Columbia College
Rabi Scholars Program

7th Annual
Science Research Symposium
12 October, 2012

Presentation Abstracts

CONTENTS

****

Rohan Bhandari: Physics, CC'13

Increasing the Timing Precision of the Liquid Argon Calorimeter of the Large Hadron Collider

Mentor: Professor John Parsons, Department of Physics, Columbia University

Even though the Liquid Argon Calorimeter has excellent timing precision, certain physics analyses, such as the search for evidence of supersymmetric models, require even greater resolution. Because of this, a timing calibration and resolution study using events with a Z particle decaying to two electrons was carried out to optimize the precision. The calibration required five corrections. The run number correction takes into account timing changes that occur between runs, such as those from seasonal changes and maintenance work. The front end board and channel offsets account for the discrepancies between the clocks of the different boards and sampling times, respectively. The timing can also be distorted if large amounts of energy are measured by a cell of the calorimeter. The energy-dependent correction adjusts for this. Lastly, there is a correction applied for cases in which the collision does not occur at the exact center of the detector. After all the corrections were applied, a timing resolution of ≈300 picoseconds is reached, given a cell with a large energy deposit.

****

Nathan Booth: Physics, CC'14

Elementary Matrix Decomposition in Real Quadratic Fields

Mentor: Professor Marc Masdeu-Sabate, Department of Mathematics, Columbia University

This project was centered on finding decompositions of 2x2 matrices with determinant 1 whose elements relate to certain groups in specific ways. A paper written by L. N. Vaserstein established that these matrices can be written as products of "elementary matrices," matrices of a very specific form. This is equivalent to the problem of writing continued fractions in quadratic fields. We attempted to make that theorem explicit by writing an algorithm to perform the decomposition whose existence the paper proved. Such an algorithm would take as input a 2x2 matrix of the correct form, and output a series of matrices which are factors of the input matrix. Development of this algorithm required using methods from various other papers about the groups and matrices involved. All algorithm programming was done using the Sage open source mathematics software. The algorithm has been created, but is not as consistently effective as we would like, so we are still working on it.

****

Rena Chen: Astrophysics, CC'14

Synthesis of Cadmium Oleate and Oleate-Bound Cadmium Selenide Quantum Dots

Mentor: Professor Jonathan Owen, Department of Chemistry, Columbia University

Quantum dots are semiconductor nanocrystals useful in the construction of future optical electronic devices because of their unique photophysical properties. Ligands bound to quantum dots affect properties such as photoluminescence, stability, and structure. Since they absorb and emit in the visible range, cadmium selenide quantum dots have been investigated for their potential use in solar cells and light emitting diodes. The synthesis reported by Chen et al. of CdSe quantum dots from cadmium myristate, oleic acid, and selenium dioxide yields quantum dots bound by a mixture of myristate and oleate ligands. The oleate ligand is particularly useful due to the double bond in the alkyl chain. This "kink" in the carbon chain provides a unique handle for NMR and may impart greater solubility to the cadmium precursor

during nanocrystal synthesis, resulting in higher yields with less solvent. After synthesizing and purifying large quantities of cadmium oleate, we successfully modified and streamlined the CdSe quantum dot synthesis by Chen et al. using cadmium oleate in place of cadmium myristate. We found that the quantum dot reaction can be executed at higher concentrations without injecting oleic acid to stabilize growth. The cadmium oleate and oleate-bound CdSe quantum dots were characterized using NMR, UV absorption spectroscopy, and transmission electron microscopy.

****

Woo Chang Chung: Mathematics, Physics, CC'13

Characterization of the Epitaxial Growth of Bi2Se3 on h-BN Substrate

Mentor: Professor Abhay Pasupathy, Department of Physics, Columbia University

Topological insulator is a new state of matter that is of high interest to both theoretical and applied physicists. Topological insulators are insulating in the bulk domain but metallic on the surface, and they are predicted to have surprising electronic transport properties, such as locking of spin perpendicular to electron momentum and protection from scattering by time-reversal invariant disorder. Bi--$_2$Se$_3$ is a three-dimensional topological insulator with a bulk band gap around 0.3 eV, which is larger than the thermodynamic energy scale of room temperature, making it a promising material for future applications such as in spintronics. An experimental problem with growing single-crystalline Bi--$_2$Se$_3$ is the difficulty of obtaining an atomically sharp interface between the crystal and the substrate; hexagonal boron nitride (h-BN) is a nice candidate for the Bi_2Se_3 film substrate in this respect because of its amazing flatness. In the summer of 2012, I studied the epitaxial growth of Bi2Se3 films on h-BN, SiO2, and sapphire substrates by atomic force microscopy (AFM); film growth was done by collaborators at Rutgers University. AFM images of the film surfaces show that films grown on h-BN is superior to those on SiO2 in terms of flatness and crystallinity, and comparable to those on sapphire. It is of high interest how these growth characteristics translate to gated device performances, and future studies will involve fabricating a gated Bi2Se3 / BN device with Hall geometry and measuring its surface electron mobility and other transport properties.

****

Bridget Collins: Biological Sciences, CC'15

Developing novel lambda bacteriophage substrates to enhance single-molecule studies

Mentor: Professor Eric Greene, Department of Biochemistry and Molecular Biophysics, Columbia University

The study of biological processes at the single-molecule level affords a much clearer and accurate understanding of their underlying mechanisms compared to bulk studies. For example, methods of target-search during homologous recombination and translocation properties of RNA polymerase on diverse DNA substrates have been analyzed on single DNA substrates under total internal reflection microscopy (TIRF) using a DNA curtain assay with nanofabricated barriers. The Greene lab typically uses the 48.5-kb lambda bacteriophage genome as a DNA substrate upon which to visualize protein-protein interactions in single-molecule optical experiments. Sequences of interest, such as the *lac* operon, are routinely cloned into a specific site on lambda that does not interfere with essential genes. Because lambda's restriction map contains a limited number of unique sites at which to insert sequences, we designed a novel restriction map for lambda containing ten evenly-spaced restriction sites, at which locations an insertion would not interfere with essential genes. This new substrate would enhance single-molecule visualization of DNA

repair pathways by increasing the variety and diversifying the location of potential sequence insertions on lambda. The map introduces three new sites – a new NheI-BmtI, SpeI, and NotI – and abolishes two – NheI-BmtI and PvuI. To test the feasibility of such large-scale genomic re-modeling, wild-type lambda was digested with five restriction enzymes into six fragments, re-ligated, and successfully packaged into infectious particles. In the creation of the novel substrate, traditional cloning techniques were used to amplify ten fragments of lambda and re-ligate them in such a way as to ensure sequence preservation and introduce or abolish restriction sites. The novel lambda will be propagated by packaging into viral capsids followed by bacterial infection and lytic growth. To use this substrate, a method of single-restriction site insertion, using PCR primers containing two sites of complementary overhangs, was developed and tested to enable facile cloning. We are also currently exploring the potential of single-stranded oligonucleotide recombineering as a viable method of genetic manipulation. In the future, this unique lambda substrate will lead to the juxtaposition of diverse sequences of interest for a diverse array of single-molecule experiments.

****

Kevin Guo: Mathematics, CC'15

Virus Classification with Hierarchical Motif Clustering

Mentor: Professor Christopher Wiggins, Department of Applied Mathematics and Applied Physics, Columbia University

I present Hierarchical Motif Clustering, a method for learning models for viral host classification by incorporating multiple protein subsequences (kmers) into each decision rule. I programmed a boosting algorithm to select a combination of features from a large search-space of seed kmers. At each boosting round, Hierarchical Motif Clustering selects a group of kmers as a decision rule, whose combination is highly predictive of a virus's respective host. In this way, each round can incorporate multiple kmers into a single decision rule while accounting for possible substitution, or shift mutations between virii of the same family. Furthermore, Hierarchical Motif Clustering can identify possible regions of biological significance in a virus, with the logic that PSSMs and kmers that are strong classifiers of host must contain something that allows infection. Each decision rule of our boosting model is either a kmer or a PSSM that is built through agglomerative clustering of kmers with low boosting loss. I demonstrated that a combination of kmer mismatches and Hierarchical Motif Clustering with offsets classifies better than just kmers with mismatches. Furthermore, Hierarchical Motif Clustering runs significantly faster than just kmers and without preprocessing of data. Data included 146 picorna virii with host vector (vertabrate, invertabrate, plant); 500 H1N1 virus with hosts (bird, human); 300 pH1N1 virii with hosts (human, swine); 300 pH1N1 virii with hosts (pandemic, non-pandemic); and finally 126 virii of herpesviridae with hosts (virulent, benign). In each run, Hierarchical Motif Clustering consistently recovered regions of biological significance in the viral genome with high accuracy (90%+). In future work, we will look to extend the Hierarchical Motif Clustering Boosting Algorithm to oncogenic virii datasets (polyoma virus, Human Papiloma Virus), in order to locate cancer-causing parts of the viral genome.

****

Raina Jain: Biological Sciences, CC'15

Mechanisms of long-term resistance of small molecule inhibitors acting against BRAF mutations

Mentor: Dr. Christina Pratilas, Department of Pediatric Oncology, Memorial Sloan Kettering Cancer Center

The RAF/MEK/ERK pathway is an area of investigation as a target for therapeutic intervention because mutations in the RAS/RAF gene families are common in human cancer. RAF inhibitors inhibit RAF-MEK-ERK signaling and thus, tumor growth, in cells that express V600E mutant BRAF. Several RAF inhibitors have been developed and shown promise in melanoma patients; however, resistance generally develops after 7-9 months of treatment. The development of resistance to RAF inhibitors has been linked to multiple mechanisms, including mutations in RAS, mutations that activate RAF dimer formation, and activation of receptor tyrosine kinase. Recent experiments aimed at studying a combination of inhibitors of both pathways to overcome resistance. Cell lines resistant to RAF inhibitors, and parental counterparts, were treated with inhibitors of both pathways. In the BRAF V600E cells resistant to the RAF inhibitor, the PI3K inhibitor had some effect on signaling and growth, while the greatest inhibition was shown by the combination of both drugs. In contrast, the parental cell line (mutation in BRAF) retained sensitivity to the RAF inhibitor, and demonstrated little effect in response to PI3K-AKT kinase inhibition.Cell counts and proliferation assays supported these data. The parental cells were inhibited by ~90% with RAF inhibition. Cells resistant to RAF inhibitors were greatly inhibited by both the pi3k inhibitor and the combination of pi3k and RAF inhibitors. This was seen using several different ATP-competitive small molecule inhibitors of PI3k. While several mechanisms of resistance to RAF inhibitors have been described in models of BRAF V600E melanoma, these data support activation of PI3k-AKT signaling as an additional mode of reducing sensitivity to RAF inhibitors, and may play a role in tumor progression in patients receiving these drugs. This research will aid in understanding the development of resistance in patients treated with vemurafenib and other RAF inhibitors, and potentially identify rational combination strategies to delay the emergence of resistance.

****

Pin-Joe Ko: Biology, CC'14

Analyzing microtubule tip protein interactions and microtubule dynamics in fission yeast

Mentor: Professor Fred Chang, Department of Microbiology and Immunology, Columbia University Medical Center

Plus-end tracking proteins (+TIPs) are a class of proteins that localize to the tips of microtubules, and play a crucial role in regulating microtubule dynamics. In this project, we use the fission yeast *Schizosaccharomyces pombe* as a model to understand how +TIPs regulate microtubule dynamics. *S. pombe* are useful in studying microtubule dynamics because there are only a small number of microtubule bundles in fission yeast, and there are only eight known +TIPs: mal3, alp14, tip1, tea1, tea2, tea4, klp2, and klp5. Mal3 (an EB1 homologue) may be a master regulator of the microtubule plus end. Here we show the effects of deleting mal3 (*mal3Δ*) on +TIP levels to get a sense of tip protein interactions. Tea1, tea2, tea4 and klp2 are all unable to localize to microtubule tips in *mal3Δ* cells. Alp14 intensity is decreased, though analysis of movies suggests that reduced quantities are caused by different microtubule dynamics rather than a direct dependence on mal3. Klp5 is unaffected by *mal3Δ*, confirming that the localization of klp5 is independent of mal3 expression. Tip1 is able to localize partially to microtubule tips without mal3.

****

Nilay Kumar: Physics, CC'15

Jet shapes as discriminants in Higgs to diphoton vector boson fusion

Mentor: Professor Emlyn Hughes, Department of Physics, Columbia University

The Standard Model of particle physics explains in its current formulation a truly wide variety of particle phenomena. However, the mechanism through which fundamental particles attain their mass has only recently (and rather tentatively) been observed experimentally at the LHC. This mechanism is predicted by the Standard model to manifest itself through the presence of the electrically neutral spin zero Higgs boson. Indeed, in July of 2012, CERN formally announced the discovery of a boson with properties that seem to be consistent with those expected of the Standard model Higgs (SM Higgs). However, more data is needed to confirm that this is so; quantities such as production and decay channel cross-sections, angular correlations of decay products, etc. must be precisely determined. In particular, vector boson fusion (VBF) Higgs production is a theoretically interesting quantity that has yet to be extensively studied in the data. VBF is the dominant Higgs production channel that is solely electroweak in nature, and as the Higgs mechanism's primary purpose is to mediate electroweak symmetry breaking, the VBF regime provides an important check of the Standard Model.

The Higgs search analysis, while extremely sensitive to Higgs production, is not optimized for discrimination between various production modes (VBF vs ggH, etc) – this project studies the use of jet shapes in such discrimination. The two jet shapes studied here are the calorimeter width of jets and the number of tracks associated with each jet. It is generally expected that VBF jets have narrower widths and fewer tracks than non-VBF jets, which could yield discrimination power. In this work we perform non-VBF background composition studies (via simulations) and show that it has a predominantly VBF-like signature. Consequently, jet shapes seem to be impractical as discriminants in cut-and-count analyses, given the low statistics in VBF physics. However, we postulate that jet shapes may find some use in future multivariate analyses.

****

Alexis Kurmis: Chemistry, CC'13

Immuno-SERS Techniques for Localization of Proteins in Samples from Artworks

Mentor: H.Y. Lee, Metropolitan Museum of Art

Different types of paints, glues, and other art materials contain different proteins, depending on what natural materials they are made of. For example, tempera paint is made using eggs, and would therefore contain ovalbumin, a glue or paint made using milk would contain casein, and ones made using extracts of animal skin would contain collagen type I. Information about what materials were used to create artworks is useful for both art historians and conservators. Many methods for identifying proteins are bulk analysis techniques, however, and do not conserve information about layers that may be present in a sample. One example is an enzyme-linked immunosorbent assay (ELISA), where a system of antibodies can be used to identify proteins and gums.

The goal of this summer was to improve the technique of using surface enhanced Raman scattering (SERS) combined with immunological methods to gather information about materials in paint layers. This involved using a SERS nanotag-reporting system to localize specific proteins in cross sections of paint samples using techniques based on ELISA. This required the preparation of cross-sections in acrylic resin by dry polishing; the activation, purification and construction of the SERS-tagged secondary antibodies;

immunological techniques, and analysis using Raman spectroscopy. The biggest challenge encountered was the nonspecific binding of the antibodies to other layers of the cross sections, so tests were conducted to find the best blocking solution to prevent this. Soy milk was found to significantly improve results when compared to the blocking system used in the ELISA method, but it is not entirely effective in preventing all nonspecific binding. Future tests to be done include the use of siloxanes as blocking agents and the pre-incubation of primary and secondary antibodies before application to the cross-section.

****

Dan Margulies: Chemical Physics, CC'13

Exact Solutions for Interference Effects in Modeled Molecular Conductance

Mentor: Professor Latha Venkataraman, Department of Applied Physics, Columbia University

Based on my previous research through the Rabi program, I explored the relationship between the shape (topology) of molecules and their electronic properties using a tight binding Green's functions approximation for the electronic transmission function. Using several fundamental equations from linear algebra and transmission theory, I was able to determine several illuminating results about the role of interference due to branches and side chains within larger molecular structures. The self-energies due to coupling the side branches were determined analytically and applied to a general n-atom chain. Side branches were found to introduce competing pathways in the conducting system of the molecule, while side branches which dead-ended introduced destructive cross-interference which has been observed experimentally. The strength of these coupling effects varied according to the number of atoms in the chain, exactly as expected.

****

Julia Oktawiec: Chemistry, CC'13

The Zinc-Catalyzed Polymerization of Lactide

Mentor: Professor Ged Parkin, Department of Chemistry, Columbia University

The *tris*(2-pyridylthio)methyl ligand, [Tptm], has recently been used to synthesize a variety of zinc complexes, such as the methyl, hydride, *bis*(trimethylsilyl)amide, and trimethylsiloxide derivatives: [κ^3-Tptm]ZnMe, [κ^3-Tptm]ZnH, [κ^3-Tptm]ZnN($SiMe_3$)$_2$, and [κ^4-Tptm]ZnO$SiMe_3$. These compounds have been found to serve as useful starting materials for the synthesis of other derivatives. In addition to their use as synthetic precursors, [κ^3-Tptm]ZnH, [κ^3-Tptm]ZnN($SiMe_3$)$_2$, and [κ^4-Tptm]ZnO$SiMe_3$, and other related zinc complexes have been found to be efficient initiators for the ring-opening polymerization of lactide, the cyclic diester of lactic acid, to form polylactide. Polylactide is biodegradable and can be formed using renewable resources, but its applications are limited by the use of currently popular catalysts that feature toxic metals such as tin. As a result, there is interest in finding effective initiators with cheap and biocompatible metals, such as zinc. In this project, [κ^3-Tptm]ZnH was utilized for the synthesis and characterization of new zinc complexes incorporating the [Tptm] ligand. Kinetic and mechanistic studies of the compounds on the ring-opening polymerization of lactide were performed.

****

Jungsik Park: Phuysics, CC'13

Studying Raman spectra of Graphene

Mentor: Professor Aron Pinczuk, Department of Physics, Columbia University

Graphene has unique two-dimensional structures of carbons. Their properties are also distinct. This made the material a hot topic in condensed matter physics, material science, and so on. Meanwhile, Raman spectroscopy allows one to study atomic structures. Different kinds of materials demonstrate different kinds of spectra, and for this reason, one can distinguish a material from others. Obtaining good samples of graphene is essential, and by using Raman spectroscopy, we are able to check if a sample has graphene that is pure enough to be studied. To illustrate, if the asserted graphene contains defects, this is shown by Raman spectra of it. Also, if it has too many layers of carbon to be called graphene, this is again illustrated by the Raman signals of it. Therefore, Raman spectroscopy is indispensable in conducting proper studies of graphene. In this summer, I obtained Raman spectra of graphene deposited on h-BN and Sapphire. In addition, in order to reduce the time in analyzing the obtained Raman spectra, I wrote a program which accepts the Raman spectra as a file that consists of numbers, and creates new spectra that gives us the construction of the graph as a sum of Lorentzian functions. This program will allow us to figure out the ideal growth conditions of graphene more quickly.

****

Darpan Patel: Biology, CC'14

Identification of a distinct death mechanism for the anticancer drug sorafenib: highlighting the therapeutic potential of system x_c^- inhibition

Mentor: Professor Brent Stockwell, Department of Biological Sciences, Columbia university

System x_c^- is a Na^+-independent transporter exchanging glutamate for cystine at the plasma membrane, implicated in drug resistance, metastatic potential, stem-cell like maintenance, cell viability, and tumor growth. Inhibition of system x_c^- by the small molecule erastin triggers ferroptosis, an iron-dependent, non-apoptotic cancer cell death program. We sought to characterize the therapeutic potential of erastin-related system xc activity by using more complex *in vitro* models. Multicellular tumor spheres (MCTSs), formed by inhibiting protein-interactions necessary for adhesion to a solid substrate, better mimic the genetic heterogeneity, cell-cell interactions, hypoxic nodes, and other structural features of solid tumors. Erastin retained lethality through a ferroptotic mechanism in MCTSs, suggesting possible antitumor potential. System x_c^- activity is often responsible for chemoresistance to many anticancer agents, spurring us to test erastin and 1-[S,R]-buthioninesulfoximine, which inhibits synthesis of the predominant cellular antioxidant glutathione, for their ability to sensitize cancer cells to a panel of anticancer compounds. An unexpected synergy was found between erastin and sorafenib, a multi-kinase inhibitor of Raf-1, VEGFR, and PDGFR. While sorafenib has been thought to execute cancer cell death through a caspase-dependent apoptotic pathway, inhibitors of ferroptosis effectively suppressed sorafenib-induced death. More tellingly, in an enzyme-coupled glutamate release assay, used to measure the direct effect of compounds on system x_c^- activity, reduction of glutamate transport by sorafenib was approximately equal to that of erastin, suggesting that sorafenib may be eliciting direct system x_c^- inhibitory activity—a previously unidentified molecular target for this drug. This identification of sorafenib as an approved anticancer agent that can induce ferroptosis through system xc inhibition, in tandem with conservation of the ferroptotic death program in more complex *in vitro* cancer models, highlights the therapeutic potential for targeting this pathway *in vivo*.

Katharina Shaw: Chemistry, CC'13

Interchanging the miRNA Dependence of Hepatitis C Virus

Mentors: Drs. Charles Rice, PhD and Robert Darnell, MD/PhD at The Rockefeller University

Liver-specific Micro-RNA (miRNA) 122 facilitates hepatitis C virus (HCV) replication by recruiting a RISC-like complex containing Argonaute 2 to the 5' end of the HCV genome. This requires basepairing between the miR-122 seed site and two sequences in the 5'UTR of the HCV RNA. A consequence of HCV replication in hepatocytes is the functional de-repression of host miR-122 targets, or the so-called "miR-122 sponge effect." To determine whether HCV's utilization of miR-122 during replication specifically mediates this sponge effect, I sought to exchange the miRNA dependence of HCV. Overlap PCR methods were utilized to generate HCV mutants capable of binding alternative miRNAs – their replication competency was determined after transfection of three different cell types through luciferase assays and real time quantitative PCR. The M15 mutant, designed to bind miR-15 in place of miR-122, replicates in Huh7.5 cells. Additionally, M15 replication is boosted in the presence of miR-15 mimic and is insensitive to LNA-122, making M15 a promising candidate for a miR-122 independent virus. Further inhibition studies are necessary to prove M15 is miR-15 dependent. If M15's miRNA dependence proves to have been swapped, M15 provides an avenue by which to study the "miR-122 sponge effect" and its specific role during viral replication.

****

Hyoun Ju Sohn: Physics, CC'13

18-Amide Self-Assembly on Graphite & Graphene: Observations of Ostwald Stage on Graphite and Self-Assembly on Graphene

Mentor: Professor George Flynn, Department of Chemistry, Columbia University

2D crystal self-assembly of organic molecules has been at the center of attention due to its potential to validating intriguing Nano-range molecular interactions. The method of liquid-solid interface STM scanning is useful in cases in which solvent influence is also studied. A platinum-iridium STM tip scans within the solution, yet above the molecule conglomeration on the substrate while measuring tunneling current to construct topological data. 18-amide is an 18-carbon chain with a benzene ring and amide group attached in succession at one end. 18-amide self-assembly has been previously studied and observed to form 6 different configurations depending on concentration and solvent type. In this paper, first we observe transitional stages within self-assembly of 18-amide on graphite. The ostwald stage is observed for 18-amide in phenyloctane on graphite. Transitions between phases I and II take place, as evidenced by consecutive scans of differing domain distribution of phase I & II. In addition, self-assembly of 18-amide on graphene is studied using the same conditions used on graphite (1mM of 18 amide in phenyloctane). Graphene is a single sheet of graphite and has been studied to possess many interesting characteristics such as high robustness and electrical conductance. High atomic resolution of self-assembly on graphene was not retrieved, although low-resolution scans show similar self-assembly behavior of 18-amide as that on graphite. Parallel lines with an average distance of 5nm apart despite copper film corrugations are an example.

****

Tyler St. Denis: Biochemistry, CC'15

Efforts towards the total synthesis of rufescenolide: a biosynthetic key of [2.2.2] octane **lignan natural** products

Mentor: Professor Scott Snyder, Department of Chemistry, Columbia University

The Snyder group has long been interested in the total syntheses of various unique oligomeric natural products, including several that possess distinctive [2.2.2]-bicyclic motifs. These include the helicterins as well as the yunnaneic acids, molecules that have served as templates for the development of novel synthetic approaches and the development of new reactions. They have also provided a means to explore biogenetic hypotheses for their formation in Nature. In this poster, we will recount how our efforts to prepare a recent related isolate, a compound known as rufescenolide, affords support that our overall synthetic approach may mirror that deployed in Nature in her synthesis of this unique [2.2.2]-bicycle.

****

Wook Hyon Yoon: Biological Sciences, CC'15

Mechanistic analysis of the conformational reaction cycle of EttA

Mentor: Professor John Hunt, Department of Biological Sciences, Columbia University

The ABC-F protein family, despite having multiple representatives in eubacteria and eukaryotes, has evaded a clear functional characterization. Unlike other characterized ABC proteins, ABC-Fs do not participate in membrane transport or power mechanical processes. EttA, an energy-sensing translational throttle A, is a protein translation factor that gates ribosome entry according to ADP-ATP ratio. By fluorescently labeling this protein and running binding experiments with ribosomes, we aimed to further clarify the function of EttA. In order to do so we needed to engineer two mutants of Etta with only one solvent-exposed cysteine by substituting out one of two solvent-exposed cysteines in wild-type EttA. After the mutant strains of EttA were purified the expression of the mutants were assayed and compared to wild-type EttA. Through SDS gel electrophoresis, the expression of the two mutants was found to be sufficient for fluorescence labeling. Despite the attempt, the two mutants of EttA could not be labeled due to the two native cysteine residues buried inside the protein structure. Thus, this set of experiments has confirmed that it is necessary to engineer a new mutant with an engineered cysteine in a desired location that will be accessible. After this mutant is labeled, binding experiments with ribosomes will be performed to further elucidate the function of EttA.

****

Samuel Zeng: Biological Sciences, CC'15

Induced β-cells Require Maturation Period prior to Full Functionality

Mentor: Professor Qiao Zhou, Harvard Stem Cell Institute

Afflicting over 25 million Americans, Type 1 diabetes involves the autoimmune destruction of β-cells, leading to an inability to regulated glycemia. A crucial step in curing this disease, therefore, is replenishing the depleted β-cell population. One approach has been to try and differentiate stems cells into functional β cells as replacements. But of late, there have been attempts to directly reprogram one adult cell form into another. The appeal of this approach is a potentially shorter production time, as well as greater *in vivo* potentials. In 2008, Zhou etc al demonstrated the first successful reprogramming of pancreatic exocrine cells into β-cell* . These induced β-cells were shown to be morphologically indistinguishable from endogenous β-cells, and were capable of ameliorating hyperglycemia in streptozotocin treated mice. However, the glycemic conditions of these experimental mice were worse off than

wild types. This current study looks into greater depth at the maturation process and epigenetic changes of cellular reprogramming of the exocrine cells in hopes of ultimately discovering methods of optimizing the transdifferentiation process.

The reprogramming of pancreatic exocrine cells, specifically acinar cells, into induced β-cells relies on a combination of three virally delivered transcription factors, Ngn3, MafA, and Pdx1. We have discovered these cells must undergo a crucial developmental period prior to achieving equivalent functionality to that of endogenous β-cells. On day 10, these cells first express insulin; day 30, they respond to glucose but cannot effectively regulate glycemia; day 60, they effectively regulate glycemia. A microarray assay of gene expressions has revealed differences in expressions in each of these stages. As could be seen, the passage of time leads the percentage of genes enriched in both induced and endogenous β-cells to increase, reflecting the maturation process. Consistent patterns of gene expression we have identified include genes that are only transiently upregulated, as well as those continually upregulated or downregulated with maturation. Additionally, a number of genes were found to be transiently downregulated. We will look into the specific genes belonging to said patterns in hopes of identifying a key pathway or mechanism driving the transdifferentation process.

****

Sicong Zhang: Mathematics, Physics, CC'14

Cluster variables and perfect matchings of subgraphs of dP_3 lattice

Mentor: Professor Gregg Musiker, Department of Mathematics, University of Minnesota

A cluster algebra is a mathematical object introduced in the past ten years which arises in diverse areas of mathematics. Starting from a quiver (directed graph with no 2-cycles) and variables at each vertex, we can mutate the quiver and variables in a sequence of chosen vertices following a specific rule. A remarkable property is the so-called Laurent phenomenon: cluster variables can be expressed as Laurent polynomials (polynomials possibly with negative power terms) in the initial variables, with integer coefficients. It has long been conjectured that the coefficients are in fact nonnegative, which motivates finding combinatorial interpretations for cluster variables.

We looked for examples where the Laurent expansion of cluster variables corresponds to the weight of finite bipartite graphs. In particular we studied a quiver with six vertices (appearing in the context of string theory) under a periodic sequence of mutations, and proved that the cluster variables equal a monomial times the weight of a sequence of bipartite graphs, whose underlying lattice is related to the quiver itself. Setting all initial variables to 1, cluster variables would count the number of perfect matchings of the corresponding graphs. The proof applied a technique called graphic condensation, where perfect matchings of two graphs are superimposed and then decomposed into perfect matchings of two different graphs.

****