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2017-2018

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September 8, 2017 - Norm Bell, Safety talk for all students working in labs. This is mandatory!!

September 15, 2017 - "Strategies for designing and delivering a scientific presentation" (by Matt Carter, Assistant Professor of Biology)
It takes time, effort and skill to design and deliver an engaging scientific talk that audiences understand and remember. In this one-hour presentation, we will discuss three aspects of designing an outstanding scientific talk: (1) organizing complex scientific information into a clear narrative; (2) using PowerPoint or Keynote software to visually communicate scientific concepts; and (3) improving verbal and nonverbal delivery during a presentation. This seminar is open to anyone and is especially applicable to senior thesis students.

September 22, 2017 - Adam Siepielski, University of Arkansas
"A cautionary tale of woe and intrigue in explaining species diversity"
Spectacular levels of species diversity exemplify most biological communities: plankton in freshwater and marine systems, beetles in a tree, plants in tropical forests or grasslands, and microbes in the human gut. What allows so many ecologically similar species to locally coexist? Progress into this vexing problem has primarily focused on identifying ecological differences among species that could promote coexistence. However, missing are critical tests determining whether or not ecological differences among species do indeed promote coexistence via their effects on population regulation. Likewise, the role of evolution in shaping the ability for species to coexist via its demographic effects is often missing. Yet, evolution is relentless. I'll explore these ideas using a diverse assemblage of aquatic insect predators - damselflies, which are a close relative of dragonflies. The work will reveal some of the complexities and joys of studying species diversity from ecological and evolutionary perspectives. Given the importance of biodiversity, understanding how diversity is maintained remains and will remain an important and active area of study in the biological sciences.

September 29, 2017 (BIMO Class of 1960 Scholar) - Zuzana Tothova ('01), Harvard
"Targeting cohesin mutations in leukemia"
Myelodysplastic syndromes (MDS) and acute myeloid leukemia (AML) represent a group of diseases of the bone marrow hematopoietic stem cells, which are characterized by ineffective production of normal blood cells. While tremendous progress has been made in defining the genetic basis of MDS with the advent of next generation sequencing, little is known about the basic mechanisms by which newly identified drivers cause transformation. Patients with MDS have a poor overall prognosis given limited treatment options. Better understanding of the mechanisms by which these novel genetic drivers contribute to transformation will offer biological insight into myeloid diseases and inform the design of urgently needed new therapies. One of the protein complexes recurrently mutated in MDS and AML is the cohesin complex – a ring-like structure that wraps around the DNA and facilitates sister chromatid cohesion, DNA repair and chromatin organization. It is not understood how cohesin mutations lead to MDS or leukemia, or whether cells with these mutations have vulnerabilities that can be exploited therapeutically. I will discuss our data showing that the loss of STAG2, the most frequently mutated cohesin subunit, results in assembly of mutant cohesin complexes, disruption of critical DNA looping interactions and leads to transcriptional deregulation. Importantly, we reveal novel therapeutic vulnerabilities associated with these changes, which has informed design of new clinical trials.

October 6, 13, 20, 2017 - Thesis Talks (two of these three dates, depending on Mountain Day)

November 3, 2017 - Abhyudai Singh, University of Delaware
"Systems Biology in Single Cells: A Tale of Two Viruses"
In the noisy cellular environment, expression of genes has been shown to be stochastic across organisms ranging from prokaryotic to human cells. Stochastic expression manifests as cell-to-cell variability in the levels of RNAs/proteins, in spite of the fact that cells are genetically identical and are exposed to the same environment. Development of computationally tractable frameworks for modeling stochastic fluctuations in gene product levels is essential to understand how noise at the cellular level affects biological function and phenotype. I will introduce state-of-the-art computational tools for stochastic modeling, analysis and inferences of biomolecular circuits. Mathematical methods will be combined with experiments to study infection dynamics of two viral systems in single cells. First, I will show how stochastic expression of proteins results in intercellular lysis time and viral burst size variations in the bacterial virus, lambda phage. Next, I will describe our efforts in stochastic analysis of the Human Immunodeficiency Virus (HIV) genetic circuitry. Our results show that HIV encodes a noisy promoter and stochastic expression of key viral regulatory proteins can drive HIV into latency, a drug-resistant state of the virus.

February 9, 2018 - Byron Weckworth, Panthera, Director Snow Leopard Program CANCELLED
"Conservation in practice: from academics to grass roots"
The guiding principles in conservation dictate the importance of preserving biodiversity, maintaining ecological complexity and upholding evolutionary potential, as well as identifying that biodiversity has intrinsic value and that untimely extinctions should be prevented. Conservationists play many roles across various fields within the basic sciences and resource management. Conservation in practice requires successfully navigating the feedback

loop between the new ideas and approaches provided by science and the field experience and research needs of resource managers, and then implementing the results into management and policy directives. Yet, in some cases, successful conservation dispenses with the formalities of this exchange in favor of local, grass roots interventions. Drawing from my own professional experiences in wildlife research and conservation, we will review results from studies of phylogeography, population genetics and ecology, predator-prey dynamics and social surveys, and examine the success and failure of their application to endangered species listing efforts for the Alexander Archipelago wolf, management of threatened woodland caribou in western Canada, and human-snow leopard conflict in Qinghai, China.

February 23, 2018 - Alumni Reunion with Emily Maclary '10, Michael Abrams '11, Gordon Smith '13, Betsy Hart '14 and Nitsan Goldstein '15. The purpose of the reunion is to provide our students a window on the process of finding and gaining admission to graduate Ph.D or MD/Ph.D programs. The reunion has two parts. First, a panel discussion will be led by our visiting alumni who are now in Ph.D, MD/Ph.D or post-doctoral programs (in TBL 112 @ 2pm). Second, the panel will be followed by a poster session where students can talk individually with the panelists about their current research and about other topics related to moving forward towards a career in basic or medical research (in TBL 211 @ 3pm).

March 2, 2018 - Shaeri Mukherjee, UC San Francisco
"Lessons learned from intracellular bacteria—how to remodel and rewire the host cell"
The unfolded protein response (UPR) is an important cytoprotective pathway in the Endoplasmic Reticulum (ER) that is manipulated by several pathogens. Interestingly, while previous work demonstrated that most pathogens induce the UPR, we have discovered that the intracellular pathogenic bacteria, Legionella pneumophila (L.p.), both activates and inhibits it. The UPR is sensed by three ER membrane sensors: ATF6, PERK and IRE1. IRE1 has a lumenal domain and cytoplasmic endoribonuclease and kinase domains. We have shown that two L.p. effectors belonging to the glucosyltransferase family, Lgt1 and Lgt2 (Lgt1/2), block the IRE1-mediated XBP1u mRNA splicing. Glucosyltransferases are common among pathogen toxins but an effect on mRNA splicing has never been observed. Along with the UPR's canonical role of sensing unfolded protein stress in the ER, it has also been implicated in the innate immune response. Therefore, this novel IRE1 role has energized efforts to understand previously uncharacterized relationships between pathogens and the UPR. Molecular dissection of this interaction will unravel novel mechanisms of bacterial pathogenesis and provide tools for probing and manipulating the UPR, which is implicated in numerous human diseases.

March 9, 2018 (BIMO Class of 1960 Scholar) - Tannishtha Reya, UC San Diego
CANCELLED
"Stem Cell Signals in Cancer Heterogeneity and Therapy Resistance"
Our research focuses on the signals that control stem cell self-renewal and how these signals are hijacked in cancer. Using a series of genetic models, we have studied how classic developmental signaling pathways such as Wnt, Hedgehog and Notch play key roles in hematopoietic stem cell growth and regeneration and are dysregulated during leukemia development. In addition, using real-time imaging strategies we have found that hematopoietic stem cells have the capacity to undergo both symmetric and asymmetric division, and that shifts in the balance between these modes of division are subverted by oncogenes. Further, regulators of this process, including the cell fate determinant Musashi, are critical players in driving progression of solid and liquid

cancers and could serve as targets for diagnostics and therapy. Ongoing work is focused on understanding the mechanisms that drive therapy resistance after drug delivery, as well as developing high resolution *in vivo* imaging approaches to map normal stem cell behavior and interactions within living animals, and to define how these change during cancer formation.

April 6, 2018 - Sonya Auer, Williams College
"The pace of life: Functional and evolutionary links between energy metabolism and the life history"
Life history traits differ markedly among populations and species but tend to fall together along a "slow–fast pace of life continuum", even after accounting for differences in body size. At the slower end of this continuum are organisms that mature at a later age and larger size, reproduce at slower rates, and have longer lifespans; organisms that mature early and at a smaller size, reproduce at a rapid rate, but die young are at the faster end of the continuum. Metabolic rate reflects the energetic cost of living and is also thought to set the pace of life, but whether and how it co-varies with the life history is not well understood. We will explore different hypotheses for how metabolic and life history traits are expected to co-vary, evaluate key assumptions underlying these hypotheses, and assess current evidence for both functional and evolutionary links between these traits.

April 13, 2018 - Beronda Montgomery, Michigan State University
"Seeing the Light: Color Vision and Developmental Acclimation in Cyanobacteria"
Photosynthetic organisms exhibit finely tuned abilities to sense and respond to changes in their ambient environment. As light is used to drive photosynthesis, which results in the production of chemical energy and important reductants, the perception of light and the resulting physiological and developmental changes that occur are among the most important adaptations in these organisms. Cyanobacteria respond to changes in light in a process known as chromatic acclimation, which tunes physiology and photosynthetic pigmentation to light cues. Recently, we have discovered that some cyanobacteria also tune cellular morphology and subcellular structures in response to external environmental cues. The photoreceptors and associated signaling pathways used to tune cellular responses and thus organismal fitness in cyanobacteria will be described.

April 20, 2018 - Nicholas Betley, University of Pennsylvania
"A Neural Circuit for the Suppression of Pain by a Competing Need State"
Hunger and pain are two competing signals that individuals must resolve to ensure survival. However, the neural processes that prioritize conflicting survival needs are poorly understood. We discovered that hunger attenuates behavioral responses and affective properties of inflammatory pain without altering acute nociceptive responses. This effect is centrally controlled, as activity in hunger-sensitive agouti-related protein (AgRP)-expressing neurons abrogates inflammatory pain. Systematic analysis of AgRP projection subpopulations revealed that the neural processing of hunger and inflammatory pain converge in the hindbrain parabrachial nucleus (PBN). Strikingly, activity in AgRP → PBN neurons blocked the behavioral response to inflammatory pain as effectively as hunger or analgesics. The anti-nociceptive effect of hunger is mediated by neuropeptide Y (NPY) signaling in the PBN. By investigating the intersection between hunger and pain, we have identified a neural circuit that mediates competing survival needs and uncovered NPY Y1 receptor signaling in the PBN as a target for pain suppression.

April 27, 2018 - David Seward ('00), University of Vermont
"Parlez-vous VUS? Functional genomics in the age of clinical sequencing"
Panel based next-generation sequencing (NGS) assays are emerging as a dominant testing modality to assess tumor variant profiles in clinical oncology. Data generated from these assays are crucial for selecting targeted therapies and supplying prognostic information. Unfortunately, the variants detected by these assays often lack sufficient evidence to assign functional impact, necessitating the use of the unsatisfying term "variant of uncertain significance" (VUS). How and if these variants affect a patient's disease and clinical course is unknown. By definition, the population frequency of any given VUS is low, and therefore the incentive to functionally characterize it, lacking. This represents a major limitation in tumor genome sequencing and is responsible for significant uncertainty and anxiety experienced by patients and clinicians. Admittedly, the possibility that a given VUS will have a population scale impact is remote. In fact, it is probable the majority of VUS are functionally irrelevant. However, when considering NGS panel testing in the context of cancer, a definitively benign result can be as clinically impactful as a definitively pathogenic one. In either case, the ability to rapidly and accurately assess variant function would allow improved individual patient care and move us closer to true precision medicine, while simultaneously informing our basic understanding of cancer biology. In part, my work aims to establish protocols enabling near-real-time functional assessment of VUS identified by NGS clinical assays. Our long term goals include understanding variants and variant profiles in the context of disease thereby transforming the way we practice molecular and genetic pathology.

May 4, 2018 - Thesis Poster Presentations from 1:00-2:30pm **on the 2nd floor of Thompson Biology**