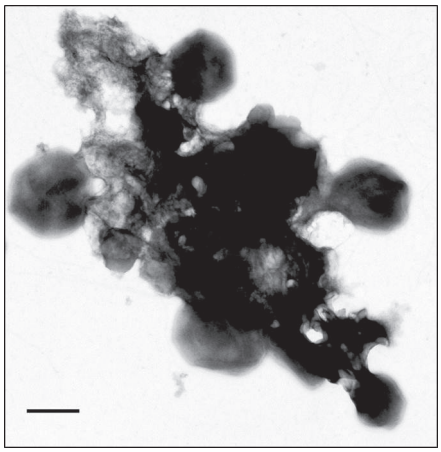

Fig. 1. Negative-stain transmission electron microscopy of *Hyperthermus hephaistosi* with attachment to iron oxide particles. The scale bars represent 700 nm.

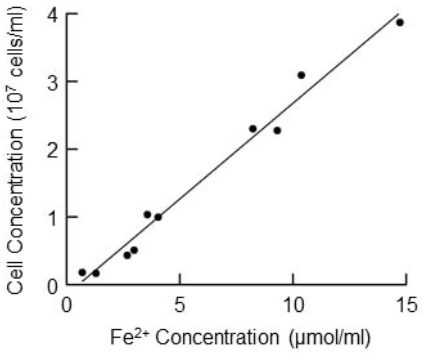

Fig. 2. Cell yield of *Hyperthermus hephaistosi* based on Fe^{2+} production (Y_{Fe2+}) calculated from a best-fit linear regression line through cell concentrations versus Fe^{2+} concentrations for one growth curve at 87°C.

We report their rates and constraints of Fe^{2+} production and the mineral end-products of their growth using using Mössbauer spectroscopy.

Characterization of growth: *Hyperthermus* sp. Ro04 and *Pyrodictium* sp. Su06 were grown anaerobically at 90°C and pH. 6.8 in Kashefi Marine Medium C [5] unless otherwise stated. The oxidizing agent was 100 mmol per liter of laboratory-synthesized ferrihydrite. The carbon and energy sources were peptides for Ro04 and H_2 and CO_2 for Su06. For each growth experiment, cell concentrations were determined at multiple time points using acridine orange stain and epifluorescence microscopy and Fe^{2+} concentrations were determined spectrometrically using the ferrozine assay.

Characterization of mineral products: Mössbauer spectra were determined for various iron oxide standards, abiotic controls, and biogenically reduced iron oxides from Ro04 and Su06. Pre- and post-growth iron oxides were dried and sealed in bottles in an anoxic chamber prior to analysis. Mössbauer spectra were acquired at Mount Holyoke College using 16 different temperatures ranging from 4 K to 295 K and calibrated relative to the spectrum of a 25 μm Fe foil. Both the Mexdist and Mexfield programs from the University of Ghent, which solve for the full Hamiltonian, were used to model the spectra. Errors on results for well-resolved components are usually ca. 0.02-0.04 mm/s for isomer shifts, quadrupole splitting and linewidths, ~0.1-0.3 Tesla for magnetic hyperfine fields, and 1-3% (absolute) for relative areas of distributions.

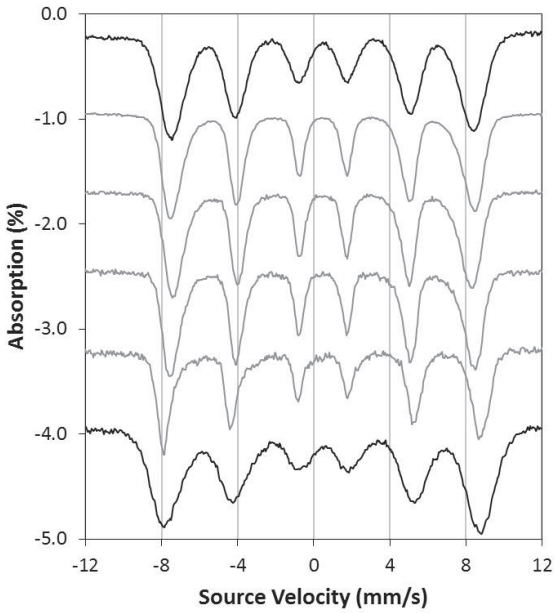

Fig. 3. Mössbauer spectra at 4 K of the iron oxide starting material (1), uninoculated growth medium before (2) and after (3) incubation at 90°C for 24 h, and the medium following growth of *Hyperthermus hephaistosi* to late logarithmic growth phase (4), along with nanophase ferrihydrite and magnetite standards. The reported IS and QS for the room temperature magnetite standard pertains only to the doublet.

Results and Discussion: A large variety of minerals are found in actively venting sulfides at hydrothermal vents. These minerals that have precipitated to form these sulfides have beginnings either from seawater or from hydrothermal fluid; they play a significant role in microbial composition especially in influencing the growth of microbes that can utilize these minerals. High-temperature-loving iron reducers, be they heterotrophs or autotrophs, are found ubiquitously and serve as a set of microbes that can take advantage of this milieu of minerals. This study provides a building block to understanding the intricate microbe-mineral interactions that must occur in order for life to use an insoluble electron acceptor.

Pure cultures were obtained from actively venting sulfide structures and the two novel hyperthermophilic iron reducers isolated from these samples. We have so far characterized growth rates of both organisms and correlated it with growth yield and Fe^{2+} production rates. Mineral transformations were also determined for both organisms and their mineral end products show differences in which minerals are produced by biogenic iron reduction. Both growth data and mineral data can help us determine possible location of these organisms and could also suggest the presence of these organisms in terrestrial analogs if potential biosignatures are found.

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A nanopatterned cell-seeded cardiac patch prevents electro-uncoupling and improves the therapeutic efficacy of cardiac repair

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Background: The heart is an extremely sophisticated organ with nano-scaled anisotropic structure, contractility and electro-conductivity; however, few studies have addressed the influence of cardiac anisotropy on cell transplantation for myocardial repair. Here, we hypothesized that a graft's anisotropy of myofiber nanoorientation determines the mechano-electrical characteristics and the therapeutic efficacy.

Methods and Results: We developed aligned- and random-orientated nanofibrous electrospun patches (aEP and rEP, respectively) with or without seeding of cardiomyocytes (CMs) and endothelial cells (ECs) to test the hypothesis. Atomic force microscopy showed a better beating frequency and amplitude of CMs when cultured on aEP than that from cells cultured on rEP. For the in vivo test, a total of 66 rats were divided into six groups: sham, myocardial infarction (MI), MI+aEP, MI+rEP, MI+CM–EC/aEP and MI+CM–EC/rEP ($n \geq 10$ for each group). Implantation of aEP or rEP provided mechanical supporting and thus retarded functional aggravation at 56 days after MI. Importantly, CM–EC/aEP implantation further improved therapeutic outcomes, while cardiac deterioration occurred on the CM–EC/rEP group. Similar results were shown by hemodynamic and infarct size examination. Another independent in vivo study was performed and electrocardiography and optical mapping demonstrated that there were more ectopic activities and defective electro-coupling after CM–EC/rEP implantation, which worsened cardiac functions.

Conclusions: Together this study provides a functional characterization and therapeutic efficacy of nanopatterned anisotropic cardiac patch. Importantly, the results demonstrate the significance of cardiac anisotropy recapitulation in myocardial tissue engineering, which is valuable for future development of translational nanomedicin

eIF2α expression and phosphorylation in response to nutritional status and stressors in zfl cells

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In a zebrafish embryonic fibroblast cell line, zfl, two forms of eIF2α are expressed, eIF2α-1 and eIF2α-2, with eIF2α-1 expressed ~5-fold higher than eIF2α-2. These two gene products are 96 % identical at the amino acid level, although the genes are found on two different chromosomes, chromosome 20 and chromosome 17, respectively, and are under the control of different promoters. Both are identical in the phosphorylation site and kinase docking site. Wild-type eIF2α-1, but not the Ser51Ala variant, is phosphorylated in vitro by activation of GCN2, PERK, PIC and HRI. Phosphorylation in zfl cells is increased by a variety of conditions; starvation, leucinol, ER stress, PIC and N-methylprotoporphyrin, an agent that depletes heme, suggesting activation of the eIF2α kinases GCN2, PERK, PKR and HRI, respectively. All these eIF2α-kinases are present in the zebrafish genome. Interestingly, eIF2α phosphorylation increases in zfl cells after transfection by Amaxa nucleofection, with phosphorylation directly proportional to transfection efficiency.

The decapping activity of vaccinia virus D10 protein enhances viral replication and virulence in mice

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All cellular and most viral mRNAs have a 5'-methylated cap structure that protects mRNA from degradation by exonucleases and enhances translation. Vaccinia virus (VACV), a member of the poxvirus family, is a large DNA virus that replicates exclusively in the cytoplasm of host cells. It encodes enzymes for mRNA synthesis and processing, including a multisubunit RNA polymerase, a capping enzyme and a polyA polymerase. Remarkably, VACV also encodes decapping enzymes that can destabilize viral and host cell mRNAs by hydrolyzing their 5' cap structures. Vaccinia virus gene expression is regulated in early, intermediate, and late stages. The majority of host cell mRNAs undergo rapid degradation at the beginning of the intermediate/late phases of infection. Previously, we demonstrated that the intermediate viral protein D10 has intrinsic decapping activity and that replacement of the D10 gene with GFP increased the stability of viral and host mRNAs and reduced virus replication in cultured BS-C-1 cells. Here, we further analyzed the role of the decapping activity of D10. Two decapping mutant viruses were constructed: D10mu contained point mutations in the catalytic domain that abolished the decapping activity; D10stop contained two stop codons that abolished D10 synthesis. Both D10mu and D10stop displayed milder negative phenotypes in cultured cell lines compared to the previous D10 deletion mutant and were only slightly impaired relative to the wild-type virus. Nevertheless, viral early and late transcripts as well as cellular GAPDH mRNA persisted longer in cells infected by D10mu and D10stop, consistent with a role of D10 in regulating mRNA stability. Despite the mild phenotypes in cultured cell lines, D10mu and D10stop showed significantly lower virulence in mice. Groups of BALB/c mice were infected intranasally with three doses of D10mu, D10stop, or wild-type viruses. Daily monitoring for mice weight loss revealed that D10mu and D10stop were more attenuated than the wild-type virus and had higher mice survival rates. Additionally, D10mu and D10stop had 10 times lower titers in the lungs and 500- to 100,000-fold lower titers in the non-respiratory organs than the wild-type virus. Similarly, in primary mouse embryonic fibroblast cells, the yield of D10stop and D10mu is 7 to 10 times lower than that of the wild-type virus. The fact that D10mu and D10stop generated similar phenotypes both in cells and in mice suggests that decapping is the major function of the D10 protein. In contrast to other mechanisms by which vaccinia virus targets specific cellular pathways, we suggest that the decapping activity of D10 contributes to the virulence of vaccinia viruses in a global manner by destabilizing most cellular mRNAs including those that produce proteins with anti-viral functions. Deep sequencing of viral and cellular mRNAs in cells infected with wild-type and D10 mutant viruses is being performed to test this idea.

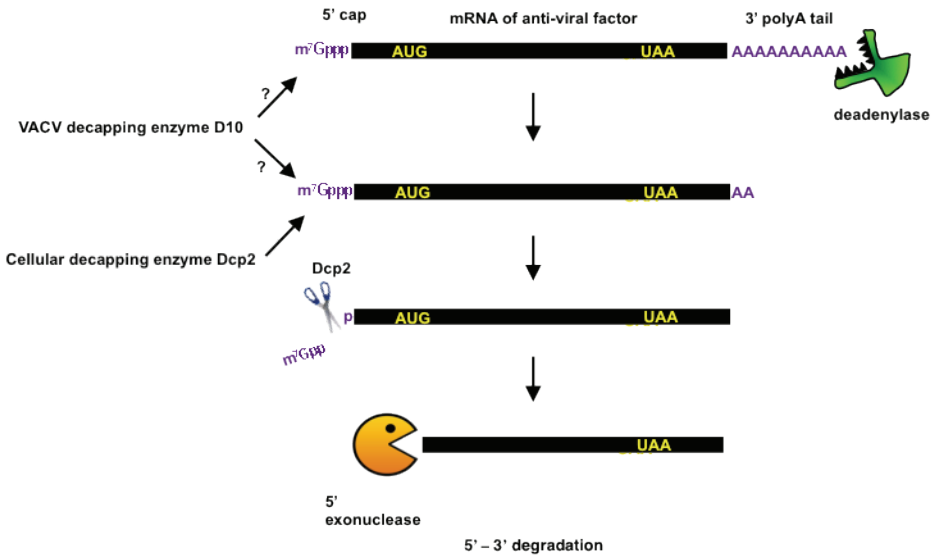

Fig1. Possible pathway for degradation of a cellular anti-viral mRNA by vaccinia virus decapping enzyme D10.

Electrical characterization of cells using DEP spring

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Dielectrophoresis (DEP), a label-free cell separation technique based on the dielectric properties, has significantly advanced biomedical research in diverse applications ranging from blood stem cells purification to cancer cells isolation from heterogeneous populations. The ability to measure the dielectric properties of individual cells is critical not only for effective DEP sorting, but also for enhancing the current knowledge of cell biology. Here, we propose a novel method: the DEP spring, which uses the force balance between the DEP force and the hydrodynamic force to measure the dielectric properties of individual cells in a continuous and high-throughput manner. When the cells are flowing through the rectangular microfluidic channel, the coplanar electrodes generate an invisible barrier which pushes away the cells (Figure 1). This invisible DEP barrier acts like a nonlinear compressive spring because it has a position dependent reacting force against the hydrodynamic force. Therefore, from the balance position (δ) and the hydrodynamic force, we can infer the strength of the DEP force and the cellular dielectric properties. To show that DEP spring can probe the dielectric properties of cells, we put the live and dead HL-60 cells and applied a frequency sequence switching between low and high frequencies (500kHz/15MHz). The live and dead cells had different DEP response to the frequency sequence because the live cells had complete membrane while the dead cells did not (Figure 2). The DEP spring method embeds the DEP characterization into single images of cells so it is more efficient than velocity measurement methods which require cell tracking in videos. With this method, we can characterize ~1000 distinct cells/min with clear cell images. It combines the high-throughtput DEP characterization of cells with high-content microscopy images and therefore provides a strong tool for cytometry and DEP cell sorting.

Structure activity relationship (SAR), crystallography and computational binding free energy prediction of a new class *F. tularensis* enoyl reductase (FabI) inhibitors

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Purpose: *Francisella tularensis* is a gram negative bacterial pathogen that causes tularemia, a serious zoonotic infection. Because *F. tularensis* is associated with high mortality, a low infectious dose, and can be cultivated and aerosolized easily, the Centers for Disease Control has categorized *F. tularensis* as a Category A priority pathogen. One attractive target for the development of novel antimicrobial agents against Gram-negative organisms is the NADH-dependent enoyl reductase (FabI) enzyme in the FAS-II pathway. Herein, we report detailed SAR analyses, X-ray structure and antibacterial action of a second generation benzimidazole compounds.

Methods: The enzyme inhibition activity was monitored using an optimized fluorescence intensity assay. Minimum inhibitory concentration (MIC) studies were performed using the CLSI broth microdilution assay method. Protein structures were solved using x-ray crystallography. The quantitative structure activity relationship (QSAR) model and the binding free energy prediction model were constructed using SybylX2.0 and Amber 12.0 respectively.

Results: With this series of benzimidazole compounds we have lowered the enzymatic activity from the sub-micromolar range to the low nanomolar range. Crystallography studies confirm the binding mode of these inhibitors and explain the observed SAR. MIC studies presented here show low microgram/mL activity against F. tularensis, B. anthracis, S. aureus, and MRSA. The preliminary QSAR model quantifies the observed SAR and the optimized binding free energy prediction model provides satisfactory prediction on benzimidazole enzymatic activities.

Conclusions: We report SAR, structural analyses confirming the binding mode of a new class of FabI inhibitors with promising antibacterial activity against several clinically relevant organisms, including the Category 'A' pathogen, F. tularensis. The computational models will provide prediction on benzimidazole enzymatic activities and guide the synthesis of future benzimidazole compounds.

This work was supported in part by National Institutes of Health Grant U01 AI077949 and a Pre-doctoral fellowship from the American Heart Association, Mid-West Affiliate 13PRE14800030.

Poster Presentation, Abstract ID P34

Impaired ability of inhibitory interneurons links with eplieptogenesis using a Dravet mouse model

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Haploinsufficiency of SCN1A gene which encodes Nav1.1 channel causes Dravet Syndrome (DS), the severe myotonic epilepsy onset in infancy with psychomotor delay during development. Previous studies reported that spontaneous seizure and premature death were observed in heterozygous DS animals. However, the dysfunction of circuit in dentate gyrus of the heterozygous DS mouse related with epileptogenesis is still unclear. Here, a knock-in mouse harboring a non-sense mutation point in Scn1a was generated, and exhibited major DS phenotypes such as spontaneous seizures and greater susceptibility to heat-induced seizures. In hippocampal dentate gyrus, a significant loss of Nav1.1-GABAergic interneuron number as well as impaired firing activity of PV-interneurons was observed. An imbalanced synaptic transmission of attenuated inhibitory drive and augmented excitatory drive were found. The reduced dendritic complexity and increased dendritic spine density in granule cells were revealed by Golgi staining. Our findings suggest that loss of Nav1.1 channels impaired the function of inhibitory interneurons and the dendritic structure of downstream neurons, which linked with hyperexcitation of neural network and epileptogenesis.

Poster Presentation, Abstract ID P35

A novel dual fluoroscopy imaging for determination of THA kinematics: *in-vitro* and *in-vivo* Study

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Introduction: Measurement of accurate 6 degrees of freedom (6DOF) kinematics in patients with of total hip arthroplasty (THA) is critical in understanding edge loading, impingement and dislocation. This study quantified a novel dual fluoroscopy imaging system (DFIS) for measurement of in-vivo kinematics of THA patients.

Materials &Method: In order to validate the DFIS, Roentgen Stereophotogrammetric Analysis (RSA) was used as gold standard in both *in-vitro* and *in-vivo* tests. Titanium beads were implanted in both pelvis and femur. Both the cadaveric hip and the THA patient hip with RSA beads were scanned with CT for 3D hip model reconstruction. A passive flexion/extension motion of the cadaveric hip and a gait cycle of the patient on a treadmill were imaged using the DFIS. The models of THA and the fluoroscopic images were then imported to a customized software for pose registration. 6DOF of the implants were then registered by matching its projected silhouette to the features of fluoroscopic images. The hip kinematics was also reproduced using the titanium beads (RSA). The accuracy of the DFIS technique was evaluated by calculating root mean squared errors (RMSEs) between the kinematics measured from DFIS tracking technique and RSA for *in-vitro* and *in-vivo* experiments.

Results: The RMSEs of the DFIS tracking technique were less than 0.74 mm and 0.74° for translation and rotations for measurement of THA kinematics during in-vitro dynamic flexion/extension. Corresponding values were less than 0.55 mm and 1.20° for a THA patient during in-vivo gait.

Discussion & Conclusion: The results of the current study demonstrated that the THA kinematics determined using the DFIS and RSA are within 1mm and 1°. This suggests that DFIS is a promising tool for accurate measurement of in-vivo THA kinematics during functional activities in patients with THA.

Poster Presentation, Abstract ID P36

Expanding genetic codes for protein modifications

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The naturally occurring pyrrolysine (Pyl) incorporation machinery was discovered in methanogenic archaea and some bacteria. In these organisms, Pyl is cotranslationally inserted into proteins and coded by an in-frame UAG codon. Suppression of this UAG codon is mediated by a suppressor tRNA, tRNAPylCUA, that has a CUA anticodon and is acylated with Pyl by pyrrolysyl-tRNA synthetase (PylRS). The PylRS- tRNAPylCUA pair can be directly applied to incorporate Pyl and other lysine derivatives into proteins at amber mutation sites in E. coli and mammalian cells. In the approach of amber codon suppression, evolved PylRSs were selected to synthesize the proteins genetically with lysine and phenylalanine derivatives which contain native or mimic of post-translational modifications or active chemical functional groups for protein labelling and protein folding studies. Using rational design and directed evolution, some engineered PylRS variants have shown substrate polyspecificity. We developed facial high-throughput screening method to identify multiple non-standard amino acids (nsAAs) that can be used for chemical biology and synthetic biology studies. These developments greatly expand the inventory of genetically encoded nsAAs and our abilities to do protein engineering in these cells.

Poster Presentation, Abstract ID P37

3D printing of interdigitated Li-ion microbattery architectures (3D-IMA)

Teng-Sing Wei[1], Ke Sun[2], Bok Yeop Ahn[1], Jung Yoon Seo[2], Shen J. Dillon[2], and Jennifer A. Lewis[1]
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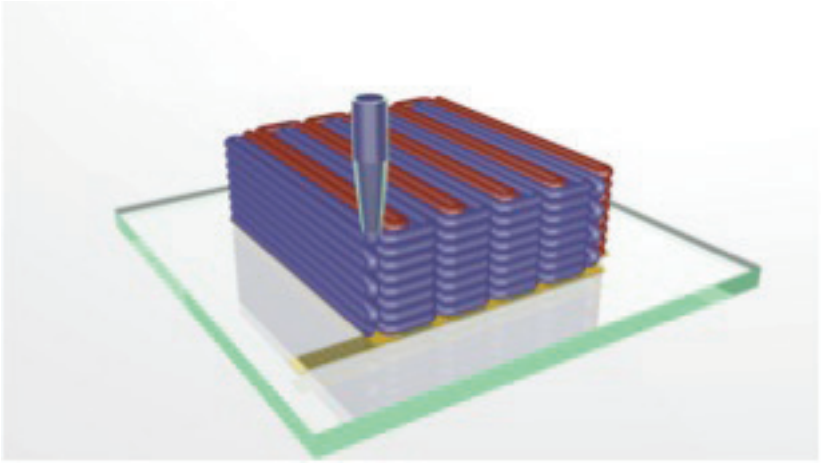
Developing compact high energy density power sources will enable autonomous micro/nano devices used in next generation microelectronics. Ideal structures combine intimately positioned electrodes with short diffusional path lengths assembled in a three-dimensional structure. Emerging applications require highly integrated patterning approaches for defining the spatial location and composition of metal oxide and carbon-based electrodes as well as polymer separators and electrolytes. Typical fabrication approaches require complex lithography or etching processes, which are either costly or difficult to scale into the third dimension. In this presentation, we describe recent efforts in fabricating 3D Li-ion microbattery with interpenetrating high-aspect ratio architectures via layer-by-layer printing. The concentrated viscoelastic inks composed of Li4Ti5O12 or LiFePO4 nanoparticles were carefully tailored for the desired rheological, drying and printing behavior. Both fabrication and electrochemical characterization of these 3D interdigitated microbattery architectures (3D-IMA) will be discussed.



Genome-wide identification of Bcl-3 and p50 target genes in disuse muscle atrophy

Chia-Ling Wu, Susan C. Kandarian*, Robert W. Jackman.
Department of Health Sciences, Boston University, Boston, MA.

NF-κB plays a central role in regulating atrophy processes during skeletal muscle atrophy. Our lab has previously shown that P50 and Bcl-3, a κB transcription factor and its transcriptional co-activator, are both required for inducing disuse atrophy. However, less is known about the molecular mechanisms of the atrophy-resistant phenotype seen in *nfkb1*$^{-/-}$ (lack of P50 protein) and *bcl-3*$^{-/-}$ mice. The purpose of this study is to identify genes that are targets of P50 and Bcl-3 in disuse atrophy at genome-wide level. We first measured global gene expressions of plantar flexor muscles from wild type, *nfkb1*$^{-/-}$ and *bcl-3*$^{-/-}$ mice with or without 6 days of hind limb unloading. Genes that were upregulated in wild type mice due to unloading but not in the knockout mice were considered as P50 or Bcl-3 direct or indirect target genes. 185 or 240 genes were identified as P50 or Bcl-3 target genes in disuse atrophy, respectively, and most of them were involved in proteolysis and transcriptional regulation. Interestingly, all P50 target genes were also identified as Bcl-3 targets; we next sought to identify Bcl-3 binding targets in disuse atrophy using ChIP-*seq*. In atrophied muscles, there were increased Bcl-3 binding to the promoter of the genes encoding for E3 ligases, N-end rule proteins, kinase and glycolysis enzymes. By studying the expression changes of Bcl-3 binding targets, we mapped a Bcl-3 regulated gene network that may be responsible for driving the atrophy processes due to unloading. One Bcl-3 direct target in disuse atrophy, **Mu**scle specific **R**ing **F**inger protein **1** (MuRF1), was studied in detail by qPCR, ChIP-*seq*, and reporter assays. These results provided the first direct confirmation that the Bcl-3 and P50 bound to NF-κB binding sites to transactivate MuRF1 during muscle atrophy. Taken together, our data support that Bcl-3 is the global regulator of genes involved in the proteolysis and the change in energy metabolism that are essential components of muscle atrophy due to disuse. *This research is supported by NIH AR041705 and AR060217.*

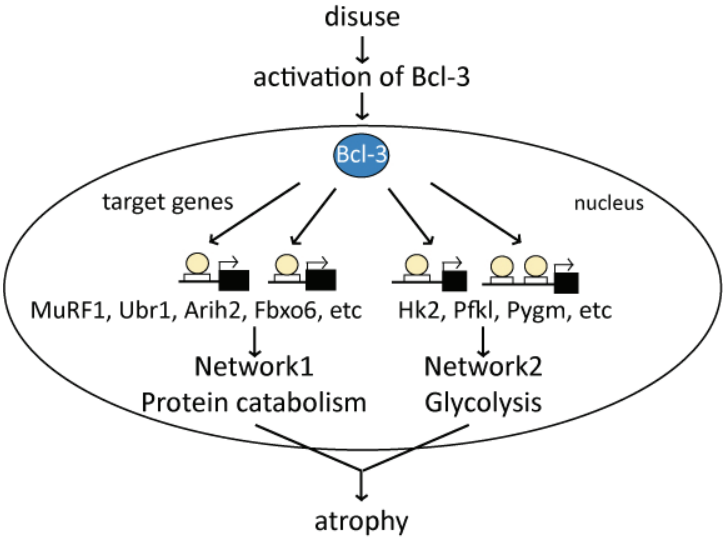


Figure Schematic model showing Bcl-3 as the global regulator of genes involved in proteolysis and glycolysis that are essential components of muscle atrophy due to disuse.

Identification of direct binding proteins of Synphilin-1 using chemical cross-linking and mass spectrometry

Xiaobin Xu[1], Han Hu[2], Anatoli B. Meriin[2], Mark E. McComb[2], Michael Y. Sherman[2], Catherine E. Costello[1,2]
[1]Boston University, Department of Chemistry, Boston, MA, 02215, United States, [2]Boston University, School of Medicine, Boston, MA, 02118, United States

Misfolding and aggregation of proteins causes neurodegenerative diseases. Synphilin-1 is a protein that promotes the formation of protein aggregates and aggresomes, and is implicated in Parkinson disease. Synphilin-1 contains several protein binding motifs, which are essential for the formation of protein aggregates and aggresomes. However, the interacting proteins of Synphilin-1 and their roles in the formation of aggregates and aggresomes have not been identified. In this study, we utilized tandem affinity purification and label-free quantitative proteomics to profile networking proteins with Synphilin-1. We have identified 57 Synphilin-1 networking proteins. The functional enrichment and pathway analysis showed that many of the associated proteins are involved in chromatin modulation, RNA and protein metabolism. Furthermore, we developed a proteomic strategy to identify Synphilin-1 direct binding proteins and their interacting domains using isotopically tagged cross-linking in combination with mass spectrometry. Using this approach, 17 direct binding proteins of Synphilin-1 (including 16 newly discovered interactions) have been determined. The adjacent coiled-coil domain (CC) and ankyrin-like repeat domain 2 (ANK2) of Synphilin-1, which have been determined as aggregate promoting domains in our previous studies, were revealed as the main region that bound interacting proteins. The directing binding proteins of Synphilin-1are mainly involved in RNA metabolism. This result indicates that Synphilin-1 may participate in RNA processing to regulate the formation of aggregates and aggresomes. Several Synphilin-1 interacting proteins have been selected to study their biological functions, especially their roles in the formation of aggregates and aggresomes. For examples, deletion of one of Synphilini-1 interacting proteins, protein kinase CK2, using RNA interference, inhibit the formation of aggresome.

This research is supported by NIH P41 RR010888/GM104603, S10 RR015942, S10 RR020946, and NHLBI contract HHSN268201000031C (to CEC), and GM R01 086890 (to MYS).

Poster Presentation, Abstract ID P40

Dendronized gold nanoparticle for siRNA delivery

Yi-Cheun Yeh, Sung Tae Kim, Apiwat Chompoosor, Sarit S. Agasti, David J. Solfiell, and Vincent M. Rotello
Department of Chemistry, University of Massachusetts Amherst

Gold nanoparticles (AuNPs) functionalized with dendritic ligands provide a scaffold for effective small interfering RNA (siRNA) delivery. AuNPs were capped with different generations of triethylenetetramine (TETA) terminated ligands via Murray place-exchange reaction, resulting G0-AuNP, G1-AuNP and G2-AuNP. These dendronized ligands feature biodegradable glutamic acid scaffolds and cationic TETA moieties that interact electrostatically with negatively charged siRNA. Higher generation of TETA functionalized AuNPs, G2-AuNP, presented higher loading efficiency of siRNA and generated stable self-assembled nanoplexes at NP/siRNA ratio of 2. To investigate the siRNA delivery efficiency of G2-AuNP, siRNA mediated knockdown of beta-galactosidase (beta-gal) expression was studied in SVR-bag4 cells. The result indicated the G2-AuNP down-regulated beta-gal expression by ~50% with minimal toxicity. Dendronized AuNPs possess the benefits of polymeric delivery vehicles while minimizing toxicity through use of non-toxic core functionality.

Poster Presentation, Abstract ID P41

H3R2me2s modulates effector protein binding to H3K4me3

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Department of Genetics, Harvard Medical School, and Department of Molecular Biology, Massachusetts General Hospital, Boston, MA

Epigenetic regulation plays pivotal roles in nuclear activities like gene expression, DNA repair, and DNA recombination, and at the systemic level is critical to embryonic development. Modifications of histone tails is one of the several mechanisms that remodel chromatin structure to allow DNA-related processes to be executed, and how histone modifications are involved in these processes have been under intense investigation. Modified histone residues do not possess enzymatic activities, rather they serve as docking sites for effector proteins to interact with chromatin. To elucidate the functions of histone modifications, it is therefore critical to not only identify their genome-wide distribution, but also their binding proteomes. Trimethylation of histone H3K4 (H3K4me3) is one of the most studied histone modifications and is considered the histone mark for active chromatin, associating with actively transcribed promoters, the origins of DNA replication, and is required for DNA recombination. It has been postulated that by recruiting their binding partners, histone modifications direct effector proteins to their genomic target sites. However, the facts that H3K4me3 is distributed at the promoter region of all actively transcribed genes, and more than thirty H3K4me3 binding proteins have been identified to date suggesting that the H3K4me3 alone is not enough recruit proteins specifically.Previously, we identified a novel histone modification, symmetric dimethylation of Histone H3R2, or H3R2me2s, and showed that H3R2me2s colocalizes with H3K4me3 throughout the eukaryotic genomes. To elucidate the roles of H3R2me2s in epigenetic regulation, we developed a novel peptide pull-down assay to identify effector proteins binding to different histone modifications. Our pull-down assay combined with protein mass-spectrometry analysis identified a subset of H3K4me3 binding proteins that no longer bind to H3K4me3 in the presence of H3R2me2s. The results suggest that H3R2me2s plays a role to modulate effector protein binding to H3K4me3, which may help improving the specificity of effector protein recruitment to H3K4me3.

Attendees

Name	Job, Organization
Chan, Kun-Wei	Graduate Student, MYU Medical Center
Chan, Leo	R&D Manager/Senior Scientist, Nexcelom Bioscience LLC
Chan, Stephanie Chan	Student, MIT
Chang, Chang	Graduate Student, UMass Medical School
Chang, Chia-Chih	Research Assistant, UMass-Amherst
Chang, Dekuan	Research Fellow, Dana-Farber Cancer Institute
Chang, Han-Wen	Graduate Student, UMDNJ
Chang, Hao-Ming	Research Fellow, Boston Children's Hospital
Chang, Ho Chung	Director of Science and Technology Division, Taipei Economic and Cultural Representative Office in the U.S.
Chang, Hsiao-Han	Graduate Student, Harvard University
Chang, Hsuanyeh	Patent Attorney, Burns & Levinson LLP
Chang, Shu-Wei	Ph.D. Candidate, MIT
Chang, Tschen-Wei	Graduate Student, UMass-Amherst
Chang, Tsun-Kai	Graduate Student, UMass Medical School
Chang, Tzu-Pei	Doctoral fellow, St. John's University
Chang, Wei-Tang	Postdoctoral Fellow, Massachusetts General Hospital
Chang, Yu Wei	Student, Columbia University
Chang, Yu-Fang	Postdoctoral Fellow, Cornell University
Chen, Li-Hsin	Postdoctoral Fellow, National Yang-Ming University
Chen, Brenden	Postdoctoral Fellow, Mount Sinai
Chen, Bruce	Master Student, Columbia University
Chen, Chen-Hao	Graduate Student, Harvard University
Chen, Chi-Li	Scientist, Tetraphase Pharmaceuticals
Chen, Chia-Yen	Student, Harvard School of Public Health
Chen, Chiao-Lin	Postdoctoral Fellow, Harvard Medical School
Chen, Chien-Fu	Postdoctoral Fellow, Columbia University
Chen, Chun-Hau	Postdoctoral Fellow, BIDMC
Chen, Chun-Ti	Postdoctoral Fellow, Boston College
Chen, Edwin	Research Fellow, Brigham & Women's Hospital
Chen, Hsi-Ju	Graduate Student, UMass Medical School
Chen, Hsiao-Rong	Graduate Student, Boston University School of Medicine
Chen, Hsin-Yi	Postdoctoral Fellow, The Wistar Institute
Chen, Hsing-Yu	Postdoctoral Fellow, University of Rochester Medical Center
Chen, Hsiuyi	Student, UMass Medical School
Chen, Huei-Mei	Postdoctoral Fellow, Harvard University
Chen, Hui-Chen	Postdoctoral Fellow, MSKCC
Chen, I-Wen	Ms., Cornell University
Chen, Jeff Chen	Harvard Student, Harvard University
Chen, Jingkang	Student, Columbia University
Chen, Justin	Graduate Student, MIT
Chen, Kai-Yuan	Graduate Student, Cornell University

Chen, Lihren	President, National Cheng Kung University Alumni Association New England
Chen, Michael	Postdoctoral Fellow, Boston Children's Hospital
Chen, Po-Hao	Postdoctoral Fellow, Robert Wood Johnson Medical School
Chen, Poshen	Student, UMass Medical School
Chen, Rose	Research Associate, Genzyme
Chen, Shau Kwaun	Postdoctoral Fellow, University of Utah
Chen, Sheng-Hong	Postdoctoral Fellow, Harvard Medical School
Chen, Shih-Pin	Physician/Research fellow, Taipei Veterans General Hospital/ Mass General Hospital
Chen, Wei-Yu	Postdoctoral Fellow, Brigham and Women's Hospital, Harvard Medical School
Chen, Wen Yi	Postdoctoral Fellow, Stanford University
Chen, Y. Jenny	Patent Attorney, Wolf Greenfield & Sacks
Chen, Yen-Hao	Student,
Chen, Ying-Chou	Postdoctoral Fellow, MIT
Chen, Ying-Ja	Scientist, Pronutria
Chen, You-Shin	Graduate Student, Georgetown University
Chen, Yu-Chen (Winston)	PhD student, University of California, San Diego
Chen, Yu-Fan	Ph.D. Candidate, UMDNJ
Cheng, Chieh-Yang	Ph.D. Candidate, Cornell University
Cheng, Sofie	Marketing Specialist, Abnova
Cheng, Yenfu	Graduate Student, MIT/Mass Eye and Ear Infirmary
Chiang, Chun-Te (Patrick)	Research Fellow, Massachusetts General Hospital, Harvard Medical School
Chiang, Hao-Sen	Research Fellow, Massachusetts General Hospital
Chiang, Wei-Yin	Postdoctoral Fellow, Brigham & Women's Hospital
Chiou, Paul	Consultant,
Chiu, Chen-Jui	Manufacturing Engineer, Medical device comapny
Chiu, Hua-Sheng	Ph.D. Candidate, Columbia University
Chiu, Po-Lin	Postdoctoral Fellow, Harvard Medical School
Chiu, Shang-Yi	Postdoctoral Fellow, Dana-Farber Cancer Institute
Chiu, Tiffany	Assistant Manager –Tour Sales & Operations, Sunshine Travel
Chiu, Yu-Hsin	Postdoctoral Fellow, BIDMC/Harvard
Chou, Chia-Ching Chou	Ph.D. Candidate, MIT
Chou, Danny	Postdoctoral Fellow, MIT
Chou, Hsin-Jung	Graduate Student, UMass Medical School
Chou, Hui-Ting	Postdoctoral Fellow, Harvard Medical School
Chou, Tehui	Scientist, Genzyme
Chou, Wen-Chi	Postdoctoral Fellow, Hebrew SeniorLife/Harvard Medical School
Chou, Yi-Ying	Postdoctoral Fellow, Harvard Medical School
Chu, An-Hsiang	Graduate Student, Tufts University
Chu, Chia-Ying	Assistant Professor, National Taiwan University
Chu, Hsueh-Ping	Research Fellow, Massachusetts General Hospital
Chu, Hunghao	Research Fellow, Boston Children's Hospital
Chu, Pei Wen	Ph.D., University of Utah
Chuang, Cheng-Chi	Group Leader, Genzyme

Chuang, Jui-Chang	Principal Scientist, Shire
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- 促進台灣與美國間學術科技交流合作
  To promote Taiwan-US science and technology(S&T) collaboration.
- 倡導科技產業投資及技術轉移
  To promote S&T industrial investment & technology transfer.
- 加強台灣與美國產、官、研、學界互訪
  To enhance bilateral personal exchanges between government agencies, academic, research institutions and industries in Taiwan and their counterparts in the USA.
- 延攬海外科技人才
  To recruit overseas talent and experts.
- 參與海外科技社團舉辦之科技活動
  To attend the workshops and conferences of Chinese-American S&T community organizations.
- 協助國內蒐集科技資訊
  To help with collection S&T information.
- 服務區域包括大華府地區、美東地區、美東北地區、美東南地區及美中地區共 24 州
  Service area including 24 states （ME, VT, NH, MA, CT, NY, RI, PA, NJ, DE, MD, VA, WV, NC, SC, GA, TN, AL, FL, KY, OH, MI, IL, IN, D.C.)

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