Characterizing the Genetics of Chronic Lymphocytic Leukemia

Brandon Isao Yi Chiang (Brandon) Ing, Senior, Biochemistry
Mary Gates Scholar
Mentor: Timothy Tidwell, Molecular & Cellular Biology
Mentor: Marshall Horwitz, Pathology

While there are many known treatments for cancer, few of these treatments address the biological mechanism by which cancer arises. One such mechanism involves mutations in DNA repair proteins, which fall in the category of the Structural Maintenance of Chromosome (SMC) proteins. SMC proteins function in pairs to form the core subunits of cohesins involved in sister chromatid cohesion, condensins involved in chromosome condensation, and an unnamed complex involved in DNA repair. We focused on a particular cancer - Chronic Lymphocytic Leukemia (CLL). CLL leads to an overproduction of B-lymphocytes that spread to the blood and lymph nodes, causing the bone marrow to fail. This results in a low blood count and a weak immune system. CLL occurs sporadically; however, as with other types of cancer, it can sometimes be inherited as a Mendelian trait. We began by screening families where CLL is inherited as a single gene disorder and used genetic linkage plus genomic sequencing to identify a likely candidate gene, C14orf145, which we found to be homologous with SMC proteins. Because SMC proteins function in pairs, we conducted an in-vitro Yeast Two-Hybrid (Y2H) assay, which relies on the growth of yeast cells that have taken up protein-protein complexes. In using the Y2H assay, the c14orf145 protein product was screened against the protein products of all known human genes. We have already identified several interactions using the Y2H assay and we are now in the process of repeating our experiments to better confirm these interactions. The next step will be to conduct directed sequencing of C14orf145 from families who have recently had members diagnosed with CLL. The C14orf145 gene may therefore hold clues for the onset of CLL but more immediately, it can potentially be a gene for testing as a risk factor for CLL.

Antibiotic Cycling and Drug Resistance

Sara Michele (Sara) Drescher, Senior, Biology (General), Individualized Studies
Mary Gates Scholar
Mentor: Benjamin Kerr, Biology

Antibiotic resistance is a serious medical concern, however, there is not yet enough known about the effects of specific drug regimes on resistance development. There are two aspects to the threat of resistance: the ability of microbes to withstand the antibiotics, and the ability of these microbes to persist in the absence of antibiotics. Resistance development usually involves a trade-off against other abilities, such that resistant types are usually less fit than susceptible types when antibiotics are not present. The ability to survive in the presence of antibiotics makes it difficult to treat infections, and the ability to persist without antibiotics allows spread from patient to patient. Our project investigates the relationship between antibiotic exposure and the development of fit, but resistant, types. We are using Escherichia coli and the antibiotic rifampicin to test two dimensions of treatment regimes: the length of cycling periods (1, 4, and 16 days between antibiotic level changes) and the type of cycling (high to zero antibiotic, mid- to low antibiotic, or constant [non-cycling] intermediate antibiotic level). When our 32 day evolution series is complete, we will analyze strain fitness (using growth rate as a metric) in a range of media environments. This will establish the effect of various treatments on the level of resistance achieved by the bacteria, as well as their potential to persist in the environment once treatment is complete. Bacteria which are highly resistant to antibiotics, but have low fitness in the absence of drug, are likely to be outcompeted by drug-sensitive bacteria and not persist in the environment. Those with low fitness in antibiotic can more effectively be treated with drugs. We hope to determine which type of antibiotic use leads to the least resistance or persistence.
Finding Masses of Supernova Progenitors
Zachary Grove (Zach) Jennings, Senior, Physics, Astronomy
Mentor: Benjamin Williams, Astronomy
Mentor: Jeremiah Murphy, Astronomy

When massive stars reach the end of their lifetimes, they erupt in enormous explosions known as supernovae, which leave behind shocked gas and dust known as supernova remnants (SNR). The evolution of these massive stars is a poorly understood area of stellar physics, partially due to a lack of data on the physical properties of these exploding stars. In the past, it has been necessary to, by pure chance, have Hubble Space Telescope (HST) images of the star before it exploded in order to make accurate measurements of its age and mass. We present a new technique in which we instead calculate the age distribution of stars that surround these SNR by examining color-magnitude diagrams of these fields. This in turn allows us to estimate the age and mass of the supernova progenitor star. Our technique has the tremendous advantage of not requiring direct imaging of the precursor star, allowing us to use the large quantity of HST archival data for SNR fields. Successful application of this technique allows us to increase the number of known masses of progenitor stars from a handful to hundreds. We have already applied this technique to seventeen SNR in the galaxy M31, as well as to the famous Supernova 1987a in the Large Magellanic Cloud, where our estimate agrees with the mass measured from serendipitous precursor imaging. We present the results of this initial analysis, and detail our plans to further examine a total of 135 SNR in the galaxies M31 and M33.

SESSION 1C

GENES AND POPULATIONS
Session Moderator: Benjamin Hall, Biology
Mary Gates Hall 228
1:00 PM to 2:30 PM
* Note: Titles in order of presentation.

Genetic Variation of Rhododendron arboreum Populations in South Asia
Ngan Kim Hoang, Senior, Biochemistry, Biology (General)
Howard Hughes Scholar, Mary Gates Scholar
Shaoqun (Simon) Zhou, Junior, Biology (Plant)
Howard Hughes Scholar, Mary Gates Scholar
Mentor: Benjamin Hall, Biology

Rhododendron arboreum is an unusual species within the genus Rhododendron, known for its ability to grow into a tall tree. Its subspecies in Asia are identified by differences in leaf indumentum and corolla color. The Chinese subspecies, ssp. delavayi, which some authors consider to be a different species, is morphologically distinct from the two Himalayan subspecies. To provide an additional means of taxonomic categorization, we examined genetic variation among these subspecies by DNA analysis. In particular, we are closely examining the ssp. delavayi that grows in Yunnan, China in order to gain a comprehensive understanding of the relationships within R. arboreum. Our analyses focus on allelic variation within the non-coding sequences—introns and intergenic regions—of nuclear DNA. These were identified and analyzed using primers for the Polymerase chain reaction (PCR) in adjacent single copy exon sequences. The exons were identified in various large blocks of Rhododendron williamsianum genome sequence by BLAST searches against plant genome databases. The R. williamsianum-derived primer sequences facilitated our search for genotyping markers to examine wild-collected R. arboreum samples by PCR and agarose gel electrophoresis. To date, we have successfully sampled 65 plants from 13 populations throughout Yunnan for 15 markers. The data suggested that there is more allelic variation in the Eastern Yunnan populations compared to the Western ones while it is intermediate in the middle region. This decrease in genetic variability suggested a possible migration event of ssp. delavayi populations from South China into the Himalayan region. Integration of these data into previous results from the Himalayan region provided a better understanding of genetic variation of R. arboreum.

SESSION 1E

SHAPING HUMAN BEHAVIOR: INTERACTIONS OF COGNITION AND SOCIAL CONTEXT
Session Moderator: Judith A Howard, Sociology
Mary Gates Hall 234
1:00 PM to 2:30 PM
* Note: Titles in order of presentation.

Can Autistics Redefine Autism?: The Cultural Politics of Autistic Activism
Karon (Ronnie) Thibault, Junior, Interdisciplinary Studies (SEB)
Mentor: Benjamin Gardner, Interdisciplinary Arts & Sciences

This research introduces a highly engaged community of autistics who insist on a public distinction between their efforts of self-activism and non-autistic agents who advocate on their behalf. What ‘autism’ means, whose interests are reflected in its social representations, and what impact these productions have on public perceptions of the autistic experience, are not well studied or understood. I examine how ‘autism’ is expressed and embodied through conflicting narratives put forth by media, institutions, scholars—and—autistics. Analyzing cultural divisions within this ‘humanly
expressive’ system of difference contextualizes the meaning of autism within an emerging cultural struggle over representation and justice. The study draws experiential evidence of autistic voice; a narrative they argue is largely hidden from society. In this study I ask, can autistics redefine autism? How will this definition reframe their position in political discussions about them? This examination illustrates emerging cultural tensions over autistic representation and justice; who has the right to speak for the autistic community, and how the value of ‘autistic being’ is characterized in the public domain. I draw on textual, media, and narrative analysis to reveal a population fighting for representation within the popular discourse of autism, which frames their experience as tragic, afflicted, and deficient. Activists battle metaphorical stigmas reproduced by non-autistic agents who rely on the deficit model of autism to garner economic and public support. They further argue these reproductions encourage the conditions for social stigma, stereotypes and abuse. This deficiency discourse propels autistics into a paradox forcing them to characterize what autism is not—an absurd consequence produced by their constant exclusion from the public discussion of what autism is.

SESSION 1L

NEUROSCIENCE: DEVELOPMENT, BEHAVIOR, AND ENDOCRINOLOGY

Session Moderator: Horacio de la Iglesia, Biology
Mary Gates Hall 284
1:00 PM to 2:30 PM

* Note: Titles in order of presentation.

Quantifying the Effect of the Nuclear Orphan Receptor GCNF in Retinoic Acid Signaling
Andrew Yiu (Andrew) Chan, Junior, Neurobiology, Biochemistry
Mary Gates Scholar
Mentor: David Kimelman, Liberal Arts
Mentor: Benjamin Martin, Biochemistry

The zebrafish, like all vertebrates develop progressively from the neck down to the end of the tail. This process requires many cell-cell signaling processes. In early development, retinoic acid is a teratogen that can cause severe posterior truncations when added to embryos. Our main focus is to determine the mechanism of retinoic acid teratogenicity. In a DNA microarray, we tested the response of numerous genes involved in development in response to the inhibition of GCNF in the presence of added retinoic acid.

Circadian rhythms are daily rhythms that dictate physiological and behavioral patterns. Disruption of the brain’s master circadian pacemaker, the hypothalamic suprachiasmatic nucleus (SCN) can result in health problems including reproductive disorders. In mammals, ovulation happens when a surge of gonadotropin-releasing hormone (GnRH) induces a surge of luteinizing hormone (LH), which stimulates the ovary to release an egg. This GnRH surge is time-of-day dependent, but how the GnRH cells “decide” when to surge is unknown. Our goal is to discover the neural pathways through which the SCN times ovulation. Using unilateral SCN lesions, we found that intact neuronal projections from the SCN are necessary for the GnRH surge. The unilateral loss of GnRH coincided with decreased expression of kisspeptin mRNA (Kiss1); kisspeptin is the strongest known physiological activator of GnRH cells. The SCN projects both to Kiss1 positive cells in the anteroventral periventricular nucleus (AVPV) and to GnRH cells, from its dorsomedial (dm) and ventrolateral (vl) subregions, respectively. We were able to behaviorally separate the daily rhythms of these two subregions, which revealed that the LH surge and upregulation of AVPV Kiss1 both depend on output from the dorsomedial SCN specifically. The dmSCN contains a population of neurons that produce vasopressin as a neurotransmitter; this population projects heavily to the AVPV. Acute pharmacological treatment with vasopressin in the AVPV is known to
cause an LH surge but only at certain times of day. This indicates the need for at least one other circadian oscillator to be coordinated with the SCN vasopressin output to trigger the LH surge. We provide evidence that the AVPV is capable of filling this role.

Session 1P

Engineering Devices and Mathematical Foundations

Session Moderator: Kristi Morgansen, Aeronautics & Astronautics
Mary Gates Hall 389
1:00 PM to 2:30 PM

* Note: Titles in order of presentation.

Sending Power Wirelessly via Resonant Magnetic Field
Jordan Thomas (Jordan) Reed, Senior, Physics
Kara Renee Kagi, Senior, Electrical Engineering
Brian Thomas Govier, Senior, Physics
Mentor: Alanson Sample, Electrical Engineering
Mentor: Benjamin Waters, Electrical Engineering
Mentor: Joshua Smith, Computer Science & Engineering, Electrical Engineering

With the increasing ubiquity of battery powered devices such as cell phones and laptops, it has become more and more desirable to improve their mobility by eliminating the need to be plugged into an outlet. One prominent example of wireless power transfer is known as the power mat, which wirelessly charges a cell phone or camera over a distance of a few cm using the magnetic flux created by an inductive circuit. Under the same principal, circuits that utilize large-size wire coil inductors oscillating at the same resonant frequency allows power transfer to take place wirelessly through the magnetic flux created by the coupled circuits over much larger distances. Previous efforts concentrating on the use of magnetically-coupled inductors to propagate practical amounts of power through air over distances on the order of a few coil diameters have been successful. However, in order to increase the efficacy of this technology, the system ought to be both simple and inexpensive. By testing different oscillator designs that utilize different transistors, a small and inexpensive oscillator circuit was developed to replace the expensive components of the original design. Past studies have shown power-transfer efficiencies of 70% in a 2ft range with the use of the expensive amplifier. As such, the efficiency of this system was expected to produce similar results. Using several magnetically resonant coils designed to oscillate around the same frequency, a DC power source, and an oscillator circuit to drive the system at the desired frequency, we have been able to demonstrate power transfer over distances of about one coil diameter. To produce data that is significant to real-world applications, this system is being characterized over a 1 meter distance. Within this distance, efficient wireless power transfer has many practical uses, from powering laptops to implanted medical devices.

Poster Session 2

Balcony, Easel 102
2:30 PM to 3:30 PM

Rhododendron Evolutionary History Reconstruction using Ty1-copia Retrotransposons
Kali Tyler (Kali) Witherspoon, Senior, Biology (Molecular, Cellular & Developmental)
Mentor: Benjamin Hall, Biology

Retrotransposons exist as genetic elements within chromosomal DNA that can replicate themselves and move to new locations within a genome, using a process involving an RNA intermediate. Retrotransposons are the most widespread class of transposable elements, being abundant in the genomes of humans, insects, yeast and plants, where they comprise as much as 70% of the genome. The two most common retrotransposon families, Ty1-copia and Ty3-gypsy, occur across eukaryotic phyla and have a similar genetic organization. In their chromosomal form, they are flanked by direct repeats of a regulatory sequence called the long terminal repeat (LTR). The region between the two LTR’s contains sequences that encode a core RNA binding protein (GAG) and a polyprotein made up of protease, integrase, reverse transcriptase and RNAase H domains: all of them enzymes required for Ty element replication. This project has involved a search of genomic sequences from Rhododendron williamsianum for Ty1-copia elements, using their LTR and protein-coding regions as queries. We obtained sequences of several intact and many incomplete Ty1-copia retrotransposons from R. williamsianum. Most of the copies encountered are nonfunctional ones, either because of deletions of essential sequences or the occurrence of other types of mutations, for example nonsense or frameshift changes. Given that some of the individual Ty-1 insertions have been present at the same site through long periods of Rhododendron species divergence, the nonfunctional mutant Ty-1 copies are considered to be ancient. We estimated that there are about 200 active Ty1s in the genome. The location of a specific Ty1-copia LTR sequence in the genome was used as a phylogenetic marker to compare R. williamsianum with other species of Rhododendron. We also used the sequences to study the evolutionary history of the Ty1-copias within the genome as a whole.

Poster Session 2

Balcony, Easel 101
2:30 PM to 3:30 PM
Toward a Highly Resolved Phylogeny of *Fortunea* Rhododendrons
Judith (Judy) Carlson, Junior, Biology (Molecular, Cellular & Developmental)
Mentor: Benjamin Hall, Biology

Historically, rhododendrons and other plants were classified using traits such as flower and leaf morphology or geographical location to posit relationships. This practice is limited by the number of phenotypic traits detectible between species. Phylogenetic analysis based on DNA sequence reveals numerous new traits consisting of Single Nucleotide Polymorphisms (SNPs) and other mutations among and between species and has made it possible to directly infer lineages. My research is focused on Rhododendron subsection *Fortunea*, comprising some 45 species. The goal is to gather DNA sequence information from many parts of the genome and to use it in establishing a phylogenetic tree for *Fortunea*. This requires finding insertion or deletion (indel) markers throughout the genome that are specific to some species, but not others. Previous research in the lab has produced a phylogeny of *Fortunea*; however, the data used to construct the tree was from three specific genes, cataloguing every SNP and mutation for each species in those genes. My research is aimed at unveiling large indels within many disparate regions of the genome: I theorize that combining the intergenomic data I am collecting with the data from specific genes will generate a more highly resolved phylogeny of subsection *Fortunea* than presently exists. To collect this data, I use PCR primers to amplify sections of the genome (specifically introns and intergenic regions) in six diverse species and compare the *Fortunea* sequence to the known sequence of a related subsection. I then design specific *Fortunea* primers to amplify regions spanning any indels that I find, using these to genotype all of the species in the subsection. So far, I have isolated six promising mutations for which I have genotyped most of the species in the subsection, revealing a foundation that I will elaborate on as I find more mutations.

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**SESSION 2D**

**GOVERNANCE, THE ENVIRONMENT, AND PRIVATE MILITARIES**

Session Moderator: Joel Migdal, Jackson School International Studies
Mary Gates Hall 238
3:30 PM to 5:00 PM

*Note: Titles in order of presentation.

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**SESSION 2K**

**MCNAIR SESSION - ADVENTURES AND INNOVATIONS IN BIOLOGICAL AND PHYSICAL SCIENCES**

Session Moderator: Gabriel Gallardo, Geography
Mary Gates Hall 287
3:15 PM to 5:00 PM

* Note: Titles in order of presentation.

Classification of X-ray Sources in the Direction of Andromeda using Optical Spectroscopy
Jerica Makiko (Jerica) Green, Senior, Astronomy, Physics
EIP Scholar, Undergraduate Research Conference Travel Awardee
Mentor: Benjamin Williams, Astronomy

A deep XMM survey has identified hundreds of bright X-ray sources from the direction of Andromeda. These sources are
mostly comprised of supernova remnants, X-ray Binaries and background Active Galactic Nuclei (AGN). We have obtained 39 optical spectra of their candidate counterparts using the 3.5-meter telescope at the Apache Point Observatory. After calibrating and extracting the objects’ spectra from the sky background, we’ve been able to classify 12 as background AGN with red shifts (1.15 < z < 2.11). Preliminary classifications of the 27 others include 9 stars in Andromeda and 1 supernova remnant in Andromeda. With these results we are beginning to constrain the background contamination in the XMM survey and to find good high-mass X-ray binary candidates in Andromeda. Furthermore, future high-resolution spectroscopy of the background AGN may allow detailed absorption studies of the Andromeda interstellar medium. With these results, we hope to gain a better understanding of the distribution of X-ray sources in the universe, and learn more about galaxies in general.

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**SESSION 2S**

**STRUCTURE-FUNCTIONAL STUDIES OF BIOLOGICAL SYSTEMS**

*Session Moderator: Ram Samudrala, Microbiology*

**Johnson Hall 175**

3:30 PM to 5:00 PM

* Note: Titles in order of presentation.

**Drug Cycling and the Evolutionary Trajectory of Antibiotic Resistance**

*Rachel V. (Rachel) Sobel, Senior, Biology (Ecology, Evolution & Conservation)*

*Mary Gates Scholar*

*Mentor: Benjamin Kerr, Biology*

The distribution of an organism’s exposure to an environment has been demonstrated to dramatically impact its evolutionary trajectory. To investigate the details of this phenomenon, we performed a serial transfer experiment, using the interaction of E. coli bacteria and the antibiotic rifampicin as a model system. All treatment wells were given the same sum amount of the antibiotic over the course of a 32-day treatment period, cycling between one of several high drug-concentration environment and the corresponding lower drug-concentration environment with a number of different cycle lengths. We are interested in the effect of the different lengths and amplitudes of the drug treatment regimen on the resistance level and overall fitness of our evolved cultures.