STARS

Summer Research Symposium

Science, Technology and Research Scholars

Yale

Kline Geology Laboratory
Lecture Hall 123

July 26 & 27, 2017

Science and Technology Research Scholars Symposium
Schedule of Presentations

Wednesday, July 26th, 2017 — Morning Session

9:00 a.m.	Melissa A. Mendizabal *Center for Green Chemistry & Green Engineering at Yale University*	Analysis of Aldehydes that Comprise Flavorants in Hookah Tobacco
9:15 a.m.	Seon Augusto De Souza Ferreira *Center for Green Chemistry & Green Engineering at Yale University*	Low Valence Homogeneous Manganese as a Catalyst for Cleavage by Oxidation of Alkenes
9:30 a.m.	Jocelyn Dicent *Department of MCD Biology*	Synthesis of Molecular Glue to Recruit Proteins to $CRL4^{CRBN}$ (CUL4–DDB1–RBX1–CRBN) E3 Ubiquitin Ligase through Copper Catalyzed Click Reactions
9:45 a.m.	Ege Ertekin *Department of MCD Biology*	Single-Cell Monitoring of DNA Damage in Aging *Saccharomyces cerevisiae*
10:00 a.m.	Guan Li *Department of MCD Biology*	Characteristics Necessary for Cancer Protein Degradation Using PROTACs
10:15 a.m.	**Morning Break**	
10:30 a.m.	Esmeralda Lugo *Department of MCD Biology*	Exploring the Role of Langerhans Cells (LCs) in Wound Healing
10:45 a.m.	Mohamed Mohamed *Department of MCD Biology*	Investigating the Localization of Adipocyte Precursor Cells (APCs) during the proliferative phase of wound healing
11:00 a.m.	Lillian Ekem *Department of Biomedical Engineering*	Towards a Novel Bio-chemo-mechanical Model of Tissue-engineered Vascular Grafts
11:15 a.m.	Jannet Rivera *Department of Biomedical Engineering*	Incorporation of Growth Factors in Cell Derived Extracellular Matrix
11:30 a.m.	Mariel Moran Quintero *Dept. of Molecular Biophysics & Biochemistry*	Investigating the Impact of a Site-Specific Cation Binding Site on Actin Filament Severing by Gelsolin
12:00 p.m.	**Lunch Break**	

Wednesday, July 26th, 2017 — Afternoon Session

1:30 p.m.	Corine Lu *Dept. of Electrical Engineering*	**S**ecurity Verification Using the Chisel Hardware Construction Language
1:45 p.m.	Lane To *Departments of Chemical & Environmental Engineering*	Solid Phase Extraction of Rare Earth Elements from Mobile Phone Electronics Waste Using N,N,N',N'-Tetraoctyl Diglycolamide Resin for Elemental Analysis
2:00 p.m.	Yesenia, G. Chavez *Brain Function Laboratory-YSM*	Exploring Neural Activity During the Communication of a Natural Smile
2:15 p.m.	Brandon Tejada *Dept. of Molecular Biophysics & Biochemistry*	Identification of Torsin2A Interacting Proteins
2:30 p.m.	Deyri S. Garcia *Department of Neuroscience-YSM*	Decreasing the Risk Conferred for Parkinson's Disease by the Mutant GBA Gene by Knocking out UGCG with CRISPR/Cas9
2:45 p.m.	**Afternoon Break**	
3:00 p.m.	Hannah Sproch *Section of Infectious Diseases, Dept. of Internal Medicine-YSM*	The Effect of *Aedes aegypti* Salivary Protein Antibodies on ZIKV Infection
3:15 p.m.	Matthew Paige *Dept. of Mechanical Engineering & Materials Science*	Modelling the Jamming Transition of Non-Confluent Epithelial Tissue through Circle Packing Simulations to Study Shape Parameter
3:30 p.m.	Arizona Greene *Department of MCD Biology*	Spatial Ordering of Phenotypes Emerges in Radial Migration of *E. coli*
3:45 pm	Katherine A. Lutz *Department of Geology & Geophysics*	Seismic Anisotropy in the Lowermost Mantle beneath North America from SKS-SKKS Splitting Discrepancies
4:00 pm	Alexa Anderson *Department of Astronomy*	Satellite Galaxy Movement in Colorspace

Thursday, July 27th, 2017 — Morning Session

9:00 a.m.	Kevin Truong *Dept. of Electrical Engineering*	Microcontroller Based Treatment of Tobacco Addiction
9:15 a.m.	Cesar A. Rodriguez *Dept. of Electrical Engineering*	Prototyping a Multi-Analyte Flexible Neural Probe for use in Brain Trauma Patients
9:30 a.m.	Karli Cecil *Dept. of Mechanical Engineering*	Prosthetic Hand Usage in Upper-Limb Unilateral Amputees
9:45 a.m.	Archibald H. Enninful *Department of Pathology -YSM*	The Role of BCL-2 Ovarian Killer Protein in the Pathogenesis of Multiple Myeloma
10:00 a.m.	Oscar Perales *Department of Pathology -YSM*	BCL-2 Ovarian Killer Regulates Erythropoiesis in a Mouse Model of Myelodysplastic Syndrome
10:15 a.m.	**Morning Break**	
10:30 a.m.	Hannah Selwyn *Department of Neuroscience -YSM*	Investigating the Role of Vasoactive Intestinal Peptide – Expressing Interneurons in State-Dependent Visual Encoding
10:45 a.m.	Jessica Tang *Cellular Neuroscience, Neurodegeneration and Repair-YSM*	The Effects of Fyn Kinase Inhibition in a Mouse Model of Tauopathy
11:00 a.m.	Angela Lin *Department of Chemistry*	Asymmetric Reductive Aminations of 3-Aminocyclohexanones using Phosphothreonine-Embedded Peptide Catalysts
11:15 a.m.	Max Mao *Dept. of Molecular Biophysics & Biochemistry*	Host-viral Protein Interactions between HIV Nef and Human AP-2 and SERINC3
11:30 a.m.	Alondra Arguello *STARS Summer Counselor*	A Look at STARS 2017
12:00 p.m	Dr. Kenneth Nelson *Director STARS Program*	Closing Remarks

Analysis of Aldehydes that Comprise Flavorants in Hookah Tobacco

Melissa A. Mendizabal[1], Hanno C. Erythropel[2,3], and Paul T. Anastas[2]

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A new trend that has gained popularity among people is the smoking of tobacco from a waterpipe, commonly known as hookah. One of the reasons for its increase in popularity is because it is sold in a wide variety of flavors, which mask the bitter taste of tobacco and make smoking enjoyable. These flavorants get their taste by the use of aldehydes, which may undergo chemical reactions that produce other toxins when they are heated by the coal during a hookah smoke session. This study focused on determining the concentrations of aldehydes and toxins present in hookah smoke. The hookah smoke was generated by simulating a smoking session using an economical analog mass flow meter from Sierra Instruments. The hookah smoke was collected by liquefying the vapor by using two containers filled with liquid nitrogen. To analyze the concentrations of the aldehydes in these flavorants of the hookah smoke, a Gas-Chromatography/Mass-Spectrophotometer machine was used. The concentrations of compounds found in the smoke were used to calculate the carryover rate percentage, a ratio of the concentrations of the aldehydes present in the shisha tobacco before a smoking session compared to the concentrations of the aldehydes present in the hookah vapor after a smoking session. The results showed that a significant amount of compounds, such as Benzaldehyde, ethyl-vanillin, vanillin, and nicotine, are still present in the smoke, thus corroborating that hookah is toxic due to the compounds that are being inhaled.

Low Valence Homogeneous Manganese as a Catalyst for Cleavage by Oxidation of Alkenes

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Ozonolysis, one of the widely-used techniques to perform the oxidation and further cleavage of carbon-carbon double bonds in alkenes, is known to be very disadvantageous. Its use of ozone represents an environmental hazard in the lower atmosphere, given ozone high toxicity and difficulties associated to its containment and disposal. Furthermore, the method itself is dyslogistic since the reaction is violent and has low selectivity. The use of manganese to catalyze the oxidation and cleavage of alkenes in the presence of hydrogen peroxide and sodium bicarbonate has been applied as a green chemistry substitute for ozonolysis. However, little is known about the mechanisms by which manganese can promote the rupture of the double bonds. This article investigated further the manganese catalysis in terms of the characteristics of the target double bond, particularly focusing on the double bond's electron density influence on the rate of the oxidation. It was verified that double bonds with low electron density are more prone to be cleaved, suggesting that nucleophilic addition to the double bond is central to the reaction mechanism.

Synthesis of Molecular Glue to Recruit Proteins to CRL4^{CRBN} (CUL4–DDB1–RBX1–CRBN) E3 Ubiquitin Ligase through Copper Catalyzed Click Reactions

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Molecular glue compounds binds to cereblon or the CRL4^{CRBN} (CUL4–DDB1–RBX1–CRBN complex) E3 ubiquitin ligase to differentiate substrate specificity. Molecular glue derivatives of thalidomide bind in a shallow hydrophobic pocket on the surface of cereblon where their glutarimide ring contributes to most of the binding. Thus, varying substituents on the phthalimide part of thalidomide introduces molecular diversity. The various substituents can potentially change the substrates and proteins that are recruited to cereblon when cereblon binding occurs. Using thalidomide as the scaffold, a series of 1,4-disubstituted 1,2,3-triazoles were introduced in the 4 and 5 positions of the phthalimide ring. An efficient synthetic route was developed for the cycloaddition reactions. A procedure of sequential bromination followed by S_N2 substitution was utilized to introduce an azide group in the 4 position of the phthalimide ring. This product was used as another starting material for the cycloaddition reactions. Synthesized compounds that fulfilled purity standards were evaluated for their ability to induce protein-protein interactions by phenotypic screening using zebrafish. Unfortunately, none of the evaluated compounds showed any phenotype. The lack of a phenotype may be the result of low compatibility of the functional groups and their position in the ring with the proteins. Developing a library of molecules is a process by which a diverse set of functional groups and positions must be evaluated. Further design and synthesis will be based on introducing triazoles on the 4 position of the phthalimide ring.

Single-Cell Monitoring of DNA Damage in Aging *Saccharomyces cerevisiae*

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Several mechanisms can lead to the loss of heterozygosity (LOH) in yeast cells. However, spontaneous LOH in yeast cells is mainly caused by mitotic recombination which is considered to be triggered by DNA damage. Previous studies conducted at a colony-level investigating LOH in aging yeast cells concluded that an ~100-fold increase in loss of heterozygosity (LOH) occurred, as mother cells aged (McMurray, & Gottschling, 2003). In our study, to examine this conclusion, a microfluidic chip was used to monitor individual cells of *Saccharomyces cerevisiae* expressing short-lived Green Fluorescence Protein (GFP). Heterozygous yeast cells were constructed by insertion of the short-lived GFP gene under the *TEF1* gene promoter in one copy of the *SAM2* locus. None of the 97 mutant cells which were monitored over their entire life-span exhibited LOH with aging. The resulting data generated three distinguishable phenotypes in terms of short-lived GFP intensity with aging: constant GFP intensity, decrease and decrease followed by an increase in GFP intensity. Our findings refute the assertion that LOH occurs in aging yeast cells. Further quantitative analysis on the full life-span dynamics of short-lived GFP expression in yeast cells and studies investigating the effect of chromosome and promoter on these dynamics could shed more light on the age-related changes in the gene expression in *S. cerevisiae*.

Characteristics Necessary for Cancer Protein Degradation Using PROTACs

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Proteolysis Targeting Chimera (PROTAC) technology is an emerging therapeutic strategy used to degrade proteins that cause cancer or other diseases. PROTACs are heterobifunctional molecules that form ternary complexes and function by recruiting E3 ubiquitin ligases such as VHL to target proteins, leading to their ubiquitination. Once the target proteins are ubiquitinated, they are then sent to the proteasome for degradation. Past work in the Crews' laboratory has resulted in several PROTACs that degrade a fusion oncoprotein known as BCR-ABL which is involved in pathogenesis in chronic myelogenous leukemia. BCR-ABL is formed by a chromosomal translocation that causes the *ABL1* gene, which encodes for the c-ABL tyrosine kinase, to fuse with the *BCR* gene. Curiously, when using a VHL-based PROTAC to engage the active site of BCR-ABL, no degradation was observed. However, effective degradation was observed when using a VHL-based PROTAC to engage the allosteric site of BCR-ABL. Additionally, both PROTACs can successfully degrade c-ABL. The current understanding of the PROTAC mechanism indicates that protein-protein interactions between the substrate protein and E3 ligase stabilize the ternary complex and must be present for efficient degradation. To investigate whether a stable ternary complex is present, a pull-down assay was conducted to isolate proteins that are directly interacting with VHL in the presence of PROTACs. Preliminary results indicate that a stable ternary complex forms between c-ABL and VHL when using both the active site binding PROTAC and allosteric site binding PROTAC. These initial results suggest that the formation of a stable ternary complex between the target protein and the E3 ubiquitin ligase may be important for degradation, but is not the main driver when using PROTACs. One factor that influences protein degradation is the process of ubiquitination in which ubiquitin molecules are covalently bound to specific amino acids such as lysine on the target protein. Thus, further investigations will involve studying how the availability of lysine residues affect target protein ubiquitination and degradation. In summary, our research aims to further advance PROTAC technology as an alternative therapeutic strategy to treat cancer and other diseases by understanding the conditions and characteristics that are necessary for protein degradation.

Exploring the Role of Langerhans Cells (LCs) in Wound Healing

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Langerhans cells (LCs) are a subtype of dendritic cells that comprise 2-5% of the skin's epidermal layer. LCs are an important component of the skin's innate immune system and help direct immune responses against infection. Previous studies have shown that LCs are found at higher densities in sites of both normal and pathological wound healing, however little is known about their role during skin repair. The aim of our research is to elucidate the contributions of Langerhans cells to wound healing. To investigate the role of these cells during wound healing, we are using the *huLangDTR* mouse model to selectively ablate LCs from the skin with the administration of Diphtheria toxin (DT). Our work here functions to optimize the conditions for ablation. Some of the factors considered were the ages of the mice and the dosage of DT. We tested a 1µg DT dosage on both 7 and 12-week mice. Two days after DT dosage, full-thickness excisional wounds were performed on the back skin of huLangDTR mice and LCs were labeled and quantified using immunohistochemistry. Younger mice demonstrated a more successful ablation compared to older mice. In summary, our research aims to demonstrate the role of LCs in wound healing in order to improve treatments for chronic wounds.

Investigating the Localization of Adipocyte Precursor Cells during the Proliferative Phase of Wound Healing

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Adipocytes have been identified in wounded tissue and are believed to play a role in wound regeneration. The changes in the populations of adipocytes, as well as other cell types, during the proliferative phase of wound healing has previously been investigated, however their spatial localizations within the wound and relative to other cell types are not fully known. Mature adipocytes are derived from adipocyte precursor cells (APCs), which have been characterized in previous studies by a variety of cell surface and transcriptional markers. In this investigation, we use both Sca1 and CD26 as markers to identify the spatial distribution of APCs in wounded and unwounded skin. We analyze skin sections before wound and 5 days after wounding. Preliminary results show that only part of the wound bed contained Sca1+/CD26+ cells in contrast to unwounded skin, where APCs were identified along the dermal layer. However, APCs were concentrated in the center of the wound bed and with a higher cell density than in unwounded skin. These initial results suggest that APCs migrate into the center of the wound bed and rapidly proliferate. Further investigation of the localization of adipocyte precursor cells at more points in the wound healing timeline as well as their positions relative to other cell types will improve our understanding of the intricate process of wound healing.

Towards a Novel Bio-chemo-mechanical Model of Tissue-engineered Vascular Grafts

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The impact of congenital heart disease is yet to be mitigated by an effective long-term solution. Tissue engineered vascular grafts (TEVG) are biodegradable scaffolds that use the host inflammatory response to remodel defective blood vessels into functional neovessels. With further development, they may offer an alternative to current approaches such as autologous vessels and synthetic conduits. The primary graft-related complication is stenosis, the incidence of which can be reduced with the inhibition of TGF-β signaling. Bio-chemo-mechanical models can predict the production and turnover of vessel constituents under normal circumstances and with TGF-β inhibition. These simulations can be used to optimize graft design and improve graft patency and performance. Quantitative analysis of in vivo graft components at 24 weeks with and without treatment with a TGF-β RI inhibitor was used to validate simulations of the production of collagen, endothelial cells, smooth muscle cells, inflammatory cells, molecular signals, and matrix proteases. Overall, empirical levels of these neovessel components in the TEVG were consistent with simulation results. However, increases in matrix proteases upon treatment with the TGF-β RI inhibitor differed from model predictions, suggesting that patency and distensibility are improved by the synthesis of matrix proteases that degrade collagen responsible for stenosis. These results assist in validating the predictions of bio-chemo-mechanical models and informing the addition of further mechanistic relations.

Incorporation of Growth Factors in Cell Derived Extracellular Matrix

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Decellularized extracellular matrix is used clinically to repair and reconstruct tissue. This natural biomaterial is still limited by its final composition; however this can be modified. Specifically, we have developed a method to incorporate vascular endothelial growth factors (VEGF) and platelet-derived growth factors (PDGF) into the matrix. Once cells are created to secrete these growth factors, they embed them into the extracellular matrix that they form. This material shows an increase in cell proliferation in comparison to an extracellular matrix that has not been altered. These results suggest that the material will also preform more effectively in an *in vivo* wound healing setting. They also demonstrate that the extracellular matrix can be modified to improve its performance.

Investigating the Impact of a Site-Specific Cation Binding Site on Actin Filament Severing by Gelsolin

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Actin is a protein that assembles from G-actin monomers into long filaments called F-actin in a process known as actin polymerization. F-actin is important for a variety of functions within a cell, such as cell shape and organization, cell motility, and mechanical support. Gelsolin and cofilin are two classes of regulatory proteins that sever actin filaments and control actin assembly and disassembly dynamics. Gelsolin binds, severs, and caps filaments at their growing end, which inhibits filament elongation. This gelsolin severing activity is regulated in cells by calcium. Cofilin binds filament sides and changes the filament mechanical properties, which promotes severing. Previous studies showed that the presence of a site-specific cation binding site on the 167th residue of the primary structure of vertebrate actin is required for cofilin to promote severing. Cofilin and gelsolin exhibit similar actin regulatory functions; therefore, we hypothesize that the site-specific cation binding site may also be important for the gelsolin severing mechanism. Yeast wildtype actin lacks the presence of this site-specific cation binding site. A mutation (A167E) was created to restore the specific cation binding site in yeast actin. Therefore, to investigate the impact of a site-specific cation binding site on gelsolin severing, polymerized F-actin filaments from rabbit skeletal muscle, yeast wildtype, and yeast A167E mutant strains were incubated with increasing concentrations of gelsolin, with or without calcium. Filament lengths were measured by staining with rhodamine phalloidin and visualizing with Total Internal Reflection Fluorescence (TIRF) microscopy. Preliminary results showed that the average length distribution of rabbit skeletal muscle actin filaments in the absence of calcium did not change significantly as the concentration of gelsolin in the sample increased; however, a shift in the length distribution of filaments with calcium conditions was observed. Further optimization is needed to visualize polymerized yeast actin under calcium conditions to make an accurate comparison between gelsolin severing events in yeast wildtype, yeast mutant, and rabbit skeletal muscle actin.

Security Verification Using the Chisel Hardware Construction Language

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After manufacturing, computer hardware is incredibly difficult, if not impossible, to patch for security issues. Rather than wait to test for vulnerabilities after manufacturing, hardware security verification preemptively ensures a hardware design, such as a microprocessor, meets specified security properties during design stages. Security verification works by first defining a set of security criteria in order to consider a system secure. In this project, a system representation of the design is created with the SecChisel hardware construction language to accurately model the behavior of the system. Through formal verification, the representation is compared to the security properties and proved secure. If vulnerabilities are found, the design needs to be fixed and retested. With especially complicated designs or with the need to test changes in quick succession, the speed of formal verification becomes an issue. In order to address this, formal verification can be parallelized in order to improve run time and speed up security verification. Parallelization splits the file read by the model checker in verification and runs the files simultaneously. Optimizing formal verification increases efficiency and usability of the hardware security verification process, allowing for safer computer systems.

Solid Phase Extraction of Rare Earth Elements from Mobile Phone Electronics Waste Using N,N,N',N'-Tetraoctyl Diglycolamide Resin for Elemental Analysis

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Effective recycling of electronics waste (e-waste) is currently difficult to achieve, and this is complicated by the fact that the elemental composition of most electronic devices and their subcomponents remains unknown. There is a great deal of information available about the major metals in e-waste (i.e., copper, gold, and iron) but minimal information about the metals present in smaller amounts, such as rare earth elements (REEs). For these valuable trace metals to be reclaimed, their presence in e-waste must be quantified; this is a substantial challenge when REEs are present alongside orders-of-magnitude more concentrated bulk metals. In order to analyze REEs independent from a common bulk metal, copper, solid phase extraction (SPE) was performed on a synthetic solution emulating the copper-to-REE ratio found in real mobile phone e-waste leachate. N,N,N',N'-tetraoctyl diglycolamide (DGA) resin was used to extract REEs from the mixture, while a copper-specific resin was used to extract copper. Effluents from the SPE were then analyzed for metal content using inductively coupled plasma-mass spectrometry (ICP-MS). Preliminary data from experiments on stock solutions containing REEs and copper individually indicate high copper recovery rates, while REE recovery varies drastically by element. Additionally, SPE with both resins on the synthetic e-waste solution yielded significantly lower REE recovery rates than SPE with DGA resin on the stock REE solution. After identifying and surmounting problems with the current SPE procedure and applying it to the real leachate, optimized extraction will give way to a more accurate analysis of the metals contained in mobile phone e-waste. Final results revealing the elemental distribution of various electronic components will be useful for future research into devising recycling strategies to recover specific metals of use for subsequent manufacturing of novel devices.

Exploring Neural Activity During the Communication of a Natural Smile

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Neural activity activated with communication of facial expressions is fundamental to social interactions, but little is known about the underlying neural mechanisms. This study uses functional near-infrared spectroscopy (fNIRS) to determine the activated neural correlates of the generation of a smile in a natural setting. A dyad of subjects was chosen; Subject 1 was instructed to view neutral or smile-inducing videos for 15 seconds. Subject 2 was instructed to watch Subject 1's face for 15 seconds. Subjects switch tasks every 15 seconds. This was done for a total of six 30 second blocks or three minutes. Two smile-inducing video runs and two neutral videos (not created with the intention of producing a smile in the subjects) were completed. Data from the functional near-infrared spectroscopy (fNIRS) machine with 40 optical nodes (20 emitters and 20 detectors) giving 58 channel layout covering frontal, parietal, and temporal areas, an electroencephalogram, electrocardiogram, response-dial indicating feeling intensity, and facial classification from an Xbox Kinect was collected. The deoxygenated hemoglobin concentration signal from fNIRS was compared for each task and related to smile intensity, defined by an automated facial classification program. This study is the first, to our knowledge, to use simultaneous EEG and fNIRS recordings with nearly full-head coverage of optodes and electrodes to investigate smile-specific effects. Our preliminary findings aim to discover neural mechanisms associated with viewing the smile of a real person.

Identification of Torsin2A Interacting Proteins

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Torsin2A is one of the four ATPase associated with diverse cellular activities (AAA+) Torsin proteins, residing in the lumen of the nuclear envelope (NE) and endoplasmic reticulum (ER). Previous experiments involving the knockout of the Torsin2A protein in HeLa cells resulted in a stark increase in herniations within the lumen nuclear envelope in a triple-TorsinA/B/3A deficient genetic background, suggesting a critical yet unexplored function (Laudermilch, *et al.,* 2016). However, insufficient knowledge regarding the cellular interaction partners and activators of Torsin2A inhibits the understanding of why this phenotype occurs. While it is known that LAP1 and LULL1 serve as essential, ATPase-activating cofactors for TorsinA, TorsinB, and Torsin3A, the cofactor(s) for Torsin2A remains unknown. To further existing knowledge of the Torsin2A protein, the interacting proteins for Torsin2A were investigated by employing a proximity ligation technique. This method relies on a genetic fusion of the Torsin2A protein and Ascorbate Peroxidase 2 (APEX2), which biotinylates proteins in close proximity. Tor2A – ER APEX2 and ER APEX2 (negative control) synthetic genes were constructed and transfected into quadruple TorsinA/B/2A/3A knockout HeLa cells (4KO). The cells were analyzed via immunofluorescence microscopy, verifying the authentic NE/ER localization and functionality of the fusion proteins that are specified by both synthetic genes. Finally, NEs of Torsin 2A – ER APEX2 transfected 4KO HeLa cells and ER APEX2 transfected 4KO HeLa cells were isolated. This was followed by the isolation of biotinylated species and a mass spectrometry-based analysis of these species to identify the relevant proteins and to estimate their abundance in each sample. The resulting data generated a list of nearly 300 possible Torsin2A-interacting protein candidates. Our findings validate the functionality of the proximity ligation approach but also motivates and informs the development of strategies for further optimization to arrive at a short list of high-confidence interaction partners that merit a detailed follow-up investigation.

Decreasing the Risk Conferred for Parkinson's Disease by the Mutant GBA Gene by Knocking out UGCG with CRISPR/Cas9

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Mutation in glucosylceramidase beta (GBA), coding for the lysosomal enzyme glucocerebrosidase (GCase), causes the loss of function of this enzyme. The GBA mutation has been established as the most common genetic risk factor for Parkinson's Disease (PD), however the underlying mechanisms of how this occurs are still unclear. It is hypothesized that accumulated uncleaved lipid, caused by the enzymatic loss-of-function, promote α-synuclein aggregation, resulting in neuronal death with age. Suppression of the downstream effects of the GBA mutation could decrease the risk factor for PD. UDP-Glucose Ceramide Glucosyltransferase (UGCG) was targeted as a candidate to decrease this downstream effect since it is upstream of GBA and it produces the lipid to be cleaved by GCase. CRISPR/Cas9, a genome editing tool, was used to knockout UGCG in human embryonic kidney (HEK) cells. The majority of the HEK cells that were successfully transfected with the plasmid died and expressed either little fluorescence or no fluorescence at all. The death of these cells suggest that a UGCG knockout can be lethal *in vitro.* Previous studies on mice have shown that the knockout is also lethal *in vivo*. But the 5% fluorescence illustrates viability, thus we hypothesize that the fluorescent cells had a heterozygous knockout. Further investigation on UGCG heterozygous knockouts could reveal heterozygous UGCG knockouts potential to decrease the downstream effect of GBA-associated Parkinson's Disease.

The Effect of *Aedes aegypti* Salivary Protein Antibodies on ZIKV Infection

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Currently, Zika virus (ZIKV) is an important area of research due to its global prevalence and variety of clinical features. ZIKV belongs to the family *Flaviviridae* and has been linked to Guillain-Barré syndrome as well as birth defects including microcephaly. The Flavivirus is primarily transmitted by *Aedes aegypti* mosquitoes. Previous literature has demonstrated that *Ae. aegypti* saliva enhances the replication and pathogenesis of Flaviviruses such as Dengue and West Nile, and likely augments ZIKV infection as well. Therefore, the focus of this research is to determine if antibodies that bind to salivary gland (SG) proteins provide a protective effect against ZIKV infection. Both *in vivo* and *in vitro* studies were conducted. During the *in vivo* experiments, AG129 mice were inoculated with SG antibodies prior to infection by mosquitoes. After infection, mice were monitored for weight loss and disease pathogenesis over the period of several weeks, and blood samples were collected to monitor ZIKV titers. During the *in vitro* experiments, macrophage cell lines were treated with antigenic SG proteins to determine their effect on cytokine expression. If an increase in expression was observed, tests were conducted to determine if antibodies that bind to SG proteins could inhibit this effect. Preliminary results for the *in vivo* experiments indicate that multiple SG antibodies are able to improve survival rate of mice. In addition, two SG proteins studied in the *in vitro* experiments, SP and AILP, resulted in increased cytokine expression; anti-AILP antibodies were able to inhibit the effects of AILP. Future studies hope to learn more about the role of *Ae. aegypti* SG proteins during Flavivirus infection and contribute to the development of Flavivirus vaccines and therapeutics.

Modelling the Jamming Transition of Non-Confluent Epithelial Tissue through Circle Packing Simulations to Study Shape Parameter

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When the jamming transition occurs in epithelial cell monolayers, the tissue becomes structurally rigid, which is vital to a number of biological processes ranging from fruit fly wing development, to asthmatic airway deformation, and cancer metastasis. Previous computational modelling of tissue jamming has been completed using the vertex model; however, this model is only capable of simulating confluent systems, while non-confluent systems occur commonly in tissue and tumors. To simulate these non-confluent systems, a simple circle packing model of particle jamming was modified to study the geometry of the Voronoi space available to each cell in the jammed state, while maintaining a non-confluent packing density. Geometric analysis was completed by computing the shape parameter, a ratio of perimeter and area, for each individual cell, and calculating the system mean. The distribution of these average shape parameters identified a critical shape parameter value that corroborated previous studies with the vertex model, indicating that this critical value was correlated to the available Voronoi space of individual cells, irrespective of packing density. The mean and mode of these distributions decreased as system size was increased; however, this increasing system size was observed to simultaneously increase packing density. It is plausible that these two system-size dependent behaviors were correlated, with higher packing density implicating a lower average shape parameter. An extension of this work to deformable particle models will improve understanding of the relationship between shape parameter and packing density, as well as their distinct influences on the jamming transition of non-confluent epithelial tissues.

Spatial Ordering of Phenotypes Emerges in Radial Migration of *E. coli*

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Collective behavior and diversity are both beneficial to communities as a means to overcoming unpredictable or hostile environments, but while collective behavior requires coordination, diversity tends to disrupt it. Bacteria exhibit collective behavior during group migration despite individual variation in chemotactic ability. A recent study in the Emonet lab demonstrated that *E. coli* resolve this conflict through spontaneous spatial ordering of phenotypes within a migrating band, such that the chemotactic ability of each individual is matched to its position along a self-produced gradient of attractant caused by nutrient consumption. This spatial ordering of phenotypes was observed for *E. coli* migrating in one dimension along a channel. However, it was unclear whether this spatial ordering would remain for bacteria migrating as density rings across a surface, because in this geometry, bacteria diffuse as the rings expand outward. To address this question, a one-dimensional simulation for bacterial migration was modified for radial migration, and bacterial growth was added. This simulation indicates that spatial ordering of phenotypes is maintained during radial migration, but it is influenced by the degree to which phenotype is maintained during replication.

Seismic Anisotropy in the Lowermost Mantle beneath North America from SKS-SKKS Splitting Discrepancies

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Seismic anisotropy has been identified in the lowermost mantle of the Earth, the D" layer, in numerous studies, although the mechanisms which generates this anisotropy in the D" layer are not well known. This anisotropy can cause discrepancies in shear wave splitting which makes observing these discrepancies a prime way to identify locations of anisotropy in the D" layer. Using SKS-SKKS seismic wave pair splitting discrepancies, which occur as these seismic wave phases sample different regions of the lowermost mantle, we examined data from 17 long-running seismic stations in the eastern US, along with 157 stations of the temporary US Transportable Array. We identified 267 high-quality SKS-SKKS wave pairs and measured the splitting intensity for each phase. Of the 267 pairs, 13 exhibited discrepancies in splitting intensity of 0.4 or greater. These pairs with pronounced splitting discrepancies were located beneath Texas and northern Mexico. This region with pronounced discrepant shear wave splitting suggests that anisotropy is present in the lowermost mantle beneath Texas and northern Mexico.

Satellite Galaxy Movement in Colorspace

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The Satellites Around Galactic Analogs (SAGA) Survey aims to collect data on satellite galaxies orbiting 100 host systems similar to the Milky Way to establish a cosmological context for the Milky Way and examine the "Missing Satellites Problem." This paper presents the verification process of color-cuts within color-color diagrams instituted by the SAGA team as being valid despite aging and color changes of the satellites. Using Flexible Stellar Population Synthesis, satellite galaxy "tracks" were created and compared to the color-cut boundaries. The behavior of bright satellite galaxies and their correlation with metallicity was illuminated. Furthermore, it was verified that objects in gr vs. ri, gr vs. ug, and gr vs. rw1 color-color diagrams would stay within their specified color-cut boundaries as they aged. Therefore, the SAGA team can continue using their current color-cut boundaries to expedite the satellite identification process.

Microcontroller Based Treatment of Tobacco Addiction

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This paper discusses the use of Arduino and Raspberry Pi (RPI), two mini-computers, in the treatment of tobacco addiction and nicotine withdrawal. Popular methods of quitting tobacco products include nicotine patches and quitting "cold turkey". Nicotine or the lack thereof in these two methods can cause various side effects to potential quitters such as nausea, headaches, and nicotine cravings. A special device 'TopDrop' was created to tackle nicotine withdrawal for cigarettes and chewing tobacco. The TopDrop device comprises of a cigarette dispensal unit and a chewing tobacco mixing system. For the cigarette system, users load cigarettes into the cigarette holder and the two microcontrollers (Arduino and RPI) control when the cigarette is dispensed. The Arduino automates the dispensing and the Raspberry Pi decides when dispension should occur. For the chewing tobacco system, different quantities of nicotine free tobacco and regular chewing tobacco are mixed and then distributed. Future directions of the chewing tobacco system are to automate ratio mixing between the two types of tobacco so that over time the withdrawal symptoms of nicotine will be lessened. TobDrop is cladded in clear acrylic to help protect all the electronics on the inside of it. Electromagnets are also used to lock the user in order to prevent users from accessing tobacco that are already in the box. All in all, these five functions are implemented to aid individuals who want to quit using tobacco products either on their own or with the help of a clinical professional.

Prototyping a Multi-Analyte Flexible Neural Probe for Use in Brain Trauma Patients

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Flexible neural probes (FNPs) have become the standard technology for implantable probes in surgical procedures. Traditional FNP designs have a single sensor, where multiple FNPs are implanted in a patient's brain to process neurological data. A multi-analyte probe design employs the use of various sensors to gather data from brain trauma patients. The goal of the prototyping process was to develop a multi-analyte FNP that can house multiple sensors. Probe molds were designed using SolidWorks CAD software and printed using a high-resolution 3D printer. Polydimethylsiloxane (PDMS) was prepared with curing agent and pulled through the probe molds using a vacuum to allow the probe to solidify into a flexible cylindrical form. A recursive design philosophy of mold design, FNP preparation, and probe experimentation was applied to the prototyping process to ensure that the FNP was compatible with the electronic sensors housed in the PDMS. The first mold prototype was in cylindrical design and was hollow to test if PDMS could cure on the inside and be extracted as a single piece. Later, a mold with convex windows along the inside of the probe was printed to house sensors on the Kapton strip. Once it was confirmed that PDMS could be poured into this design, a device to house the probe mold was created to secure the electronics configuration within the mold. At the current development stage, the experimental results indicate that PDMS is an effective material for an implantable FNP.

Prosthetic Hand Usage in Upper-Limb Unilateral Amputees

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Research on upper-limb unilateral amputees and their prosthetic devices has become increasingly popular in recent years. However, it has yet to focus on daily tasks that are highly relevant and important in everyday living. Our goal is to determine how amputees use their prosthetics within the home setting while completing everyday tasks in order to determine what aspects of the devices should be focused on while conducting future research and designing future prosthetics. To do this, we asked a selection of upper-limb unilateral amputees to wear head-mounted GoPro video cameras and record between one and eight hours of videos of themselves doing everyday chores and activities around their homes. An analysis was then performed on the videos that involved 1 hour and 6 minutes of videos of each participant. The videos were watched and the grasps observed in the videos were recorded for the start and end time of each grasp, as well as the type of grasp being done. By doing this, we discovered that the amputees are using their prosthetics to do far fewer prehensile grasps than expected. However, it was also determined that the amputees used their prosthetic hands/arms to complete a high number of non-prehensile grasps, which was not an anticipated result. In summary, the project focuses on analyzing amputees completing daily life tasks through videos and, from this analysis, learning in what ways they use their prosthetics.

The Role of BCL-2 Ovarian Killer Protein in the Pathogenesis of Multiple Myeloma

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Multiple Myeloma accounts for almost 2% of all cancer deaths in America, with a close to 50% fatality rate due to the development of resistance to chemotherapeutic agents. BCL-2 Ovarian Killer (BOK), a pro-apoptotic member of the BCL-2 family of apoptotic proteins, is frequently deleted in many different types of cancer and under-expressed in numerous Multiple Myeloma cell lines. Hence, we hypothesize that BOK may play a key role in the pathogenesis of Multiple Myeloma. Preliminary results have shown that *Bok* is still expressed in the Multiple Myeloma cell lines OPM2, U266, ARK and ARP-1. To study the possible effects of the deletion of BOK in Multiple Myeloma, the *Bok* gene was knocked out using the CRISPR-Cas9 system. We hypothesize that the deletion of *Bok* may result in changes in the Unfolded Protein Response (UPR), a pro-survival mechanism which is triggered in response to cellular stress. The deletion of BOK may favor autophagy over apoptosis, and lead to the proliferation of the cancer cells. To test this, the BOK knock-out cell lines will be treated with a panel of ER stress agents to determine if the deletion of Bok confers any pro-survival abilities to the cell. Overexpression of XBP-1, a transcriptional factor has been implicated in the pathogenesis of Multiple Myeloma based on its role in the regulation of the UPR. Hence, our study makes use of the XBP-1 TG, XBP-1BOK KO, and the BOK KO mouse models to determine if the deletion of *Bok* attenuates or accentuates the progression of Multiple Myeloma. Any phenotypic changes, characteristic of Multiple Myeloma will be monitored as the disease progresses as well as elevations in serum IgG1 and IgM levels. We observed that our mouse models did not exhibit elevated serum IgM and IgG1 levels until close to 20 weeks of age after running a Sandwich ELISA. Understanding how BOK regulates apoptosis in Multiple Myeloma will help in the development of novel therapeutic agents.

BCL-2 Ovarian Killer Regulates Erythropoiesis in a Mouse Model of Myelodysplastic Syndrome

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BCL-2 Ovarian Killer (BOK) is a pro-apoptotic member of the BCL-2 family of proteins best characterized for its putative ability to induce apoptosis in response to Endoplasmic Reticulum (ER) stress. While studying BOK's pro-apoptotic role in the Nup98-HoxD13 (NHD13) mouse model of myelodysplasia, lower hemoglobin levels were observed in NHD13 *Bok*$^{-/-}$ mice, which raised a potential connection between BOK and the regulation of erythropoiesis in cells experiencing ER Stress. This investigation aims to study the role BOK in the regulation of red blood cell synthesis under different ER stresses. Furthermore, this investigation aims to study the effects of a BOK knockout on the expression of the proteins that constitute the Unfolded Protein Response (UPR), the pro-survival pathway that protects cells from ER Stress. Mouse colony forming unit assays revealed there is a decreased amount of erythroid progenitor stem cells in the bone marrow of NHD13 Bok$^{-/-}$ mice which hinted at a diminished ability to produce RBCs in the absence of BOK. Additionally, RT-QPCR analysis showed decreased expression of CHOP, a protein involved in the UPR, in the RBC progenitors of NDH13 BOK$^{-/-}$ mice. Lastly, in vivo stimulation of erythropoiesis after induced hemolytic anemia revealed no significant difference in hematocrit recovery between WT and *Bok*$^{-/-}$, mice while supra-physiological RBC production induced with erythropoietin (EPO) revealed that *Bok*$^{-/-}$ mice did not attain hematocrit levels as high as those for WT mice. These results suggest that in addition to its pro-apoptotic function, BOK may have other regulatory roles within the cell, and specifically a role in regulating erythropoiesis when certain RBC progenitors experience ER Stress.

Investigating the Role of Vasoactive Intestinal Peptide – Expressing Interneurons in State-Dependent Visual Encoding

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Patterns of cortical activity differ dramatically across different behavioral states, such as sleep, wakefulness, and arousal. The diverse populations of GABAergic interneurons have been hypothesized to play a key role in state-dependent cortical function. Previous work has identified interneurons co-express Vasoactive Intestinal Peptide (VIP) as potential key regulators of state-dependent activity in cortical circuits. VIP interneurons are extremely sparse, making up ~ 1% of all cortical neurons, and unique in that they primarily synapse onto other inhibitory interneurons. To assess the specific contributions of VIP interneurons to state-dependent sensory encoding in the primary visual cortex, we used a combination of pharmacogenetics, in vivo 2-photon laser scanning microscopy (2PLSM), and innate behavioral patterns in mice. We used Designer Receptors Exclusively Activated by Designer Drugs (DREADDs) to temporarily inhibit VIP interneuron firing in the primary visual cortex (V1) upon the injection of a synthetic ligand, clozapine-N-oxide (CNO). Recordings of activity in Somatostatin (SOM)-expressing interneurons, a primary target of VIP interneurons, were made using 2PLSM during presentation of visual stimuli of differing contrasts and orientations. We assessed the role of VIP interneurons during transitions between two distinct behavioral states. Activity of SOM cells indicated a decrease in visual responsiveness as compared to wild type mice both before and after the injection of CNO, indicating that VIP cells were unhealthy. Histology was performed on mice after two and three weeks of DREADDs expression time, and both results indicated VIP interneuron death. These results suggest that DREADDs are not an adequate tool for assessing the role of VIP interneurons in visual encoding. Further investigation into alternative tools, such as cell type-specific expression of the Diphtheria Toxin Receptor (DTR), to manipulate VIP interneuron activity is currently being conducted. This alternate tool provides the possibility of investigating the effects of long-term VIP interneuron firing disruption on visual encoding. Using these tools, we can begin to identify the cell-type specific roles of inhibitory interneurons on sensory processing in the healthy brain, as well as understand how their disruption contributes to disease.

Asymmetric Reductive Aminations of 3-Aminocyclohexanones Using Phosphothreonine-Embedded Peptide Catalysts

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Organocatalysts have emerged in recent years as a new complementary approach in asymmetric catalysis that can tackle the new challenges and limitations associated with achieving high enantioselectivity for broader and more complicated substrate scopes. One such subset in this family, chiral phosphoric acid (CPA) catalysts, have been established as powerful, wide-ranging, and versatile, exhibiting high enantioselectivity in synthetic reactions of interest. While most effective CPAs are derived from 1,1'-bi-2-napthol (BINOL), which provides an atropisomerically locked C_2-symmetric structure as a chiral environment, efforts to develop diverse catalytic templates that depart from this model have been slow. In taking a biomimetic approach with insight gained from the phosphorylation of proteinogenic amino acids, a common post-translational modification in biological systems, the incorporation of phosphothreonine (pThr) into minimal peptides as a new catalytic system was investigated. pThr-embedded peptides depart from the dominant BINOL-derived structure, yet have shown to have potential as highly selective CPAs and bifunctional catalysts. Phosphopeptides were synthesized with conventional peptide coupling methods and reductive amination of 3-aminocyclohexanones mediated by Hantzsch ester, an NADH mimic, were carried out. Significantly, enantioselectivities of up to 90:10 favoring the *cis*-product were observed in comparison to the BINOL-CPA favorance of the *trans*-product with 12:88 e.r. This selectivity of pThr-containing peptides was attributed to secondary interactions between the catalyst and directing groups on the substrate. Studies suggested the phosphopeptides folded into a reproducible secondary structure that provided a favorable stereochemical environment, which contributed to the high enantioselectivity. Hence the approach combined the concepts of 1) the natural ability of enzymes to fold and be phosphorylated and 2) the strength of BINOL-derived CPAs as Brønsted acid catalysts to produce a new class of CPAs.

Host-viral Protein Interactions between HIV Nef and Human AP-2 and SERINC3

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HIV uses viral proteins to increase virulence through domination of the host immune system. Recently, an HIV protein, negative regulatory factor (Nef) has been identified in manipulating host membrane trafficking to antagonize cellular antiviral defense molecules. One such restriction factor antagonized by Nef is the host protein SERINC3 (Y. Usami, *et al.,* 2015). Through clathrin-mediated endocytosis via adaptor protein complex-2 (AP-2), Nef removes SERINC3 from the plasma membrane inhibiting its antiviral function. However, how Nef, SERINC3 and AP-2 interact remains unknown. To investigate these interactions, chimeric proteins of Nef fused to cytosolic regions of SERINC3 (Nef-S3LX) were purified to homogeneity and tested for binding in a GST-AP-2 pulldown. Significant binding between cytosolic regions can lead to further analysis towards structural determination, potentially elucidating molecular interactions between Nef, SERINC3, and AP-2. The result will provide insight into how HIV hijacks cellular membrane traficking to antagonize the host defense molecule SERINC3.

Acknowledgments

We wish to thank the following for their contributions to the Yale STARS Summer Program 2017:

Peter Salovey**,** President, Yale University
Benjamin Polak, Provost, Yale University
Marvin Chun, Dean of Yale College
Sandy Chang, Assistant Dean Yale College Science Education
Kurt Zilm, Chemistry, Convener, STARS Advisory Committee
Hector Arce, Astronomy, STARS Advisory Committee
Keith Baker, Physics, STARS Advisory Committee
Daniel Colon-Ramos, Cell Biology, STARS Advisory Committee
Enrique De La Cruz, MB&B, STARS Advisory Committee
Christine DiMeglio, Chemistry, STARS Advisory Committee
James Duncan, Biomedical Engineering, STARS Advisory Committee
Anjelica Gonzalez, Biomedical Engineering, STARS Advisory Committee
John Hall, Mathematics, STARS Advisory Committee
Burgwell Howard, Associate Dean Yale College, STARS Advisory Committee
Rise Nelson, Assistant Dean Yale College, STARS Advisory Committee
Paul Turner, E&EB, STARS Advisory Committee
Donalee Slater, Yale College Science & QR
Sarah DelVecchio, Yale College Science & QR

We would also like to express our gratitude to the Principal Investigators and Mentors who have invested so much time and energy in the scientific development of the STARS summer students; we are grateful for your dedication and service.

To our program staff who worked tirelessly with expertise and professionalism:

Christopher Lim, Ph.D. Candidate, MB&B, Graduate Assistant STARS
Robert Fernandez, Ph.D. Candidate, MB&B, Graduate Assistant STARS
Lien Nguyen, Ph.D. Candidate, Interdepartmental Neuroscience Program, Graduate Assistant STARS
Alondra Arguello, Summer Coordinator, STARS

We would also like to express our appreciation to:

Yale College

for the funding that makes this program possible.

Our best wishes and gratitude to:

Maria Moreno, MCDB, Academic Coordinator STARS Program
Kenneth Nelson, MCDB, Academic Director STARS Program
Kailas Purushothaman, Center for Teaching & Learning, Advisor STARS Program