Biology Department

Honors Research and Summer Research Open House

Wednesday, January 19
4:00pm
TBL 112

Thursday, January 20
Lab Open House
9:30am – 3:30pm

Department Chair: Lois Banta
x4330

Biology Majors….

…learn about honors research opportunities, use the following resources:

- information session with faculty
- open house (see schedule below)
- department website

The deadline to apply to the honors program is February 18th. Applications can be found online at:

https://biology.williams.edu/research/honors-research-form/

Faculty accepting honors students for **academic year 2022-2023**: Lois Banta, Ron Bassar, Matt Carter, Pei-Wen Chen, Allison Gill, Cynthia Holland, David Loehlin, Luana Maroja, Martha Marvin, Claire Ting, Damian Turner

Faculty accepting off-cycle honors students for **academic year 2022-2023**: Ron Bassar, David Loehlin, Claire Ting

Faculty accepting **summer** students for 2022: Lois Banta, Ron Bassar, Pei-Wen Chen, Allison Gill, Cynthia Holland, David Loehlin, Luana Maroja, Martha Marvin, Claire Ting, Damian Turner

Open House Schedule, Thursday, January 20		
Faculty	**Time**	**Room or Zoom Link**
Lois Banta	10am-11am	In person, Hopper Room 116
Pei-Wen Chen	4pm-5pm	In person, Hopper 110
Allison Gill	1pm-2pm	In person, Hopper 201
Cynthia Holland	1:30 – 2:30pm	In person, Hopper 114
David Loehlin	2:30 – 3:30pm	https://williams.zoom.us/j/9401305127?pwd=VlUvTVJJZ3paSktNcFdxK2IrUHZwUT09
Luana Maroja	2pm-3pm	In person, Hopper 213
Martha Marvin	10am-11am	https://williams.zoom.us/j/2443819882?pwd=S3AyYzQwNW92S3Z4Z2MrOEptUkt2dz09
Claire Ting	3pm-4pm	https://williams.zoom.us/j/99401529962
Damian Turner	11am-noon	https://williams.zoom.us/j/4190557644?pwd=WlZRRjFkaoVXWUNQOWZJYiswdm9IUT09

Please contact Matt Carter by email with questions about his lab
Please contact Ron Bassar by email with questions about his lab

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Biology Major Requirements

BIOL 101 The Cell
BIOL 102 The Organism
BIOL 202 Genetics
2 – 300-Level courses, both with a lab component
1 – 400-Level course
3 – additional electives at any level

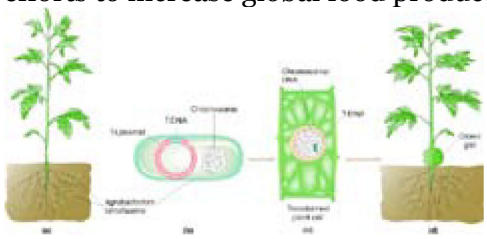
Biology Major Requirements w/Honors

BIOL 101 The Cell
BIOL 102 The Organism
BIOL 202 Genetics
BIOL 493/494 Senior Thesis
2 – 300-Level courses, both with a lab component
1 – 400-Level course
2 – additional electives at any level

Lois Banta

HSB 116 (laboratory); TBL 213 (office), x4330, lbanta@williams.edu

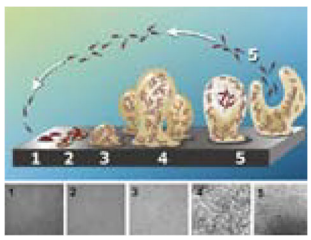
In the Banta lab, we study the interactions between the soil bacterium Agrobacterium tumefaciens and its host plants. In particular, we are interested in the transport of a large fragment of DNA across the membrane system surrounding the bacterium, and in the plant defense responses elicited by the bacterium. Infection of susceptible plants by A. tumefaciens results in crown gall tumor formation. The disease mechanism involves the transfer and integration into the plant genome of a specific DNA molecule (T-DNA) from a bacterial tumor-inducing (Ti) plasmid. Sequences on the T-DNA encode enzymes responsible for the biosynthesis of plant growth hormones; expression of these genes in the host plant leads to uncontrolled hormone production and hence unregulated plant cell division ("plant cancer"). This naturally occurring process of DNA transfer to plants is widely used to introduce new genes into plants, but its utility is limited by the fact that some plants, including the agriculturally important grains rice, wheat, corn and barley, are poor hosts. Thus, advances in our understanding of the mechanism of DNA delivery, and in particular the contributions made by bacterial proteins that are required for infection of some but not all hosts, may further the work of those scientists engaged in efforts to increase global food productivity.



Source: Griffiths, et al., An Introduction to Genetic Analysis (7th ed.)

Many bacteria including A. tumefaciens form biofilms, complex aggregates of bacteria, held together by polysaccharides, that are resistant to antibiotics and immune attack. Dental plaque and slime on rocks or metal in water are examples of biofilms; in the lungs of cystic fibrosis patients, biofilms serve as a clinically significant reservoir of bacteria. We have been exploring how the Type VI Secretion System (T6SS), implicated in virulence in several other human pathogens, plays a key role in Agrobacterium's ability to form biofilms. We will continue to investigate why bacteria deficient in the T6SS exhibit enhanced attachment to biotic and host plant surfaces.

We also discovered that this T6SS mutant is less able than its wild-type parent to infect host plants efficiently, and we believe this is because substrates secreted by the T6SS are needed to dampen host defenses. Additional data from our lab have led us to hypothesize further, however, that those same substrates can also trigger defense responses through a previously unknown mechanism. Future students will have the opportunity to continue the work of current students Irfa Qureshi '22, Sofia Neaher '22, Amy Wang '24 and Cooper Desmond '24, who are comparing the defenses mounted by Arabidopsis plants against T6SS mutant versus wild-type bacteria. The goal of our research in the coming year is to further characterize this novel pathogen-recognition pathway, using protein biochemistry, plant genetics, and molecular and cell biology approaches.



Formation of bacterial biofilmsSource: biology.binghamton.edu/davies/research.htm

Ron Bassar

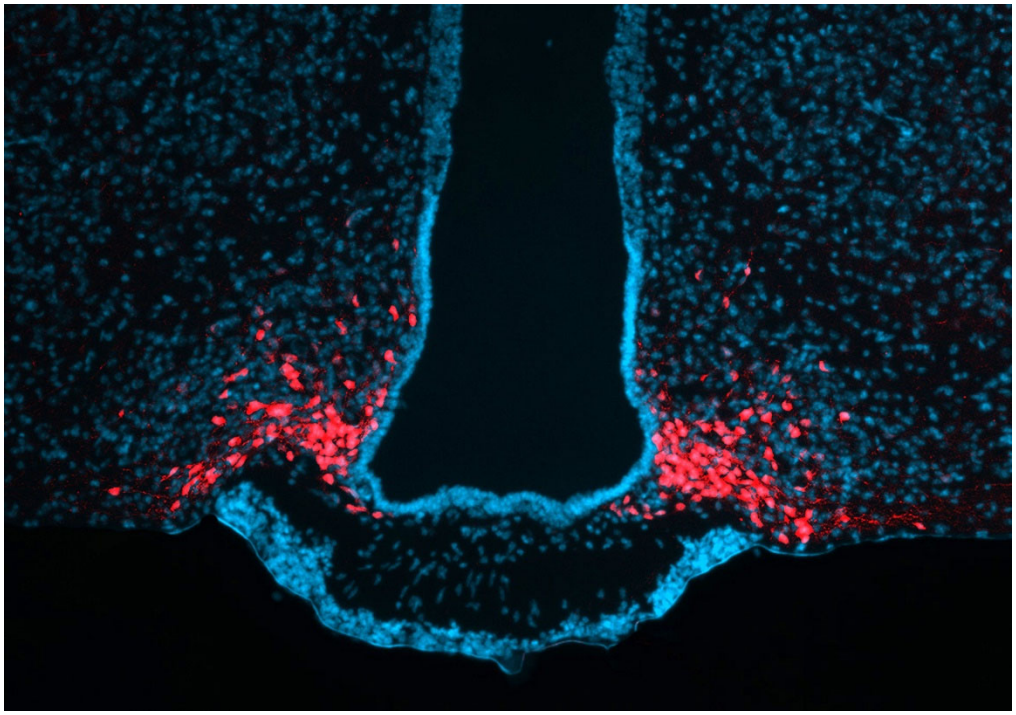
TBL 019 (laboratory); TBL 204 (office), x2119, rdb4@williams.edu

Darwin thought that evolution by natural selection occurred very slowly, over hundreds if not thousands of years. Evolutionary biologists now know that evolutionary changes in species can happen very quickly, over a relatively few generations. The consequence of this rapid evolutionary change is that ecological and evolutionary processes interact on the same timescale, sometimes drastically altering the outcomes of each. Research in the Bassar lab focuses on developing theory and conducting empirical research aimed at understanding the causes and consequences of this interaction in the generation and maintenance of biological diversity. Past research has demonstrated the role of biotic interactions in life history evolution, how these biotic interactions and their evolutionary outcomes alter community and ecosystem structure, and how abiotic factors, such as climate change, alter these dynamics. Current research is building upon this theme by testing the influence of short-term evolutionary change on species coexistence in structured populations. All research involves an ongoing synergism between theory and data using Trinidadian stream communities. We develop theory and then test predictions from theory with experiments in natural populations, semi-natural mesocosms, and the laboratory. As such, there are opportunities to conduct research in using any of these approaches.

Matt Carter

TBL 018 (laboratory); TBL 218 (office), mc10@williams.edu

To ensure that an animal obtains an optimal amount of sleep, food, and water, the brain must sense the internal and external environment and influence behavior by producing sensations we describe as “tired/awake,” “hungry/full,” and “thirsty/quenched.” The ultimate goal of my lab is to elucidate the neural basis of these homeostatic systems and behaviors using mice as a model organism. Which neuronal populations and neural networks in the brain play an important role in maintaining homeostasis, and how does their activity affect animal physiology and behavior?



Appetite-inducing neurons in a mouse brain. Neurons in the mammalian hypothalamus that produce the Agouti-related protein (AgRP) neuropeptide sense nutritional information in the blood and orchestrate an increase in food-seeking behavior. In this photomicrograph, AgRP neurons are transduced with red fluorescent protein and appear red. All cells are labeled with a DAPI stain and appear blue. In some lab projects, we selectively stimulate or inhibit AgRP neurons and measure changes in food intake behavior.

To address these questions, my lab uses classical and cutting edge neuroscience techniques. Neuroanatomical, imaging, and electrophysiological methods demonstrate which brain regions are active during specific behavioral states. Optogenetic and chemogenetic methods allow for the ability to stimulate or inhibit neurons in the brain of freely moving, behaving animals. Neuroanatomical and microscopy techniques show the structure of neural circuits. Taken together, these approaches allow us to dissect neural systems and circuits that regulate behavior.

By taking an integrative approach and performing experiments at the anatomical, molecular, physiological, and behavioral levels of investigation, we hope to make substantial contributions to understanding these homeostatic behaviors, and ultimately how they affect the health of the entire organism.

Pei-Wen Chen

HSB 110 (laboratory); HSB 130 (office), x3536, pc7@williams.edu

Concurrent remodeling of cellular membrane and actin cytoskeleton occurs in many biological processes such as cytokinesis, phagocytosis and cell migration. Broadly, my lab is interested in understanding the mechanisms underlying the coordinated change in various cellular membrane and actin structures as this coordination is fundamental for normal physiology and often disrupted in pathological conditions like cancer cell invasion and metastasis.

Specifically, we use focal adhesions (FAs) in mammalian cells as a model structure to investigate the role of Arf GTPase-activating proteins (Arf GAPs) in regulating dynamics of membrane and actomyosin networks (Fig 1). FAs are mechanosensing organelles that not only mediate cell adhesion to the extracellular matrix (ECM) but also sense and activate signaling crucial for cell survival, proliferation and differentiation. We use a combination of approaches including molecular cloning, biochemical and biophysical analyses, quantitative microscopy and cell biology techniques in our studies.

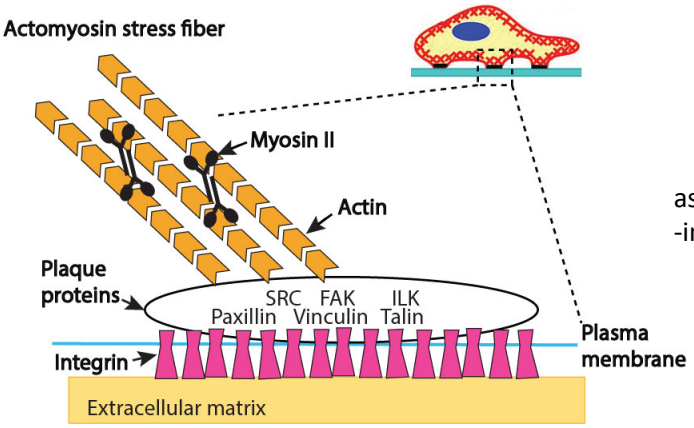


Figure 1 Components of focal adhesions.

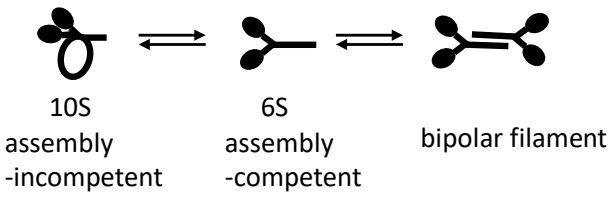


Figure 2 Conformations of Myosin II.

I. Molecular basis for the formation of Myosin II-Arf GAPs complex

Initial work will focus on one Arf GAP called ASAP1 because of its clinical relevance to cancer. ASAP1 is amplified in many human malignancies and elevated expression of which is implicated in cancer invasion and associated with poor prognosis. However, the mechanism by which ASAP1 contributes to cancer progress remains elusive. Through proteomic screens and subsequent biochemical, microscopic and functional analyses, we have identified the actin-associated motor, Myosin II as a novel binding partner and effector for ASAP1. Direct association of ASAP1 with Myosin II is essential for ASAP1 function in controlling actin remodeling, FAs and cell migration. We will generate, produce and purify mutants of ASAP1 recombinant proteins to determine the structural components in ASAP1 responsible for Myosin II-binding. We will also test if the formation of Myosin II-ASAP1 complex is modulated by other known binding partners of ASAP1, phosphoinositide PI(4,5)P2 and Arfs. By the end of the study, we will have defined the interacting motif/residues and a role of lipid in regulating Myosin II, which will position us to determine the biological function of the complex and rationally design small molecules that perturb the complex to block migration or invasion.

II. Regulation of Myosin II structural changes and bipolar filament formation

Myosin II assumes three forms: a folded assembly-incompetent monomer, an extended assembly-competent state and self-assembled bipolar filaments (Fig 2). The transition among the three forms regulates Myosin II ability to bind ATP and actin, which confers actin cross-linking and motor activity of Myosin II to generate contractility and cytoskeletal patterning in cells. Currently, there are no tools to detect Myosin II filament formation in live cells. Regulation of Myosin II filament formation in non-muscle cells has been centered on the phosphorylation of the regulatory light chain. Based on our result showing that siRNA-mediated knockdown of ASAP1 disrupted Myosin II structures in cells, we hypothesize that ASAP1 and perhaps a subset of Arf GAPs bind and control assembly of Myosin II filaments in specific time and space in cells. We will develop Föster resonance energy transfer (FRET) - based spectroscopy and microscopy assays to measure Myosin II filament formation and structural changes. We will first use purified Myosin II under conditions known to affect filament formation and computational modeling to establish the assay. We will then expand the study to live cells to test our hypothesis of Arf GAPs as a new class of Myosin II regulators.

III. Regulation of membrane and actin dynamics by Arf GAPs in cancer invasion and metastasis

There are multiple ways that ASAP1 may contribute to cancer invasion and metastasis. We will examine alternative hypotheses that can explain the effects of ASAP1 on cell movements and invasion. Given the known role of Arfs in membrane traffic, ASAP1 may control the secretion of collagen I and/or metalloproteases or delivery of integrin receptors to modulate cancer cell invasion. It is also possible that ASAP1 may regulate or under the regulation of signaling pathways such as RhoA and ROCK to affect actin dynamics and cell migration. Several cell-based assays, immunoblotting and immunofluorescence staining will be used in these projects.

Allison Gill

HSB 201 (laboratory); TBL 219 (office); x2811; alg4@williams.edu

My lab investigates how plant-microbe interactions influence the biological and biophysical processes that cycle carbon (C) and nutrients throughout terrestrial ecosystems. These processes critically govern how ecosystems will respond to ongoing global changes such as increasing atmospheric CO_2 concentrations, warming temperatures, and anthropogenic nitrogen deposition. Soils in particular represent the largest terrestrial C store, and much of our work centers on understanding how biological activity and responses to global change inform the size and stability of the soil C pool. Approaches in my research group integrate long-term field studies, laboratory experiments, and data synthesis activities. Some ongoing projects are described below. Please get in contact if you are interested in learning more and getting involved!

Interactions between substrate chemistry and nitrogen enrichment on saprotrophic fungal metabolic activity, using a model *Arabidopsis* system. Fungi are important decomposers in terrestrial ecosystems and produce enzymes that break down soil organic compounds to access C and N resources for growth, but fungi vary in their resource acquisition strategies and enzymatic capabilities. This variation may influence their specific responses and competitive interactions following N addition. To understand the fungal metabolic response

Fig. 1: White rot polypore, *Pycnoporus cinnabarinus* growing on *Arabidopsis* tissue.

to changes in nutrient environments across variable substrates, we use laboratory decomposition experiments in which pure fungal cultures are grown on senescent *Arabidopsis thaliana* tissue engineered to express varying lignin and carbohydrate chemistry. This approach allows us to target specific decomposer mechanisms and connect the detailed understanding enabled by laboratory experiments to broader patterns identified in the field.

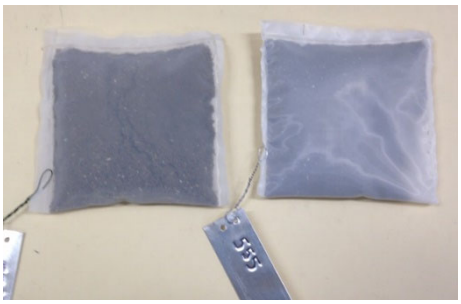


Fig. 2. Soils sealed in 50 um mesh (left) that allows for mycorrhizal fungal ingrowth and 1 um mesh that excludes mycorrhizal fungal hyphae.

Role of mycorrhizal fungi in mediating soil carbon pool responses to nitrogen fertilization, Cedar Creek, Minnesota. Mycorrhizal fungi, or fungi that maintain a mutualistic association with plants, play a critical role in the process of soil C accumulation or loss, as well as the nature of soil C responses to N fertilization. We previously conducted a field experiment evaluating the influence of competitive interactions between free-living saprotrophic and mycorrhizal fungal communities on soil C decomposition in a long-term N fertilization experiment across seven forests and grasslands in central Minnesota. The sites vary in plant species composition, soil C chemistry, and dominant mycorrhizal association. We are currently characterizing rates of microbially-produced enzyme activity, which break down structural compounds and carbohydrates and release nutrients in soils, as well as the degree of physical protection of soil C fractions to develop mechanistic understanding of the role of C chemistry, fungal decomposer activity, and fungal community interaction sin mediating the soil C response to N fertilization.

Mechanisms of soil carbon stabilization and ecosystem responses to nitrogen fertilization at Hopkins Forest. While the activity of plants and decomposer microbes largely define the amount of C substrates 'added' to soils, as well as the rate of C consumption through the process of decomposition, soil physical structure strongly influences soil C accessibility, and thus the likelihood of microbial attack and release to the atmosphere. This summer, our group is initiating a new N fertilization and C substrate addition experiment at Hopkins Forest, replicated in two areas of the forest with varying soil minerology. Current research students are characterizing pre-treatment microbial community composition using 16S and ITS amplicon sequencing, as well as the decomposer activity of the community using extracellular enzyme assays. This summer, we will characterize plant communities across experimental plots and measure rates of litterfall production and whole soil respiration prior to the initiation of experimental treatments in the fall. The experiment is globally unique and provides a wide range of opportunities to ask questions about plant, microbial, and biogeochemical responses to N fertilization.

Cynthia Holland

HSB 114 (laboratory); HSB 132 (office), ckh2@williams.edu

About half of all modern pharmaceuticals are derived from or inspired by compounds found in nature, yet the biosynthetic pathways for many natural products remain unknown. These pathways generally use basic metabolic building blocks, like amino acids, as starting materials, which have also been largely under-investigated. Research questions in the Holland laboratory focus on the evolution of enzyme function and regulation in amino acid metabolism and natural product biosynthesis in plants.

Cardenolide biosynthesis in wallflower

Cardenolides are a chemically diverse group of natural products that act as allosteric inhibitors of Na^+,K^+-ATPase, an essential membrane ion transporter that is found in almost all animal cells. The pharmaceutical cardenolide digoxin is used to treat heart arrhythmias and is on the World Health Organization's list of essential medicines, but the cardenolide biosynthetic pathway has yet to be investigated. Using a recently published genome for a cardenolide-producing species of wallflower (*Erysimum cheiranthoides)*, our current efforts are focused on identifying and characterizing candidate genes using genomics, protein biochemistry, and analytical chemistry techniques (Fig. 1).

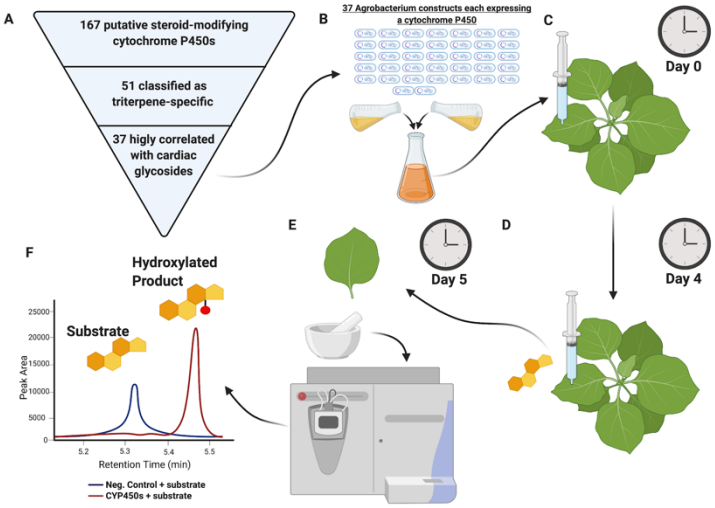


Figure 1. Identification and characterization of cytochrome P450s from wallflower. Genes were identified using bioinformatic approaches (a), and candidate genes will be cloned into *Agrobacterium* (b) for expression in *Nicotiana* leaves (c). Predicted substrates can be co-infiltrated (d) before harvesting leaves (e) and searching for the formation of

Tryptophan metabolism

Tryptophan-derived natural products and intermediates in tryptophan biosynthesis are used as flavoring agents (like the flavor of grape and bitter flavors in horseradish and mustard), fragrances, herbivore repellants, dyes, and cancer drugs, but very little is known about the substrate specificity and regulation of tryptophan biosynthesis in plants. While humans and animals must obtain tryptophan from their diet, plants and bacteria synthesize tryptophan using a 5-step, 7-enzyme pathway. Using a combination of plant genetics, biochemistry, and structural biology, our goal is to characterize the enzymes involved in tryptophan metabolism in *Arabidopsis,* maize, and fruits like strawberry and grape.

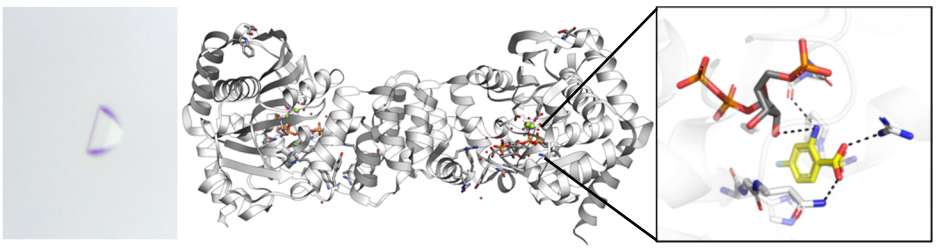


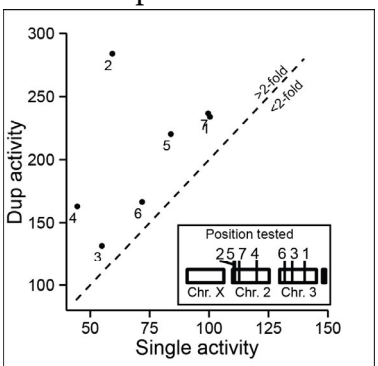
Figure 2. Structural analysis of Trp enzymes. Proteins can be crystalized (left) and models can be generated (center; PDB:4N5V) to predict the active site amino acids (right) for engineering.

David Loehlin

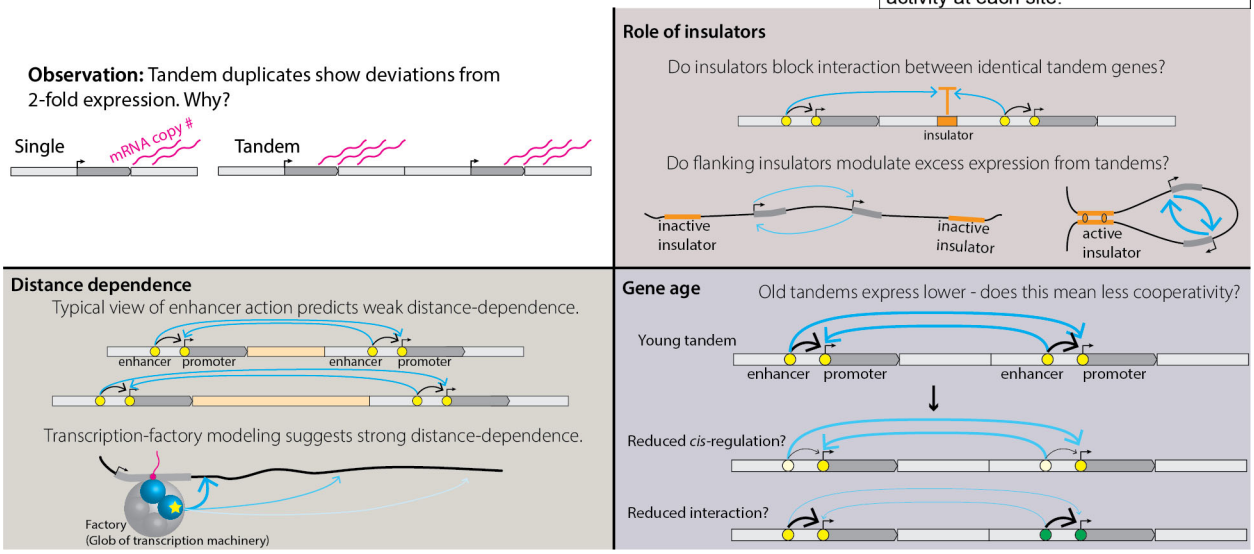
HSB 220 (laboratory); HSB 206 (office), x2244, dwl1@williams.edu

The Loehlin lab studies the structure, function, and evolution of tandem duplicated genes. These are both core elements of genomes and known causes of disease and individual variation, yet scientists have not yet mechanistically studied the "rules of the genome" that govern the level of gene expression from tandem genes. A simple prediction is that doubling the number of copies of a gene will double gene expression, but we and others have observed that this is often not the case. The lab is trying to figure out when and why deviations from two-fold expression occur.

We previously observed that tandem genes we were studying in *Drosophila* flies produced more than twice the level of matched single copy genes (Loehlin and Carroll 2016). Our basic hypothesis is that the excess expression from tandem duplicate genes is caused by identifiable genetic factors. To identify these factors, the lab uses modern genetic tools to build and modify genes at the DNA level, then we test their function by injecting them into flies and measuring RNA levels or the amount of enzyme they produce. The lab is looking at a couple of different features that we think might influence expression of a gene pair.



Expression (B-galactosidase activity) of single copy and tandem duplicate *vgQ-lacZ* reporter genes in seven chromosomal *attP* locations. Duplicate activity is significantly greater than twice single activity at each site.



Is expression of tandem genes mediated by insulators?

Certain proteins bind to specific DNA sequences called "insulators", which are thought to organize the genome into loops or "territories" within the nucleus and block regulatory interactions between the stuff on either side of the insulator. The lab is determining if tandem overexpression is caused by insulators or is independent from them. In one project, we are comparing the expression of single and tandem transgenes in the presence/absence of flanking and intervening insulators. One planned experiment is to determine the effects of removing insulator-mediating proteins on tandem gene expression. We are also using computational tools to predict native insulator sequences, then mutating the insulator sequence to see if that influences single vs tandem expression.

Is excess expression of tandem duplicates distance-dependent?
If tandem duplicates show excess expression, how important is it that they are close to one another? The lab developed a new technique, using recombination, to duplicate a native gene in the genome at varying gene-gene distances. The plan is to make a set of duplicates at varying distances and then measure the expression levels of the new tandem pairs. Does the expression level show some kind of distance-dependent curve, suggesting cooperative transcription? Is it a stair-step, suggesting a role for specific regulatory elements? What will happen when the two genes come within 6' of one another?

How do naturally occurring tandem duplicates express themselves?
Naturally occurring tandem duplicated genes experience not only the structural influences described above, but also have had their expression level shaped by mutations and natural selection. New high-quality genome sequences from *Drosophila* populations and species make it possible to identify evolutionary changes in copy number of tandem duplicate genes, characterize their expression levels, and then unpack how the two neighbor genes influence one another through targeted deletions using the CRISPR technique.

Luana Maroja

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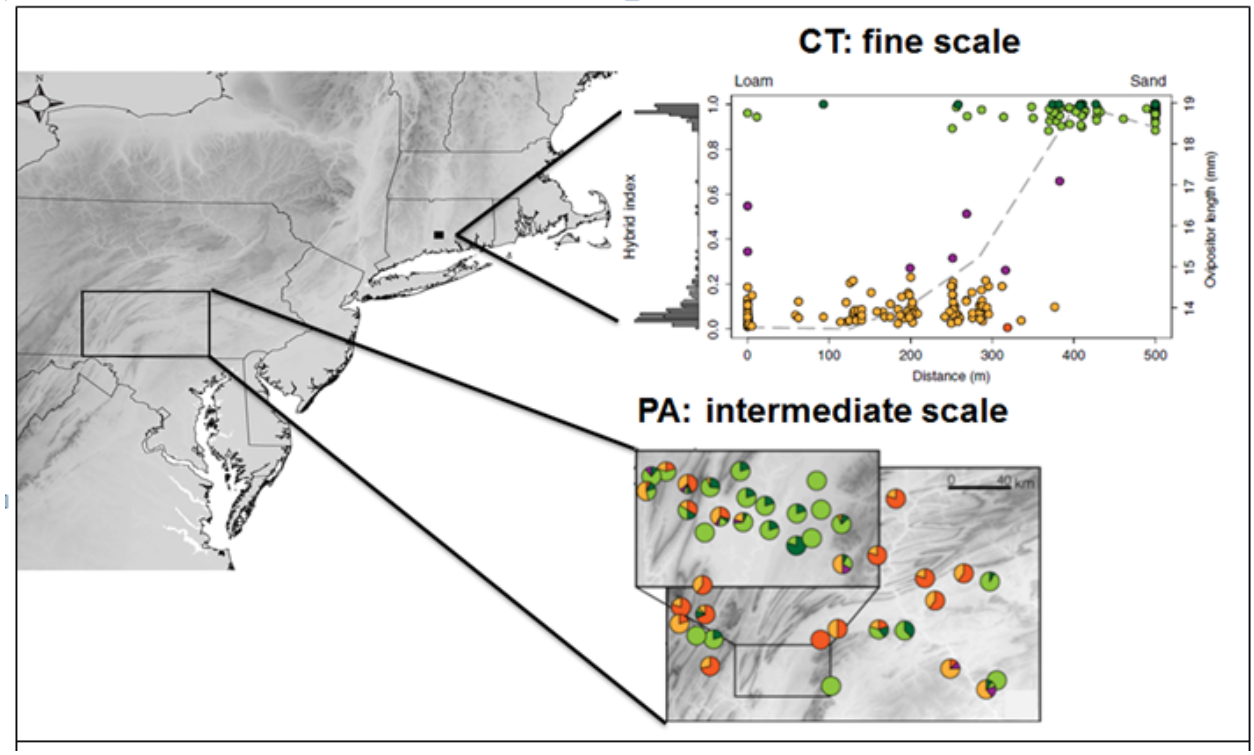
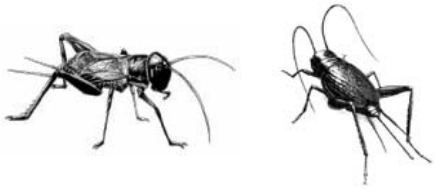
Gene flow between species: Can we find genes responsible for speciation and species isolation?



I am currently working in two species complexes, crickets and fruit flies. In both projects the aim is to help us understand the mechanisms that generate biodiversity. That is, how do two unique species evolve from one common ancestor? One way of examining this is to look at populations of closely related species that have recently diverged but are still able to mate with each other, producing hybrids and mapping families. What genes are responsible for the initial divergence and maintenance of species barriers? What are the mechanisms that impede such species eventually losing their identity through hybridization? Which genes are able to flow across the hybrid zone and which are limited to one species? What are the first genetic changes that lead to reproductive isolation?

Reproductive isolation between two field crickets, *Gryllus firmus* and *G. pennsylvanicus*



Recently diverged species, such as he crickets *G. firmus and G. pennsylvanicus*, share the majority of their DNA. This is both due to the short time they have been evolving independently and also because they can still exchange genes by producing hybrid offspring. Recently, some SNPs unique to each species and unable to pass the species barriers have been described. The very interesting observation is that most of the loci unable to cross the species barriers seem to be located in the X-chromosome, which might indicate a large X-effect in speciation or the presence of a single important X-linked locus. We are testing if any of these genetic locations determine whether the offspring of a heterospecific cross will be viable or not, to do this we will use population crosses between the two species and use next generation sequencing to scan SNPs in surviving offspring and parents that yielded fertile crosses. We will also use next generation sequencing to get a full sequence of the X chromosome and locate genes that seem to be important for speciation.

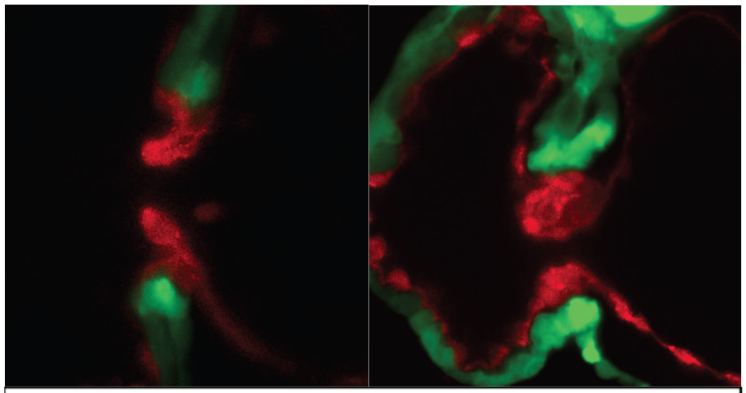
Martha Marvin

MSL 126 (laboratory); MSL 128 (office); x3546, mmarvin@williams.edu

Our chief research interests are in **cardiovascular development in zebrafish** and the molecular mechanisms underlying variations in **stress reactivity** in embryos and adults.

Adult levels of stress reactivity are in part governed by early life experience of stress. We are investigating the genes that are modulated by early life exposure to stress, with a particular focus on genes that may undergo permanent epigenetic changes in expression levels from embryonic exposure through adulthood. These candidates could be key genes in setting the stress "thermostat" throughout life. We created mutations in *fkbp5*, a stress-modulating gene, using CRISPR/Cas9 mutagenesis. We study their motion and biochemical responses following stimuli to observe how the presence or absence of fkbp5 affects their stress response.

Zebrafish are an excellent model in which to study the developing heart, the most common organ to suffer birth defects in humans. The zebrafish heart begins beating at 24 hours, but is not required for survival for the first week, permitting the study of serious defects.



Deformed zebrafish embryo heart valves caused by estrogen exposure, viewed by confocal microscopy.

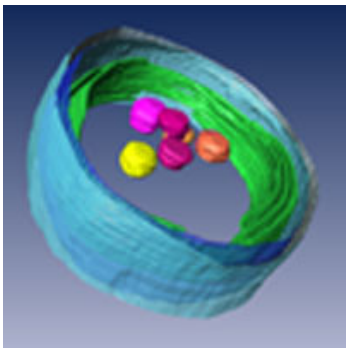
Cardiac valve growth is regulated by Notch signaling and by prostaglandins, which are more widely known as pro-inflammatory signals. Zebrafish exposed to exogenous estrogen or estrogen-

like compounds causes the loss of heart valves. We are investigating the roles of xenoestrogens, and their interaction with two estrogen receptors—the canonical nuclear receptor (ER) as well as the G-protein coupled estrogen receptor (GPER)—to clarify the developmental risks posed by exogenous endocrine disruptors.

Claire Ting

TBL 023 (laboratory); TBL 214 (office), x4053, Claire.S.Ting@williams.edu

Photosynthesis is a fundamental biological process upon which the majority of Earth's life depends. How do differences at the genome level between closely related photosynthetic organisms translate into selective physiological advantages in photosynthetic capacity and in tolerance to abiotic stress? What is the significance of existing molecular/physiological diversity for the ecology of photosynthetic organisms and the evolution of niche differentiation?



In order to address these questions my laboratory is focusing on the ecologically successful marine cyanobacterium, *Prochlorococcus* (image on the left depicts a *Prochlorococcus* cell visualized by the Ting Lab using cryo-electron microscopy). This microbe is thought to be the most abundant photosynthetic organism on our planet. In certain regions of the oceans, more than 10,000 cells can be found in a single drop of sea water. *Prochlorococcus* plays a key role in primary production and in global energy cycles, and is an excellent model for plant photosynthesis. The projects in my lab are interdisciplinary and integrate tools and concepts from fields including genomics, biochemistry, cell biology, ecology, and evolution.

Photosynthetic Physiology and Environmental Stress Response Mechanisms
Through comparative studies of closely related isolates, we are investigating the photosynthetic physiology and environmental stress response mechanisms of *Prochlorococcus*. The availability of 12 complete *Prochlorococcus* genome sequences has enabled us to formulate specific hypotheses regarding how isolates and ecotypes will respond to key environmental factors, such as light and temperature. These studies will contribute to our understanding of the survival and distribution of *Prochlorococcus* populations in the open ocean water column and how this important marine microbe will respond to global environmental change.

Comparative Genomics, Metagenomics, Metatranscriptomics
Our most recent grant from the National Science Foundation has funded our field work in the Sargasso Sea, an open ocean region where *Prochlorococcus* often dominates the bacterioplankton population. We are conducting metagenomic (characterization of genes/genomes isolated from environments) and metatranscriptomic (characterization of gene expression in natural communities) analyses in order to understand how key environmental factors impact community composition and biological activity in open ocean waters.

Ting Lab research assistants conducing field work in the Sargasso Sea.

Structural Characterization of Photosynthetic Microorganisms
Because *Prochlorococcus* cells are tiny (approximately 100 cells can be lined up side by side across the width of a human hair!), we are using state-of-the-art microscopy techniques to characterize the cellular structure and organization of *Prochlorococcus*. We have discovered that closely related isolates exhibit significant differences at the ultrastructural level, including in the number and organization of their internal membranes, where proteins involved in photosynthesis are localized.

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Resident memory T cells and the pathogenesis of asthma

Asthma is a chronic inflammatory disease of the lung which results in narrowing of the airways, breathing difficulties which can lead to death. According to CDC estimates, approximately 1 in 12 people (25 million) have asthma and asthma was responsible for 1.8 million emergency room visits in 2010. Current treatment strategies for asthma include inhaled corticosteroids that can control airway inflammation but do not cure chronic allergic asthma. Understanding the mechanisms leading to the development and chronicity of asthma is therefore critical to designing more effective therapies and to cure this disease.

Memory CD4 T cells play important roles in the initiation and regulation of asthma and have been shown to coordinate disease pathology through the recruitment and activation of effector cells like eosinophils and mast cells. Allergic asthma is driven by inhaled allergens that, over time, create populations of allergen-specific memory T cells. We have identified a new subset of tissue resident memory CD4 T cell (CD4 TRM) within the lung which are maintained independently of circulating populations and which exhibit peribronchiolar localization that ensure early exposure to inhaled matter. We have further found that CD4 TRM are generated in the lung of mice following long-term exposure to the common household allergen, house dust mite (HDM) allergen. We have found that allergen-specific TRM in the lung are rapidly activated and migrate into the airways upon re-exposure to the allergen. Lung TRM may therefore represent critical targets in new approaches to prevent chronic and recurrent asthma symptoms. I wish to investigate the role of lung TRM in the pathophysiology of allergic asthma. Furthermore I will use antigen specific immunotherapy to target the TRM population and assess the effect on disease severity and chronicity.