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2013-2014 Colloquium Schedule

September 19, 20 (BIMO 60s Scholar): Dr. Rick Morimoto, Northwestern University
"Proteostasis - Protecting the Proteome in Biology, Aging, and Disease"
Understanding the principles underlying CELLULAR QUALITY CONTROL — the integration of processes by which the cell senses, responds and adapts to environmental and physiological challenges — is among the most fascinating problems in biology. The appearance of incorrectly expressed or improperly folded proteins results in a cellular stress response involving activation of stress-induced transcription factors and leads to the elevated expression of molecular chaperones and proteases that serve to clear damaged proteins. An imbalance in protein homeostasis results in the accumulation of misfolded and aggregation-prone proteins that are poorly refolded and degraded, often accumulating as oligomeric intermediate species and aggregates in different subcellular compartments. These events are hallmarks of human genetic diseases including the polyglutamine-expansion diseases such as Huntington's disease, Parkinson's disease, Alzheimer's disease, familial ALS, prion diseases, amyloidosis, cystic fibrosis, and a-1-antitrypsin disease. Our laboratory is interested in the fundamental events that underlie the appearance of misfolded proteins and their consequence to protein homeostasis, cellular function, and organismal adaptation and survival.

September 27: Dr. Jesse Bellemare, Smith College
"Climate Change and Plant Conservation in the Forests of Eastern North America"
Climate change will be a top threat to biodiversity in coming decades. Species with small ranges, i.e. endemics, may be at increased risk of extinction, as unsuitable conditions may develop rapidly across the entirety of their ranges. Human-assisted colonization or "managed relocation" has been proposed as one option to avoid extinctions by facilitating species in tracking suitable conditions poleward. In this research we conducted a biogeographic GIS analysis to document where small-ranged endemic species are concentrated in the forests of eastern North America and how these distribution and diversity patterns might relate to past climate change and the threats posed by modern, anthropogenic climate change. We found that endemic forest plants are highly concentrated in the Southeast US, but largely absent from areas near and north of the boundary of the last glacial maximum in the Northeast and upper Midwest. The patterns detected suggest that many small-ranged species' distributions are still impacted by past climate change and that they might be slow to respond to modern challenges. In parallel to the GIS study, we also launched an on-the-ground experiment testing the feasibility of northward managed relocation with one of the small-ranged endemics investigated in the biogeographic analysis, Umbrella-leaf (*Diphylleia cymosa*, Berberidaceae). This forest herb is endemic to high elevation forests in the southern Appalachian Mountains of western North Carolina. In Fall 2008, we established a ~1000 km transect of seed sowing sites from 3 locations within the species' native range to 5 apparently suitable, but unoccupied, sites outside the range in the Mid-Atlantic and Northeast US. Germination in 2009 was relatively high overall (44%) and did not differ significantly within vs. beyond the species' range (40% vs. 46%). Survival from the seedling to juvenile stage (2009-2010) was significantly higher inside vs. outside the range (63% vs. 30%), possibly due to increased herbivory beyond the native range. However, 2010-13 survival rates have been comparable inside vs. outside the range as juveniles have

become established. Growth rates of experimental plants outside the native range have been higher than those within the range, despite increased herbivory, and sexual reproduction is possible in 2014. Overall, these results suggest that the distributions of many small-ranged forest plants may still be recovering from past climate change and that assisted colonization could be an option for some endemic species threatened by modern climate change.

October 4, 11, 18: Mountain Day / Thesis Talks

October 24, 25 (Class of 60s Scholar): Dr. Rebecca Nelson, Cornell Univeristy
"Understanding disease resistance in maize: genetic architecture, QTL and pleiotropic effects"
It is important to protect crops from the many pathogens that attack them. Breeding resistant varieties is probably the most effective single approach to disease management. The Nelson lab works on the genetic analysis of disease resistance in maize, with the aim of contributing to sustainable disease management. Many loci in the maize genome have been identified that contribute to reducing disease severity. We have proposed that quantitative disease resistance is based on diverse mechanisms, presumably involving genes involved in avoidance, perception, signaling and response. Because genes involved in development, morphology, signaling and defense may entail physiological costs and trade-offs, this raises the possibility that disease resistance is associated with other, potentially undesirable, traits. Pleiotropic effects of interest would include those resistant traits that affect crop yields; those cases in which resistance to one disease is associated with resistance or susceptibility to another; and cases in which resistance is associated with a phenotype that sheds light on the underlying mechanism of resistance. Recent findings pertaining to the issue of multiple disease resistance and pleiotropy with respect to quantitative resistance to maize will be presented. Evidence includes correlation analyses in segregating populations, fine mapping of selected QTL, association mapping for multiple traits, and analysis of mutants at candidate gene loci.

November 1: Dr. Jennifer Morgan, Marine Biological Laboratory
"Roles for Synuclein in Spinal Cord Injury and Parkinson's Disease"
Spinal cord injury causes widespread death of neurons, thereby limiting regeneration and recovery. At present, little is known about how to improve the survival of damaged neurons after injury. To address this, our lab is taking advantage of the giant reticulospinal (RS) neurons in sea lampreys (*Petromyzon marinus*), which permit an examination of post-injury cellular and molecular responses at the level of individual neurons. In lampreys, some of the identified giant RS neurons reproducibly die after injury, while others survive the injury. By studying the molecular responses in these cells, we can identify specific molecular factors that govern cell death or survival after injury, which is difficult - if not impossible - in other vertebrate experimental models. We recently discovered some interesting parallels between neurodegeneration in spinal cord injury and that observed in Parkinson's Disease. Specifically, we observed cell-specific accumulation of the neuronal protein, synuclein, into neurotoxic aggregates only in the subset of neurons that degenerate after injury. Using imaging and knockdown approaches, we have further shown that reducing the accumulation of synuclein consequently increases neuronal survival and improves axon sprouting and regeneration after spinal cord injury. Thus, synuclein accumulation is a risk factor for neurodegeneration after injury, as it is in Parkinson's Disease, suggesting that this process may be a new therapeutic target for improving recovery from spinal cord injury.

November 8: Dr. Stephen DiCarlo, Wayne State University
"Sympathetic Neuroplasticity Following T5 Spinal Cord Transection Increases the Susceptibility to Ischemia-induced Sustained Ventricular Tachycardia"
Spinal cord injury-induced neuroplasticity within sympathetic pathways causes cardiac dysfunction and increases the susceptibility to life-threatening ventricular arrhythmias. For example, using coronary artery occlusion, we documented a dramatic increase in the susceptibility to ventricular tachy-arrhythmias in conscious rats with mid-thoracic spinal cord injury (T_5X). Furthermore, using injections of cholera toxin B into the left and right stellate ganglia, as well as pericardial sac, and using the Sholl analyses, we documented

that stellate-projecting sympathetic pre-ganglionic neurons within spinal segments T_1-T_5 as well as cardiac projecting sympathetic post-ganglionic neurons within the stellate ganglia from T_5X rats have larger dendritic trees than uninjured rats. The hearts of rats with T_5X are also hyper-innervated by tyrosine hydroxylase (TH)-immunoreactive sympathetic axons. These neuroplastic changes are associated with an increased nerve growth factor content within the heart and stellate ganglia. Thus, by using a combination of techniques and lines of evidence, we documented that mid-thoracic spinal cord injury results in cardiac sympathetic hyper-innervation and increased susceptibility to life-threatening ventricular arrhythmias. These results have important implications for understanding the mechanisms responsible for the high mortality rates and incidence of cardiovascular disease in individuals with spinal cord injury.

February 7: Magdalena Bezanilla, University of Massachusetts
"Myosin and actin steer plant cell division"
Plant cells divide using the phragmoplast, a microtubule based structure that directs the motion of vesicles carrying cell wall precursors to the nascent cell plate. For decades actin has been known to be a part of the phragmoplast. While studies using actin inhibitory drugs have suggested that actin connects the phragmoplast to the cell periphery, a lack of genetic evidence for actin's role in cell division and the fact that in the absence of actin, plant cells still divide quite normally has raised doubts as to whether actin actually has a significant functional role in plant cell division. We have used genetic and cell biological approaches to demonstrate that myosin VIII associates with the plus ends of phragmoplast microtubules and resides at the cortical division site in both moss protonemal and tobacco BY-2 cells, a model for mitosis and cell division in seed plants. Furthermore we find that both myosin VIII and actin are required to guide phragmoplast expansion to the cortical division site. Our data suggest a model whereby myosin VIII physically links phragmoplast microtubules to the cortical division site via actin filaments. Myosin VIII's motor activity along actin provides a molecular mechanism for steering phragmoplast expansion.

February 21: Biology Alumni Research Reunion with Jamie Lahvic '10, Erik Tillman '10, and Emily Behrman '09.

February 27, 28 (Class of 60s Scholar): Elissa Hallem '99, UCLA
"Host-seeking behaviors of parasitic nematodes"
Skin-penetrating parasitic nematodes infect approximately one billion people worldwide and are responsible for some of the most common neglected tropical diseases. The infective larvae of skin-penetrating nematodes are thought to search for hosts using sensory cues, yet their host-seeking behavior is poorly understood. We are conducting an in-depth analysis of host seeking in the skin-penetrating human threadworm *Strongyloides stercoralis*, and comparing its behavior to that of other parasitic nematodes. We found that *S. stercoralis* is highly active relative to other parasitic nematodes, and displays robust attraction to a diverse array of human skin and sweat odorants. Many of the strongest attractants for *S. stercoralis* also attract mosquitoes, suggesting that mosquitoes and worms target humans using many of the same olfactory cues. A comparison of odor-driven behavior in *S. stercoralis* and six other nematode species revealed that parasite olfactory preferences reflect host specificity, suggesting an important role for olfaction in the host selection process. We are now investigating the neural basis of host-seeking behavior. We are also conducting a comparative analysis of neural circuit function in *S. stercoralis*, the closely related rat parasite *Strongyloides ratti,* and the free-living nematode *C. elegans*. Our results will provide insight into how sensory neural circuits differ in free-living vs. parasitic species, and may enable the development of new strategies for combating harmful nematode infections.

March 7 (BIMO Class of 60s Scholar): Mike Snyder, Stanford University
"Personalized Medicine: Personal Omics Profiling of Healthy and Disease States"
Personalized medicine is expected to benefit from combining genomic information with regular monitoring of physiological states by multiple high-throughput methods. Here, we present an integrative personal omics profile (iPOP), an analysis that combines genomic, transcriptomic, proteomic, metabolomic, and autoantibody profiles from a single individual over a 14 month period. Our iPOP analysis revealed various

medical risks, including type II diabetes. It also uncovered extensive, dynamic changes in diverse molecular components and biological pathways across healthy and diseased conditions. Extremely high-coverage genomic and transcriptomic data, which provide the basis of our iPOP, discovered extensive heteroallelic changes during healthy and diseased states and an unexpected RNA editing mechanism. This study demonstrates that longitudinal iPOP can be used to interpret healthy and disease states by connecting genomic information with additional dynamic omics activity.

March 14: Hadley Horch, Bowdoin
"He Said, She Said: Sexually Dimorphic Responses to Injury in the Auditory System of the Cricket"
The consequences of injury in adult central nervous systems are often devastating and irreversible. The auditory system of the cricket is unusual in that it is capable of compensatory plasticity after injury. Unilateral deafferentation of the auditory neurons of the prothoracic ganglia induces these cells to send dendrites across the midline, a boundary they typically respect, to form synapses with contralateral auditory afferents. Past experiments have shown that this compensatory growth is remarkably precise, reinstating interneuron-specific tuning curves within several days. Careful anatomical analysis indicates that female dendrites grow rapidly across the midline but then stall in growth by about 5 days. Male dendrites, in contrast, are slower to cross the midline, but extend, on average, twice as far as female dendrites after several weeks. Our lab is investigating a number of candidates, including the family of semaphorins, that might be involved in this compensatory response to injury. We use dsRNA to manipulate expression levels and then measure the resulting physiological and morphological recovery.

April 11: Melina Hale, University of Chicago
"Development of fin morphology and movement in the context of changing functional demands"
An animal may experience strikingly different functional demands on its body's systems through development. One way of meeting those demands is with temporary, stage-specific adaptations. This strategy requires the animal to develop the appropriate morphological states or physiological pathways to address transient functional demands as well as processes to transition morphology, physiology and function to that of the mature form. Our recent research on fishes reveals a developmental transition between pectoral fin functions, providing an opportunity to examine how an organism copes with changes in the roles of its body's systems through life history. In this talk I will discuss our finding which both surprised us and led our research in interesting new directions involving fluid dynamics modeling and respiratory physiology and well as neurobiology and behavior. Studies relating structure to function often focus on stable systems that are arguably well adapted for the roles they play. Examining how animals navigate transitional periods, when the link of structure to function may be less taut, provides insight both into how they contend with such change and into the developmental pressures that shape mature form and function.

April 18: Ajay Dhaka, University of Washington, Seattle
"Investigating Temperature and Pain:TRP Channels and Beyond"
Temperatures ranging from innocuous to noxious activate ThermoTRPs, a family of nonselective ion channels required for temperature sensation. In the Dhaka lab, we are using ThermoTRPs as an entry point to the study of somatosensation with a focus on temperature and pain sensation. In this presentation this work will be discussed as well as recent studies where we have developed the zebrafish as a model system to develop unbiased high throughput assays for the discovery of novel small molecule analgesics.

April 24: Claire Ting, Sigma Xi Talk

May 9: Thesis Poster Presentations, TBL Lobby 1:00 - 2:30