1 P.M. POSTER SESSION – THURSDAY, OCTOBER 20, 2016

POSTER AUTHOR	POSTER LOCATION	TOPIC	POSTER TITLE	ABSTRACT
BASIC LIFE SCIENCE				
Oluremi Akindele	1	Basic Life Science	IKK Expression Fine-Tunes NF-kB Pathway Activation in Response to Cytokines	Activation of IKK is a multi-step process in the NF-κB pathway that involves its recruitment to poly-ubiquitin structures that form in response to cytokines. These poly-ubiquitin structures recruit other proteins called IKK-kinases (IKKK) that trans-activate the kinase activity of IKK. Although IKK and IKKK are both activators in the same pathway, competition for binding to poly-ubiquitin structures may favor a specific ratio of both to optimally activate NF-κB. We hypothesize that recruitment of IKK and IKKK to ubiquitin structures is a control point that finely-tunes activation of the NF-κB pathway, and changes to their ratio of expression may either hyper-activate or shut down the NF-κB pathway. We adapted a model of cytokine-induced signal transduction to include ubiquitin structures to show increased expression of IKK can have an inverted U-shaped response on NF-κB activation. Using fixed-cell immunofluorescence we measured cytokine-induced activation of NF-κB and IKK expression in single cells, comparing parental U2OS with cells overexpressing IKK. Our results concur with simulations showing that the NF-κB pathway activation is sensitive to IKK level, can be shut down in cells with a high abundance of IKK, and suggest that in some signal transduction architectures, overexpression of a canonical activator can have inhibitory effects.
Margaret Bennewitz	2	Basic Life Science	Lung Vaso-Occlusion in Sickle Cell Disease Mediated by Arteriolar Neutrophil-Platelet Micro-Emboli	Vaso-occlusive crisis (VOC) is the primary reason for emergency medical care by sickle cell disease (SCD) patients. SCD patients hospitalized with VOC often develop acute chest syndrome (ACS), a form of acute lung injury, suggesting a role for pulmonary vaso-occlusion in the onset of ACS. However, the cellular and molecular mechanism of pulmonary vaso-occlusion is unknown. Multiphoton excitation enabled quantitative fluorescence intravital lung microscopy (qFILM) was used to determine the molecular mechanism of pulmonary vaso-occlusion in live mice. SCD transgenic or non-sickle control mice were intravenously (IV) challenged with 2 to 3 ng of bacterial lipopolysaccharide (LPS). Fluorescent anti-mouse Ly-6G and CD49b mAbs were administered IV for in vivo staining of circulating neutrophils and platelets, respectively. Function-blocking anti-P-selectin mAb (Fab fragments) was administered IV to assess the role of platelet P-selectin in promoting pulmonary vaso-occlusion. A nanogram dose of IV LPS selectively triggered pulmonary vaso-occlusion in SCD but not control mice. Remarkably, pulmonary vaso-occlusion involved occlusion of the pre-capillary pulmonary arteriole bottle-necks by large neutrophil-platelet embolic aggregates. IV administration of anti-P-selectin mAb Fab fragments led to the resolution of pulmonary vaso-occlusion. These results highlight

				the therapeutic potential of inhibiting platelet P-selectin to prevent ACS in SCD patients hospitalized with VOC.
Megan Bertholomey	3	Basic Life Science	Role of Estradiol in Ethanol-Motivated Behaviors	Epidemiological, clinical, and preclinical studies have identified vulnerability to alcohol abuse in females. Compared to males, female rats drink more ethanol and show greater cue- and stress-induced reinstatement of ethanol seeking following. Though estradiol is implicated in motivation for cocaine, its role in ethanol-motivated behaviors is less consistent, and no studies have evaluated estradiol's effects on the reinstatement of ethanol seeking, and index of "craving". Here, gonadally intact and ovariectomized (OVX) female rats self-administered a sweetened ethanol solution paired with a cue for 3 weeks. Following extinction, rats were tested for the effects of estrogen receptor modulation on cue+stress-induced reinstatement of ethanol seeking. OVX rats received estradiol, and intact rats received the estrogen receptor blocker, clomiphene, or PHTPP, an estrogen receptor β antagonist prior to reinstatement. Estrogen levels were positively related to ethanol drinking. OVX females showed reduced reinstatement compared to intact females, and estradiol tended to reduce reinstatement relative to vehicle. Blockade of estrogen receptors with clomiphene or PHTPP tended to reduce reinstatement in intact females. These findings suggest that estrogen plays a role in ethanol-motivated behaviors that depend on gonadal status. Clarifying the role of estradiol in ethanol-motivated behavior may guide treatment targets for alcohol dependent women.
Jennifer Boatz	4	Basic Life Science	Solid-State NMR Reveals Two Structurally Distinct Aggregates Formed by a Cataract-Associated Gamma-D-Crystallin Mutant	Human gamma-D-crystallin (HGD) is an extremely soluble eye lens protein that under certain conditions loses its solubility and succumbs to protein aggregation. The aggregation of HGD in the lens is associated with cataract formation. The P23T mutant of HGD has significantly reduced solubility, and is associated with childhood cataracts. Currently there is no mechanistic understanding of how structural changes in the protein fold result in the reduced solubility and aggregation of P23T. We use magic-angle-spinning (MAS) Nuclear Magnetic Resonance (NMR) to investigate the structure of P23T in the aggregated state in order to gain insight into the mechanism of aggregation. MAS NMR measures protein chemical shifts, which provide in depth structural information. The chemical shifts of the protein are exquisitely sensitive to structural changes. Thus, we probe in a residue and site-specific fashion how the structure of P23T HGD changes between soluble and aggregated states. Depending on the aggregation conditions, different conformations of P23T in the aggregated state are directly observed. Our data reveal that aggregation conditions not only affect the macroscopic appearance of the aggregates, but also have a dramatic impact on the aggregates' detailed internal atomic structure. Therefore, there are distinct molecular mechanisms for crystallin misfolding and aggregation.

Colin Bredenberg	5	Basic Life Science	Examining Variably Diffuse Weight Perturbations in Plastic Neural Networks	Large-scale cortical networks employing homeostatic mechanisms and synaptic plasticity rules have been shown to exhibit stability in response to small perturbations to synaptic strengths. This property can potentially serve as a mechanism for memory in the brain–learned synaptic strengths within this paradigm are resistant to small degradation effects. Previous studies applied relatively simple perturbations to probe the stability of the network–all synapses within a given population were lowered by a uniform percentage. The goal of this work has been to analyze whether more complex perturbations can reveal more information about network stability. For instance, we have shown that lowering the strength of all synaptic weights in a specific assembly by 10% was not equivalent to lowering the strength of 1/3 of the weights by 30% –synaptic strength was restored in the former case, while it degraded in the latter. The net loss in synaptic strength was equivalent, and yet different results were observed. To further test this phenomenon, a lower-dimensional stochastic Wilson-Cowan model was employed, which captures the same perturbation phenomenon, but whose simplicity allows us to draw detailed conclusions about the relationship between the size of the perturbed population and its stability.
Teresa Capasso	6	Basic Life Science	Role of BMP10 in Cardiovascular Development in Zebrafish	Hereditary hemorrhagic telangiectasia (HHT) is a genetic disease characterized by a patient's increased tendency to develop direct connections between arteries and veins rather than an intervening capillary bed. In major organs, these malformations are known as arteriovenous malformations (AVMs), whereas in skin and mucous membranes, they are known as telangiectases. AVMs are prone to rupture and may lead to epistaxis, anemia, stroke, brain abscess, and heart failure. Heterozygous loss of the TGF-beta type 1 receptor, ALK1, leads to HHT2. Bone morphogenetic protein (BMP) 9 and BMP10 bind ALK1 with high affinity in vitro. However, which ligand activates ALK1 in vivo is unknown. Therefore, we generated zebrafish harboring mutations in liver-specific bmp9, heart- and liver-specific bmp10, and heart-specific bmp10-like. bmp9 and bmp10-like mutants develop no gross phenotype, whereas bmp10 mutants develop phenotype at around 1.5 months. We have observed erythema, edema, vessel dilation, hemorrhage, heart abnormalities, and early lethality in bmp10 mutants, suggestive of an HHT-like phenotype. Furthermore, bmp10;bmp10-like double mutants develop shunts embryonically and phenocopy alk1 mutants. These results suggest that BMP10 is the critical ALK1 ligand, and that in zebrafish, bmp10-like compensates for bmp10 embryonically but not at later stages.
Xing Changrui	7	Basic Life Science	Discovery of Novel Cannabinoid Receptor 2 Selective Ligands	Cannabinoids (CB) are defined as a class of compounds that can act on Cannabinoid receptors 1 or 2 (CB1 or CB2) and affect human physiology. Both CB1 and CB2 receptors belong to G-Protein Coupled Receptors (GPCRs). However, CB1 receptor is mainly expressed in the central nervous system, while CB2 receptor is dominantly located in the peripheral nervous system and immune cells. By now, scientists have

				discovered many CB ligands that have therapeutic potentials, but the limitation of non-selective ligands is the psychiatric side effect mediated by the activation of CB1 receptor such as drug abuse and depression. In this study, we discovered (E)-3-(4-Ethoxy-3-methoxyphenyl)-2-((4-methoxyphenyl) sulfonyl)-1-phenylprop-2-en-1-one as our novel CB2 lead compound; designed and synthesized analogues for the structure-activity relationship (SAR) studies. We also did physicochemical property prediction and docking studies. Then we tested their binding affinities and selectivities; conducted in-vitro functional studies; and evaluated their potentials for therapeutic treatment. Four compounds showed high CB2 binding affinity (Ki of 10-60 nM) and good selectivity (CB1/CB2 of 20 to 1305 fold). Their off-targets effects were also predicted. Overall, these sulfone derivatives can be used to develop novel therapeutic CB2 ligands.
Si Chen	8	Basic Life Science	Drug Target Identification Using Network Analysis: Taking Active Components in Sini Decoction as an Example	Identifying the molecular targets for the beneficial effects of active small-molecule compounds simultaneously is an important and currently unmet challenge. In this study, we firstly proposed network analysis by integrating data from network pharmacology and metabolomics to identify targets of active components in sini decoction (SND) simultaneously against heart failure. To begin with, 48 potential active components in SND against heart failure were predicted by serum pharmacochemistry, text mining and similarity match. Then, we employed network pharmacology including text mining and molecular docking to identify the potential targets of these components. The key enriched processes, pathways and related diseases of these target proteins were analyzed by STRING database. At last, network analysis was conducted to identify most possible targets of components in SND. Among the 25 targets predicted by network analysis, tumor necrosis factor α (TNF-α) was firstly experimentally validated in molecular and cellular level. Results indicated that hypaconitine, mesaconitine, higenamine and quercetin in SND can directly bind to TNF-α, reduce the TNF-α-mediated cytotoxicity on L929 cells and exert anti-myocardial cell apoptosis effects. We envisage that network analysis will also be useful in target identification of a bioactive compound.
Rebecca Dalton	10	Basic Life Science	Competition for Resources in a Co-Flowering Community	Biodiversity is critical for essential ecosystem functions and services to humans. Coexistence of many species requires a delicate between inter- and intraspecific competition. This will occur if one species is slightly better at obtaining a specific resources (e.g., acquiring nutrients vs. receiving pollinator visits), but, if changes in conditions due to global climate change or habitat fragmentation occur, this balance could be disturbed and some species to drive others extinct. For example, warming temperatures are causing some flowering species to emerge and reproduce earlier in the season, while others are germinating later. If species in a community respond unequally to the same environmental cues, populations might experience higher or lower levels of interspecific competition for shared resources than in the past, which could upset the balance of competition essential for coexistence. My research

				examines the relationship between phenology and the ability of two plant species to coexist in subalpine communities in Colorado. Thus far, there is evidence of competition in natural populations between two co-flowering species, Mertensia brevistyla and Claytonia virginica. With these preliminary data, I will model how climate change will affect coexistence mediated by competition for abiotic resources.
Tian Du	11	Basic Life Science	Identifying Endocrine Resistance Drivers in Invasive Lobular Carcinoma	Introduction: Invasive lobular carcinoma (ILC) is one histology subtype of the breast carcinoma and about 95% ILC tumors are estrogen receptor (ER) positive. Endocrine treatment to block ER pathway is one important approach to treat ER positive ILC tumors but limited by endocrine resistance. To identify the underlying mechanism in acquired endocrine resistance, we developed endocrine resistant long-term estrogen-deprived (LTED) ILC cell models from SUM44PE and MDA-MB-134VI (MM134) cells. Methods: We performed RNA-Seq on the LTEDs and their parental cells. Differentially expressed genes were analyzed and validated using R package DESeq2 and qRT-PCR. Gene functional studies were performed with Ingenuity Pathway Analysis (IPA) and online tool DAVID. Results: MM134LTEDs are unresponsive to estrogen in growth while SUM44LTEDs remain estrogen responsiveness. Pathway analysis indicates that metabolism pathways (eg, cholesterol biosynthesis) are activated in MM134LTEDs, and SUM44LTEDs show activated cell cycle and DNA damage response. ER activity and E2F signatures are also predicted to be activated in SUM44LTEDs, suggesting its role in endocrine resistance. We are currently studying the phenotypes of LTED cells, and are also testing candidate genes identified in the RNA-Seq analysis. Conclusion: MM134LTEDs and SUM44LTEDs have different phenotypes and they may have different mechanisms in endocrine resistance.
Mitch Ellison	12	Basic Life Science	The Paf1 Complex Broadly Regulates the Transcriptome of Saccharomyces Cerevisiae	Paf1C is a five-subunit complex that associates with RNA polymerase II during transcription. To investigate its roles in modulating the transcriptome, we assayed transcript levels in paf1 strains using whole genome tiling arrays. This approach revealed that Paf1 regulates the levels of both coding and non-coding Pol II transcripts. In addition to regulating snoRNA termination, Paf1 appears to promote the transcription of cryptic unstable transcripts and affect levels of antisense, stable unannotated, and Xrn1-sensitive transcripts. Gene ontology analysis revealed that the expression of iron homeostasis genes is elevated in paf1Δ strains, while the expression of phosphate homeostasis genes is decreased in these cells. As shown by RT-qPCR, individual Paf1C subunits differentially affect the expression of these genes. The largest effects for iron genes were observed in paf1Δ and ctr9Δ strains. Additionally, phosphate genes were affected in an rtf1Δ strain indicating that Rtf1-dependent histone modifications may be playing an important role. These data suggest that Paf1C modulates the expression of a diverse array of transcript types in S. cerevisiae by both promoting and repressing transcription. However, individual

				Paf1C subunits appear to affect several loci differentially suggesting that each complex member may play a different role.
A. Elizabeth Hildreth	15	Basic Life Science	Identifying the Regulatory Role of the DNA Entry-Exit Site of the Nucleosome in Transcription Termination	Eukaryotic chromatin is a restrictive barrier to RNA polymerase II, which transcribes protein coding and some noncoding RNAs. Chromatin consists of repeating nucleosomes, approximately 147 basepairs of DNA surrounding an octamer of histone proteins. Transcription is controlled by factors that modify nucleosomes, allowing Pol II to contact otherwise occluded DNA. Despite a few studies showing a requirement for select histone modifications and chromatin remodelers, little else is known about the role of chromatin at the final termination step. The goal of our work is to elucidate this role using Saccharomyces cerevisiae. We used a plasmid library encoding mutant histones and a termination reporter to identify 12 residues in histones H3, H4, and H2A required for proper termination. Interestingly, many of these residues reside in or near the nucleosome DNA entry-exit site. This surface coordinates the first 30 basepairs of DNA, thus regulating stability and accessibility of the nucleosome. Analysis thus far reveals improper nucleosome occupancy at candidate loci and defective placement of a transcription-coupled histone modification. Recent results suggest that increased elongation rate may also contribute to the observed termination defect in some mutants. These data implicate the DNA entry-exit site as an important player in the regulation of transcription.
Marie Johnson	16	Basic Life Science	CRISPR/Cas9-Engineered 3.16 Mb Deletions Generate a Model System to Study Hormone Secretion Deficits in Prader-Willi Syndrome (PWS)	PWS is a multisystem disorder caused by failure to express a cluster of ~12 paternally-expressed, imprinted genes. Neonatal failure to thrive (FTT) is followed by childhood-onset hyperphagia, obesity, neurobehavioral issues, and deficits in growth hormone, GnRH, insulin, and other hormones. In a PWS mouse model with deletion of the PWS-orthologous genes, we have shown that FTT is associated with a postnatal onset of severe hypoglycemia leading to lethality and pancreatic endocrine abnormalities, including developmental defects, deficient basal and glucose-stimulated insulin secretion with concurrent hypoglucagonemia and lack of a counter-regulatory response to hypoglycemia. Thus, PWS-imprinted genes are required to prevent hypoglycemia, and for development and secretory function of endocrine cells. Using rodent cell lines that secrete insulin (or glucagon or GnRH) and express a fluorescent protein-propeptide hormone biosensor to monitor trafficking within secretory granules, we utilized CRISPR/Cas9 genome editing to engineer deletions of the 3.16 Mb PWS-imprinted domain in 5-10% of cells. Subsequently, we generated clonal control and deletion cell lines, and are currently performing molecular cytogenetics, epigenetic, and hormone secretion assays, prior to secretory granule studies. This model system will allow genetic dissection of which PWS-imprinted genes control secretion of multiple hormones and the molecular and cellular mechanisms involved.

Zariel Johnson	17	Basic Life Science	Transcription Factor TonEBP is Critical for Maintaining Pro-Inflammatory Gene Expression in Nucleus Pulposus Cells	The transcription factor TonEBP (NFAT5) promotes transcription of genes required for cell survival under hyperosmotic stress as well as genes for extracellular matrix homeostasis. These functions are crucial in the physiologically hyperosmotic, matrix-rich nucleus pulposus (NP) of the intervertebral disc. We have shown, using RNA sequencing and gain- and loss-of-function experiments, that TonEBP also positively regulates transcription of pro-inflammatory genes CCL2, IL6, TNF, and NOS2 under hyperosmotic conditions and maintains protein levels of CCL2. TonEBP controls hyperosmotic-inducibility of CCL2 via a highly conserved binding site in the CCL2 proximal promoter. Using an organ culture model to evaluate the effects of hyperosmolarity and TonEBP on pro-inflammatory transcripts ex vivo, we found that CCL2, IL6, TNF, and NOS2 were osmo-sensitive in discs from wild-type mice but in not those from haploinsufficient TonEBP heterozygous mice. Finally, we examined cross-talk between TonEBP and NF-kB signaling pathways. Interestingly, hyperosmolarity induced NF-kB activity in the TonEBP-dependent manner and NF-kB activity was required for hyperosmotic induction of IL6, TNF, and NOS2 but not CCL2. Extracellular osmolarity in the NP fluctuates with diurnal loading of the spine. Therefore, we hypothesize that the osmotic sensitivity of these transcripts represents a physiological adaptation of NP cells to their environment.
Audrey Jonas	18	Basic Life Science	Unearthing Novel Bacteriophages on Microbacterium Hosts	Bacteriophages, viruses that infect bacteria, are the most abundant biological particles on earth and have a dynamic and very diverse population. Bacteriophage genomes are mosaic, as many of their genomic elements undergo illegitimate recombination with other phages and their hosts. Isolating and characterizing new phages of different bacterial hosts builds a more complete overview of phage diversity and evolution. This work focused on actinobacterial hosts within the genus Microbacterium: gram-positive, aerobic bacteria isolated from soil, grass, and leaf litter. Over twenty novel bacteriophages have been found to infect three species within this genus: M. foliorum, M. terrae, and M. aerolatum. Analysis of plaque morphologies, virion morphologies, and genomic digests using restriction endonucleases showed diversity between the phages. Fifteen of the genomes were sequenced. Comparative analyses including gene content, dot plots and average nucleotide identities of nucleotide content, phylogenetic relationships of the gene content (Splitstree) provide insights into that diversity. This illustrates the many discoveries left to be made regarding the vast diversity of the global bacteriophage population.
Ching-Chung Ko	19	Basic Life Science	The Analsys of Toxicity by Gene 52 of Mycobacteriophage Fruitloop	The sequenced genome collection of mycobacteriophages—viruses infecting the genus of Mycobacterium—has grown to more than 1100 genomes. The majority of the mycobacteriophage-encoded genes' functions are not understood. To exploring the unknown, 202 mycobacteriophage genes were over-expressed in Mycobacterium smegmatis mc(2)155—a relative of tuberculosis-causing bacteria—to identify those that are detrimental to bacterial growth. Using this approach, gene

				52 of mycobacteriophage Fruitloop was identified as a toxic mycobacteriophage gene. A co-immunoprecipitation assay followed by mass spectrometry analysis revealed that Wag31 of M. smegmatis—an essential protein involved in cell shape and cell wall integrity—was a target for Fruitloop gene 52's protein product (gp52). Fruitloop gp52 over-expression results in a change in mycobacterial cell morphology from rod to round, a phenotype similar to that seen when Wag31 is depleted in mycobacteria. Moreover, over-expressing Wag31 allows mycobacteria to survive in the presence of Fruitloop gp52. Further analysis revealed that gp52's V45, I70, and W71 residues are important for its toxicity, while the first 28 amino acids of gp52 are not. At a time when drug-resistant tuberculosis is becoming a severe concern, elucidating the phage-encoded toxic proteins' mechanisms creates opportunities to discover new anti-tuberculosis drug targets.
Jongwon Lee	20	Basic Life Science	Development of Structural and Functional Connectivity of MNTB Axon Collaterals to the Mouse Superior Paraolivary Nucleus	The medial nucleus of trapezoid body (MNTB) is the major source of inhibition in the auditory brainstem, providing inhibitory inputs to the lateral superior olivary (LSO), as well as the superior paraolivary nucleus (SPON). Projections from the MNTB to these nuclei are tonotopically organized. In the developing LSO, the tonotopic precision substantially increases via synaptic silencing and axonal pruning. In this study, we investigated whether the refinement of individual MNTB axon collaterals in the LSO and SPON is coordinated. Anatomical reconstructions of biocytin-filled MNTB axons show the presence of tonotopy in the MNTB-SPON pathways shortly after birth (P2-4). Over the next three weeks, axons expand and add new boutons, but this growth was proportional to the expansion of the SPON, resulting in no change in the tonotopic precision. Ongoing studies to map functional connectivity using laser-scanning photostimulation further support the early tonotopic organization of the MNTB-SPON projection and the absence of tonotopic refinement during the first three postnatal weeks. Our results demonstrate that MNTB axon collaterals show a dramatically different degree of tonotopic refinement and axonal pruning, depending on whether they innervate the LSO or MNTB, indicating that axonal pruning of these inhibitory axons is determined by the postsynaptic target.
Jr-Jiun Liou	21	Basic Life Science	Platelet-Rich Plasma Impairs Chondrogenesis of Infrapatellar Fat Pad Derived Adipose Stem Cells In Vitro	Post-traumatic and focal cartilage defects of the knee affect over 3 million Americans annually. Autologous cell-based cartilage repair, e.g., matrix assisted autologous chondrocyte implantation (MACI), is limited by donor site morbidity and the need for ex vivo chondrocyte expansion. Mesenchymal stem cells (MSCs), which can be obtained in higher quantities than chondrocytes and undergo extensive expansion with subsequent chondrogenic differentiation, represent an alternative cell type for cartilage repair. We tested the use of platelet-rich plasma (PRP), previously shown to promote stem cell proliferation and tissue healing, to enhance chondrogenic differentiation of human MSCs derived from infrapatellar fat pad (IFP-ASCs). In both pellet and hydrogel cultures, PRP does not improve IFP-ASC chondrogenesis; in general, chondrogenesis was inhibited with increasing PRP

				concentrations and duration of exposure. These findings suggest that although PRP is reported to be beneficial in terms of pain relief and joint function improvement, PRP may not enhance hyaline cartilage formation.
Shi Tong Liu	22	Basic Life Science	Optimal Features for Acoustic Classification	The recognition and categorization of complex sounds is a central goal of auditory processing. In vocal animals, conspecific vocalizations or 'calls' are an ethologically central set of sounds that are perceptually recognized and distinct. Typically, the vocal repertoire of a species consist of several categories with overlapping spectral profiles, making classification using low-level cues such as long-term spectrum impossible. In addition, classifiers should account for the high variability of different vocalization tokens within each class. Here, we propose that combinations of acoustic features of intermediate complexity can be used to categorize vocalizations. We start by extracting random acoustic features from one class of marmoset calls. Using an information maximization approach, we score each feature on its ability to correctly classify this call type from all others. We then select a set of features that maximize classification accuracy while minimizing redundancy. High classification accuracy can be achieved using a small set of such features. If cortical neurons were indeed encoding such features, they would exhibit highly nonlinear and selective tuning. Such neurons have been observed in single-unit recordings from marmoset auditory cortex, supporting the feature-based classification model. Similar feature-based approaches can be implemented for more complex tasks such as speech recognition.
Jacob Meadows	23	Basic Life Science	FOXOs Suppress Lipid Peroxidation to Promote AML Progression and Chemotherapy Resistance	Acute myeloid leukemia (AML) is a blood cancer that arises from the over-production of immature white blood cells (called myeloid progenitors) that are unable to differentiate. Over 30% of AML patients do not respond to first-line chemotherapy, and a significant portion of patients that do respond eventually relapse with resistant AML, suggesting that AML cells either develop or inherently possess mechanisms to circumvent conventional chemotherapy. Previous studies suggest that AML may alter their intracellular redox environment in order to acquire chemotherapy resistance, but the specific pathways controlling are unknown. The FOXO family of transcription factors support the differentiation blockade in AML and thus promote survival. In this study, we provide evidence that FOXOs manage AML cell redox biology by suppressing the production of lipid peroxides. Interestingly, anthracyclines (e.g. daunorubicin, DNR), which are the first-line class chemotherapies for AML, rely on inducing lipid peroxidation to kill cells. Our research has shown that FOXO inhibition increases lipid peroxidation and boosts DNR-mediated AML cell death. Further, the anti-lipid peroxide agent, butylated hydroxyanisole, entirely blocks the cytotoxic effects of DNR. These results suggest that FOXOs play an important role in AML progression and chemotherapy resistance by directly modulating lipid peroxide levels.

Wynn Meyer	24	Basic Life Science	Exploring Variation in Courtship Song Throughout the *Drosophila nasuta* Clade	Courtship behavior in Drosophila is highly variable, with some aspects frequently displaying strong quantitative differentiation between closely related species. One such variable trait is “pulse song,” a vibrational pattern that contributes critically Drosophila’s stereotypical courtship ritual. The spacing of song pulses differs between closely related species in several clades and is often important for species recognition. Previously developed methods enable high-throughput characterization of pulse song in *Drosophila melanogaster*; however, these methods perform poorly in distantly related species. We here develop a general method for pulse song identification and use it to characterize song phenotypes across 13 species within the *Drosophila nasuta* clade. This clade represents a recent radiation of species with low levels of morphological and genetic divergence, making it a prime model for studying the genetic basis of reproductive isolation. We assess how pulse song has evolved throughout this clade by integrating our quantitative pulse song analyses with an estimation of species’ phylogenetic relationships. Our results suggest that the new method will be applicable to species with wide variation in pulse song. Moreover, we identify differences in pulse song between species in the *D. nasuta* clade that show promise for mapping the genetic basis of these important behavioral traits.
Nyla Naim	25	Basic Life Science	Camp Compartment Dynamics in Thyroid Cell Proliferation	Cyclic adenosine monophosphate (cAMP) is a ubiquitous second messenger that regulates multiple cell processes. Mutations causing constitutive cAMP signaling have been linked to endocrine hyperproliferative disorders. Despite its clinical significance we lack a fundamental understanding of how cAMP activates specific downstream pathways. The cAMP compartmentalization model suggests cAMP distribution is uneven and can accumulate in subcellular regions. These compartments can co-localize with effector proteins to specifically regulate downstream responses. Working in thyroid cells, we found a protein complex containing protein kinase A (PKA), exchange protein directly activated by cAMP (EPAC), and scaffolding protein Radixin. Disruption of this complex blocks thyroid stimulating hormone (TSH)-mediated proliferation. These data suggest that the Radixin complex positions PKA and EPAC in a local area of high cAMP for effective transduction of TSH signaling. We hypothesize the Radixin cAMP compartment regulates TSH-mediated proliferation. We found cAMP levels proximal to the Radixin complex are ~2-fold higher compared to the bulk cytosol. To mimic this phenomenon, we have developed novel optogenetic tools targeted to distinct subcellular compartments. Gaining a better understanding of the physical interactions and dynamics between cAMP and multiple signaling pathways may provide novel therapeutic approaches for treating diseases with aberrant cAMP signaling.
Robert Nicholls	26	Basic Life Science	A Porcine Model of Phenylketonuria	Phenylalanine hydroxylase (PAH) deficiency, traditionally termed phenylketonuria (PKU), results in neurotoxic accumulation of phenylalanine (PHE), culminating in

			Generated by CRISPR/Cas9 Genome Editing	neurodevelopmental, cognitive, and psychiatric symptoms. Although rodent models biochemically recapitulate classical PKU, they poorly model the neurological phenotype. Since pigs more closely resemble humans in brain size, anatomy, physiology and genome, we proposed PAH-null pigs as a superior animal model. By expressing Cas9 endonuclease with CRISPR guide RNAs (gRNAs) targeting sites in PAH introns in in vitro cell models, we identified optimal reagents that generate exon 6 deletions or inversions and inactivate the gene. Subsequently, zygote injections of RNA encoding a pair of gRNAs and Cas9 with embryo transfer to surrogates led to a pregnancy with two piglets delivered. Biochemical analyses showed normal blood PHE in one (141 μM) with the other having hyperphenylalaninemia (2063 μM) consistent with classical PKU. Molecular analyses (deletion-PCR, DNA sequencing) demonstrated the former was heterozygous for alleles having a deletion or gRNA target site mutations, while the PKU piglet has deletions involving each allele. Clinical and neurological phenotypes are under assessment. In conclusion, a porcine model of PKU provides a highly relevant pre-clinical model to discern mechanisms of neurological disease and to develop novel interventional strategies.
Joon Park	31	Basic Life Science	Activating the HSP70 Chaperone Ameliorates Acute Kidney Injury in Zebrafish	A widespread and potentially fatal condition called acute kidney injury (AKI) affects up to 1.5 million patients and is associated with a high mortality rate exceeding 71% of at-risk patients. Current treatment options such as dialysis or kidney transplant are poor options, and exacerbates the need for a novel therapeutic option. Enhancement of the renal epithelial cells by improving the cytoprotective capability has shown to be an encouraging potential therapeutic model. A previous study used MAL 1-271, an allosteric regulating compound, to improve protein functionality of heat shock protein 70 by stimulating ATPase activity. The methyl ester analog of MAL 1-271, AMT 628-27, has shown even greater ATPase activity given the significantly greater increase in survivability after nephrotoxic insult in a zebrafish model. The function of heat shock protein 70 has been linked to inhibiting apoptosis and is pivotal for cellular stress response. Further understanding of the activation of heat shock protein 70 on kidney repair could lead to other potential therapeutic options.
Kexin Shen	32	Basic Life Science	Identification of Selective Inhibitors for SRC-Family Kinases Implicated in FLT3-ITD+ AML	The myeloid Src-family tyrosine kinases Hck, Lyn and Fgr are over-expressed and constitutively active in acute myelogenous leukemia (AML), and may contribute to leukemic stem cell survival. Recently we found that Fgr is expressed at very high levels in a subset of primary human AML bone marrow samples, identifying Fgr as a unique drug target in AML. To develop a high-throughput screening assay for selective inhibitors of Fgr, we expressed the near-full-length kinase (SH3-SH2-kinase-tail) in bacteria and characterized it by mass spectrometry. Using an in vitro kinase assay, we demonstrated that recombinant Fgr is active and strongly inhibited by the ATP-competitive kinase inhibitor, A-419259, which has been previously shown to

				eradicate AML stem cells in patient-derived xenograft mice. Surprisingly, full-length Fgr was more sensitive to this inhibitor than the near-full-length kinase, suggesting that the unique N-terminal domain has an allosteric effect on the inhibitor binding site. Similar experiments with Src did not reveal this difference, identifying a unique feature of Fgr amenable to medicinal chemistry optimization. Ongoing studies are exploring the role of the SH3 and SH2 domains in the regulation of Fgr kinase activity in vitro, as a prelude to selective inhibitor discovery targeting this AML-associated kinase.
Zheni Shi	33	Basic Life Science	Pard3c, an Unconventional Zebrafish Par-3 Ortholog for Organogenesis: Important for Cell Survival and Proliferation, but Not for Apicobasal Polarity	Vertebrate homologs of Caenorhabditis elegans Par-3 have versatile biological functions, including the prototypical role in cell polarization; such functional versatility may be partly explained by the variety of vertebrate Par-3 homologs. Thus, revealing the similarities and differences among individual Par-3 homologs is a prerequisite for a thorough understanding of their biology in vertebrates. Here, we identified and characterized Pard3c, one of the four zebrafish Par-3 orthologs. The Pard3c sequence is most closely related to that of Pard3, a zebrafish Par-3 ortholog that has been studied extensively. Surprisingly, unlike Pard3, Pard3c does not restrictively localize apically nor is it required for epithelial apicobasal polarity; instead, Pard3c localizes broadly to the cell membranes and is required for proper levels of cell survival and proliferation during the morphogenesis of the retina, lens, midbrain-hindbrain boundary, pharynx, and pectoral fin. Thus, despite the loss of the hallmark function of regulating apicobasal polarity as other Par-3 homologs do, Pard3c yet plays indispensable roles in zebrafish organogenesis.
Huong Tran	34	Basic Life Science	Effects of Acute Alterations in Intraocular and Intracranial Pressures on the Optic Nerve Head	Elevated intraocular pressure (IOP) is the main risk factor for glaucoma, the second leading cause of blindness worldwide. It remains poorly understood how the biomechanical effects of IOP vary depending on the level of intracranial pressure (ICP). Our goal was to measure the effects of acute modulation of IOP and ICP on the optic nerve head (ONH) of the eye. In 5 eyes of 3 monkeys, IOP and ICP were each set at 4 levels (low, baseline, high, very high). The anterior lamina cribrosa (ALC) and scleral canal opening at Bruch membrane (BMO) were manually delineated. MATLAB codes were used to reconstruct 3D ALC surfaces and computed ALC depths relative to the BMO best-fit plane within regions visible in all scans of an eye and normalized to baseline in each monkey. Acute modulation of either IOP or ICP above or below baseline caused non-linear and non-monotonic deformations of the ALC, with strong interactions between IOP and ICP. The ranges for normalized median ALC depth were 72-104%, 52-122%, 61-115%, 62-107%, and 92-108% in eyes 1R, 2R, 2L, 3R and 3L. In all 5 eyes, the most anterior LCs occurred with low IOPs (<15mmHg) and very high ICP (20-45mmHg).
Jianying Zhang	36	Basic Life Science	Non-Tenocyte Differentiation of Tendon Stem Cells	Tendinopathy is a prevalent tendon disorder, and costs billions of healthcare dollars every year. Current clinical treatments for tendinopathy are largely palliative because the precise cellular and molecular mechanisms of the disorder are not clear.

			Causes Tendinopathy via mTOR Signaling	Histological analysis indicated that tendinopathy tendons have lipid deposition, proteoglycan accumulation, and calcification. Mammalian target of rapamycin (mTOR) plays an important role in the regulation of cell proliferation and protein synthesis. Previously, we showed that the leading cause of tendinopathy is the aberrant differentiation of tendon stem cells (TSCs) into non-tenocytes. However, it is not clear whether the differentiation of TSCs is regulated by mTOR. Therefore, we studied the effect of rapamycin (a specific inhibitor of mTOR) on cell proliferation and differentiation of rat TSCs. Rapamycin treatment significantly inhibited the non-tenocyte differentiation of rat TSCs as evidenced by histochemical staining of oil red O (adipogenesis), Safranin O (chondrogenesis), and Alizarin red S (osteogenesis), and by gene expression of PPAR (adipocyte-marker), SOX-9 (chondrocytes-marker), and Runx-2 (osteocytes-marker). These results suggest that non-tenocyte differentiation of TSCs could lead to the development of tendinopathy in vivo. Rapamycin may be an effective drug for preventing development of tendinopathy by decreasing the non-tenocyte differentiation of TSCs through the inhibiting mTOR activity.
Jianying Zhang	37	Basic Life Science	Characterization of Stem Cell Populations Isolated from the Sheath and Core of Human Plantar Fascia	Plantar fasciitis is very common with 3 million patients in the USA every year. Its pathogenesis is unknown, and no effective treatment is in place so far. Only the mechanical property of plantar fascia (PF) was studied, nothing is known about its tissue structure and cell type contents. In order to understand the cellular mechanisms involved in PF healing, we studied the properties of stem cells isolated from the sheath (PF-S) and the core (PF-C) of human PF. The PF-S cells formed larger colonies and grew faster than the PF-C cells. More PF-S cells expressed stem cell markers (nucleostemin, Oct-4, and SSEA-4) and positively stained by collagen type IV, CD31, and vimentin, and less PF-S cells stained by collagen I when compared to PF-C cells. Furthermore, both PF-S and PF-C cells differentiated into adipocytes, osteocytes, and chondrocytes, but the numbers of differentiated PF-S were higher than PF-C cells. These results were confirmed by qRT-PCR. This study shows for the first time that the human PF has distinct sheath and core tissues with different structures. The stem cells in PF sheath and core exhibit differential properties, which will be useful to devise new biologics approaches for repairing injured PF in clinics.
Yifei Zhao	38	Basic Life Science	Comparison of Ex-Vivo Expanded Human Alloantigen Specific Regulatory T Cells Stimulated by Multiple Antigen Presenting Cells	Regulatory T cells (Tregs) play a vital role in manipulating immune responses, indicating their potentially usage in post organ transplantation. It has been reported that multiple antigen presenting cells (APCs) succeeded in expanding human Tregs ex-vivo. However, little is known about the differences in potency and characteristics of Tregs stimulated by different types of APCs. Comparison in various aspects have been made among Tregs expanded by conventional DCs, LPS treated DCs (LPS-DCs), CD40L treated DCs (CD40L-DCs) and CD40L-sBc. In two independent experiments using different pairs of donors and recipients, LPS-DC stimulated Tregs expanded the most, CD40L-DC Tregs expanded comparable to LPS-DC Tregs, but always less than LPS-DC Tregs. CD40L-sBc Tregs expanded the least. Expression of

				CD25 was lower in DC Tregs and LPS DC Tregs, while CLA is higher in LPS DC Tregs. In one experiment, we also observed that CD40L DC Tregs are the most potent in SA, while LPS-DC Tregs and CD40L sBc Tregs are less potent, but still more efficient than DC Tregs. In one experiment, we observed all types of Tregs produce less IFN-r compared to control Teff. More experiments needs to characterize the Tregs expanded by different APCs.
NEW RESEARCH TOOLS AND TECHNIQUES				
Margarete Bower	39	New Research Tools and Techniques	Share Data with D-Scholarship	Researchers are increasingly encountering funder requirements for preserving and sharing research data. Even where no requirement exists, there is growing recognition of the benefits of data preservation and sharing for the data creators, the scholarly community and the public (Corti et al., 2014, p. 11-12). As the University's repository for scholarly research materials, D-Scholarship@Pitt can function as a home for materials of all kinds. This poster focuses on D-Scholarship@Pitt as a research tool for sharing data. The University Library System now mints DOIs for data deposited in D-Scholarship@Pitt, tracks usage via Plum Analytics, and provides a suite of services to support researchers as they deposit data. With this poster, we outline benefits of data sharing via D-Scholarship@Pitt and the library resources and services that help researchers see these benefits in action. Corti, L., Van den Eynden, V., Bishop, L., & Woollard, M. (2014). Managing and sharing research data: A guide to good practice. London: SAGE Publications Ltd.
Erin Gilchrist	40	New Research Tools and Techniques	The Macro Research Assistant Program: A Winning Solution for Acute Care Research and Undergraduate Students	Multidisciplinary Acute Care Research Organization (MACRO) is a joint clinical research enterprise of the Departments of Critical Care Medicine, Surgery, Emergency Medicine, and Medicine, focused on screening and enrollment of human subjects in acute care studies. In 2009, we set up a small student program to facilitate live screening and data collection in one Emergency Department (ED) for a single trauma study. In response to further demand and recognizing the opportunity to educate Pitt undergrads in clinical research and practice, we continued the program, and developed selection, training, and mentoring processes. Undergraduate students undergo rigorous training to become proficient at various complex lab tests as well as study protocols while utilizing innovative methods of screening and recruitment. In 2013 and 2014, we worked with the University's Health Professions Advisors, and the Office of Admissions for the School of Medicine, to further enhance the educational experience. The MACRO RA program affords significant educational opportunities for undergraduate students seeking medical and clinical research exposure, and has become an integral tool for the successful conduct of multiple acute care studies.
Asiyeh Golabchi	41	New Research	Effect of Chronic Melatonin Administration on	It is commonly assumed that the success of long-term functionality of implanted microelectrodes into the cortex for electrophysiological recording and stimulation depends on the stability of the interface between neural tissue and electrodes. The

		Tools and Techniques	Long-Term Neural Recording Quality in the Visual Cortex of Mice	possible cause for electrode failure is the formation of an inflammatory fibrous capsule and neuronal loss in the surrounding microenvironment around the recording sites. Caspase-1 or interleukin (IL)-1-converting enzyme is known to be responsible for cell death and inflammatory process. Our previous study showed the chronic recording from implanted electrode in caspase-1 knockout (KO) mice had significantly greater single-unit recording performance compared to the wild type (WT) mice and strongly suggesting caspase-1 being a promising therapeutic target for maintaining healthy electrode and neural tissue interface and high quality neural recording . Melatonin is a small molecule drug with remarkable neuroprotective effects by indirectly inhibiting caspase-1 along with non-caspase dependent apoptosis. Daily administration (intraperitoneal injection) of melatonin was given 3 days before and for 4 month after implantation to the WT male mice implanted with chronic NeuroNexuas neural electrode arrays into V1m cortex. Electrophysiological recording presents significant improved single-unit yield from the melatonin treated groups compared to the saline control groups.
Carol Greco	42	New Research Tools and Techniques	New, Brief Questionnaires to Assess Nonspecific Factors in Treatment Outcome	Objective: To introduce new, brief questionnaires that assess non-specific factors such as treatment expectations, and determine whether these factors predict pain treatment outcomes. Methods: Patients (N=178) with chronic back and/or neck pain completed the Healing Encounters and Attitudes Lists (HEAL) computerized questionnaires early in their treatment and 6 weeks later. HEAL includes: Patient-Provider Connection (PPC), perceptions of the Healthcare Environment (HCE), Treatment Expectancy (TE), Positive Outlook (PO), Spirituality (SP), and attitudes toward Complementary and Alternative Medicine (CAM). Treatments included chiropractic, physical therapy, injections, acupuncture, or medications. Results: Overall, patients' self-reported pain intensity was significantly improved during their treatment ($t=7.03$, $p<.001$). HEAL Patient-Provider Connection, Treatment Expectancy, and Attitude toward CAM predicted improvement (Clinical Global Impression of Improvement). In regression models that included adjustment for age and depression, Treatment Expectancy predicted improvement in pain intensity at 6 weeks. Patients stated that HEAL questionnaires were easy to understand and relevant to their treatment. Clinicians generally found the HEAL summaries useful and important, and they valued graphical displays of scores. Conclusions: HEAL measures are relevant to nearly any type of treatment, and nearly any clinical condition, and can enhance patient care as well as contribute to research precision.
Solomon Klombers	45	New Research Tools and Techniques	Assessing CFTR's Tolerance for Nonsense Mutation Correction in NBD1	Cystic fibrosis (CF) is a genetic disorder that results in altered salt and fluid secretion. CF is caused by mutations in the cystic fibrosis transmembrane conductance regulator protein, (CFTR) which functions as a chloride channel in epithelial cells. CFTR has nearly 2000 identified mutations, many of which cause improper folding, resulting in protein degradation and loss of function. Our project will focus on two of CFTR's nonsense mutations: G550X and S489X. Both G550X and S489X are in

				nucleotide binding domain 1 (NBD1) and result in nonfunctional CFTR. Current small molecule therapeutics are imprecise and do not provide specific replacement of the native amino acid. Therefore, it is likely that specific nonsense mutations will show differential efficiencies in correction. To test the tolerance for amino acid substitutions and potential for small molecule correction of nonsense mutations, we will generate missense mutations at positions G550 and S489, which are sites of identified nonsense mutations in the CF population. Using site-directed mutagenesis, we will assess the impact of substitutions at these loci on folding of NBD1 and full-length CFTR. These data will clarify the tolerance for amino acid substitutions at specific sites and the potential use of small molecule read-through therapies for correction.
Dongmei Liu	46	New Research Tools and Techniques	Quantification of Cumulative Multiple Organ Dysfunction Scores Identifies Phenotypic Clusters and Biomarker Patterns in Blunt Trauma Patients	Background: Trauma-induced multiple organ dysfunction syndrome (MODS) is often associated with a complicated clinical course. Using Marshall MODScore as an intermediate endpoint, we sought to identify clusters among trauma patients and to correlate the clusters with inflammation biomarker patterns as a strategy for early stratification of patients. Methods: Clinical data from 376 blunt trauma survivors with MODScores from D2-D5 were subjected to hierarchical clustering analysis (HCA) to define patient sub-groups. Inflammation biomarkers were assayed in serial blood samples (3 samples within the first 24 h and then daily up to D5). Dynamic network analysis (DyNA) was used to suggest dynamic interconnectivity among the inflammatory mediators. Results: HCA segregated patients into three distinct groups: Low MODS; Intermediate MODS; and High MODS groups. There were statistically significant differences among the three groups with regards to in-hospital adverse outcomes being all greatest in the High MODS group. Circulating levels of IL-6, MCP-1, IL-10, and IL-8 were differentially elevated upon presentation in the High MODS group. DyNA revealed a reduced interconnectivity among the inflammatory biomarkers in the High MODS group over the initial 16 h post-injury. Conclusion: Our results suggest it will be feasible to use biomarkers to stratify trauma patients into outcome-based cohorts.
Albert Liu	47	New Research Tools and Techniques	Finding the Distinct Functional Impact of Different Mutations in PIK3CA Using the Tumor-Specific Driver Identification Algorithm	PIK3CA is a commonly mutated oncogene that encodes for the catalytic subunit of the enzyme PI3K, whose pathway leads to cell proliferation and survival. We hypothesized that mutations in PIK3CA may alternate downstream signaling pathways and induce tumorigenic changes in gene expression. We used the novel Tumor-specific Driver Identification (TDI) algorithm, which finds causal relationships between somatic genomic alterations (SGAs) and differentially expressed genes (DEGs) in individual tumors, to identify target genes of PIK3CA amplification and somatic mutations, as well as target genes of specific PIK3CA mutation hotspots. The TDI algorithm found that the 424 targets of PIK3CA somatic mutation and the 187 targets of PIK3CA amplification activate a common set of target DEGs, indicating that both activate a common canonical pathway of normal PI3K. These target genes

				were highly enriched in known target genes of PIK3CA hotspot mutation H1047R derived from an independent study. More Importantly, PIK3CA somatic mutation affects the expression of 248 genes outside of this canonical pathway. Thus this alternate downstream signaling pathway induced by PIK3CA somatic mutation will clearly contribute to our mechanistic understanding of tumorigenesis and facilitate the development of targeted therapies in cancer clinics.
Jose Posada	48	New Research Tools and Techniques	Social-Context Sentence Annotation from Psychiatric Clinical Reports	Current medical natural language processing pipelines does not provide social context sentence extraction, which is critical for processing psychiatric notes and determining health outcomes of various disorders. We conducted annotation study for annotating 210 discharge summary notes collected from the WPIC which is the largest psychiatry hospital serving the Allegheny county in Pennsylvania. There were two board-certified psychiatrists annotating the reports. The final inter-annotator agreement was 75.2%, which shows good agreement between the two psychiatric annotators. We perform six rounds of annotations which included a training phase, a guideline validation stage, individual annotation stages and agreement sessions. Before the annotation, we created a guideline for the annotation study. The first step was to create a definition of social context based on SNOMED CT and DSM IV. From SNOMED CT we used the definition of the social context hierarchy and the elements below that root. For DSM we used the axis four which describe psychosocial and environmental problems. Using both definitions, along with a revision of some psychiatric reports, we came up with 11 different types. Those types are: economic, education, health care, housing, interaction with legal system, occupation, social environment, spiritual life, support circumstances and networks, transportation, and other.
Matthew Rannals	49	New Research Tools and Techniques	Molecular Profiling of an In Utero Gene Transfer Model of the Schizophrenia and Rare Autism Disorder Associated Gene, Transcription Factor 4, TCF4, Identifies Ion Channel Targets of Pathophysiology	Transcription Factor 4 (TCF4) is a clinically pleiotropic gene associated with schizophrenia and Pitt-Hopkins syndrome (PTHS). To gain insight about the neurobiology of TCF4, we created an in vivo model of PTHS by suppressing Tcf4 expression in rat prefrontal neurons immediately prior to neurogenesis. This cell-autonomous genetic insult attenuated neuronal spiking by increasing the afterhyperpolarization. At the molecular level, using a novel technique called iTRAP that combined in utero electroporation and translating ribosome affinity purification, we identified increased translation of two ion channel genes, Kcnq1 and Scn10a. These ion channels candidates were validated by pharmacological rescue and molecular phenocopy. Remarkably, similar excitability deficits were observed in prefrontal neurons from a Tcf4+/tr mouse model of PTHS. Thus, we identify TCF4 as a regulator of neuronal intrinsic excitability in part by repression of Kcnq1 and Scn10a and suggest that this molecular function may underlie pathophysiology associated with neuropsychiatric disorders.
I. Mitch Taylor	50	New Research	Development of Novel	The real-time in vivo detection of neurochemicals is highly intriguing due to their widespread implication in healthy and diseased brain function. Successful

		Tools and Techniques	Electrochemical Sensors for the Real-Time In Vivo Detection of Cocaine and Dopamine	neurochemical sensors must be selective and sensitive for the neurochemical of interest, exhibit high spatial and temporal resolution and maintain small physical dimensions to prevent insertion related tissue damage. We have developed three novel, highly successful electrochemical sensors that provide clear and robust real-time detection of dopamine and cocaine. Our in vivo cocaine sensor incorporates a cocaine-selective, electrochemically active DNA aptamer onto a single shank silicon neural recording probe. The sensor exhibits selective, robust cocaine detection in the rat dorsal striatum in response to both local cocaine infusion and intravenous cocaine injection and clear measurement of spontaneous and evoked electrophysiological activity in the barrel cortex. We have also developed two dopamine sensors that incorporate PEDOT coatings onto carbon fiber microelectrodes (CFE). PEDOT/graphene oxide coated CFEs exhibit an 880% increase in dopamine sensitivity and a 50% decrease in LOD compared to bare CFEs, whereas PEDOT/carbon nanotube coated CFEs exhibit a 4800% sensitivity increase and a potential for signal amplification by preconcentration. These sensors are a marked improvement over existing technology and will allow for greater understanding of brain function.
PHYSICAL SCIENCE AND ENGINEERING				
Amanda Boyer	51	Physical Science and Engineering	Electromyography Based Control for Lower Limb Assistive Therapy	Recent research has shown robotics based neurorehabilitation is as effective as traditional therapy. In order to help patients regain leg mobility, this project aims to create a mathematical model based on the electromyographic (EMG) signal. The EMG signal is an electrical signal the muscle emits as it contracts. Three mathematical models were tested: 1) a sigmoid artificial neural network, 2) a musculoskeletal model, and 3) a combined musculoskeletal-neural network model. The first mathematical model used was a sigmoid artificial neural network with the leg extension machine. The neural network was trained, using the error, to output the joint angle of the leg extension machine. The second model used was the musculoskeletal model. Using estimated parameters taken from a participant, the dynamics of the leg based on the position and activation voltages (EMG signal) were simulated. The output was then mapped to the range of the leg extension machine. The third used the artificial neural network to map and adjust the EMG signal in the musculoskeletal model to fit the encoder data. The first two methods did not have accurate enough results and the third was unstable. Further research adjusting these methods must be done to find an accurate model.
Riley Burton	52	Physical Science and Engineering	Computational Modeling of Wall Stress in Cerebral Aortic Aneurysms Endoscopically Coiled with	Cerebral aortic aneurysms (CAA) are abnormal focal dilations of intracranial arteries resulting from medial degeneration of the vessel walls. The most serious threat from CAAs is sudden rupture and subsequent hemorrhage. Endovascular coiling is a non-invasive procedure where CAAs are filled with detachable coils to induce blood clotting, thereby restricting blood flow in the aneurysm and lowering the tendency to rupture. The goal of this study is to investigate spatial variation in aneurysmal

			Different Packing Densities	wall stress for different coil packing densities (CPD) and to evaluate the effectiveness of coiling between simple and branched CAAs. Virtual 3D geometries of CAAs were constructed from Digital Subtraction Angiography scans of patients. CAA walls were modeled using literature mechanical property values with a uniform thickness of 0.36 mm under a constant pressure of 120 mmHg. Thrombi were modeled using material properties from uniaxial compression data. Four models were created for each patient: one exhibiting the mechanical properties of a blood clot, and three clots made with different CPDs (10%, 20%, 30%). Among filled CAAs, larger reductions in mean wall stress occurred with the presence of coils and larger CPDs. Mean wall stress reductions in simple CAAs were significantly higher than in branched models.
Kelly George	53	Physical Science and Engineering	Systematic Backbone Alteration of a Zinc Finger Domain Leads to Unnatural Mimics with Comparable Folds and Functions	The crucial characteristic of proteins that allows these ubiquitous macromolecules to perform vital and sophisticated biological roles is their propensity to fold into compact conformations. Designing polymers with specific folded conformations (termed “foldamers”) that can mimic these natural folds and functions may open doors for applications ranging from therapeutic development to entirely novel tasks. Yet, the design of such molecules remains a significant challenge. Our group previously reported an approach to generate heterogeneous foldamers by altering 15-20% of the backbone of a small protein while retaining its native tertiary fold. This method utilizes several types of unnatural building blocks in concert by substitution into natural peptide sequences. My project aims to advance this method by expanding past tertiary structure mimicry and aiming to also retain ligand binding in zinc finger domains, a target class in which tertiary fold formation is metal dependent and gives rise to sequence-specific recognition of double stranded DNA. This poster describes the design, synthesis, and biophysical characterization of backbone-modified variants of a natural Cys2His2 zinc finger, Sp1-3 (the third finger of Specificity protein 1). Results obtained suggest that two variants successfully mimic the tertiary fold, ligand binding environment, and ligand binding propensity of the natural sequence.
Gabriel Hinding	54	Physical Science and Engineering	Modeling Precision Motion of Linear Stages	Precision motion is essential in a variety of applications, and improvements can be made by redesigning the hardware, but it’s more cost effective to upgrade the software instead. Three Aerotech Inc. stages were examined with intentions of eventually developing a systematic way to virtually design and test any stage for explicit precision requirements. To do this, it was necessary to investigate various aspects of system dynamics, evaluating the increase in model accuracy achieved with each increased step of model complexity. By using a black-box model, it’s possible to focus strictly on the relationship between the input and output of the system. Thus, part of the investigation was to determine an input signal that excites the correct parameters. The stage behavior was collected using an Aerotech program, and the input/output currents of the amplifiers in each stage were

				recorded. Frequency domain data was used to create models, which were then validated using time domain step data. The amplifier in the Aerotech Inc. stages is closed loop, thus it's not surprising that the unit gain models resulted in the best time domain fit percentages. Although only three stages are examined, a successful model framework could be used for any linear stage.
Katerina Kimes	56	Physical Science and Engineering	Additive Manufacturing of Magnetocaloric Material for High-Efficiency Cooling	Magnetocaloric materials have been studied extensively within the past few decades in an effort to find alloys that exhibit a large temperature change when magnetized. These materials are used in magnetic refrigeration which is a more sustainable and efficient alternative to traditional refrigeration methods. However, no studies have been done regarding the additive manufacturing of magnetocaloric materials and their properties. Here, we focus on the characterization of the Direct Laser Deposition (DLD) of NiCoMnSn powder. Powder size distribution analysis and microscopy were performed on the powder before printing. The distribution was found to be varied over a wide range of sizes. Printed samples were characterized using VSM, DSC, SEM, and EDS techniques. VSM results showed a small hysteresis and a saturation magnetization around 50 emu/g for both samples. DSC tests showed wide peaks between 50°C and 150°C instead of a narrow peak for the phase transformations. SEM imaging showed very interesting microstructural characteristics such as grains, twinning, dendrites, and segregation. The microstructure varied greatly from bottom to top in all samples. Lastly, EDS analysis resulted in nominal composition in the twinned regions and enriched/depleted areas outside of the twins.
Seyed Moghaddam	59	Physical Science and Engineering	Multiscale Shoe-Floor Friction Model Predicts Impact of Shoe-Floor Angle on Utilized Coefficient of Friction During Slipping	Slips are a serious occupational hazard. Probability of slips increases when the available coefficient of friction between shoes and flooring (ACOF) is less than the required coefficient of friction to sustain walking. Our previous research has revealed the potential of multiscale computational models to predict ACOF. The objective of this study was: 1. To utilize the multiscale computational model to understand the impact of slipping kinematics on coefficient of friction during a slip (COFU) and 2. To use the multiscale computational model to predict the impact of shoe-floor angle on ACOF. Our experimental results demonstrated that COFU had higher values for human subjects with low (near zero) shoe-floor angles. A similar trend was present in ACOF and the shoe-floor contact area that were predicted by the model. This may explain why lower shoe-floor angles are typically associated with lower slip severity. Also, the predicted ACOF was positively correlated with experimental COFU and the values were of similar magnitude (R^2=0.42). Findings of this study indicated that multiscale modeling has the potential to understand the impact of slipping biomechanics on ACOF and COFU and that just by considering shoe-floor angle during slipping, we could predict 42% of the variation in COFU.

Shae Rosemore	60	Physical Science and Engineering	Supporting Infrastructure for Last Mile Solutions	Cars and other automobiles are expensive to own or operate in Singapore, and so many citizens rely on public transportation and more are beginning to use personal mobility devices (PMDs) such as scooters. Electric scooter (escooter) usage is increasing in the city of Singapore but is restricted due to lack of supporting infrastructure. Users are discouraged from using their product because of limited pathways, confusing or restricting road laws, lack of proper storage, and bulky scooters. This eight-week study expands on the research of previous teams to explore potential solutions to enable current and potential escooter users. The previous studies focused on the redesign of the scooter to enable easy transport when it was not in use. The methods this team used were; first-hand scooter usage, travelling to popular areas for locals or tourists, examining previous research, surveying current and potential users, examining current and future laws on escooter usage, and scaled-down prototyping. From this the team was able to conclude that focusing on an infrastructure-focused design would most benefit users. From 1:5 scale models the team was able to narrow down features and a potential locker design that would fully enclose an escooter which provides security, weatherproofing, and convenience.
Nathan Tavenor	61	Physical Science and Engineering	Designed Coiled-Coil Based Supramolecular Polymers and Metal Peptide Frameworks	Supramolecular polymers (SMPs) are typically composed of a mixture of small molecules and rely upon intermolecular interactions between those molecules to impart large-scale structure akin to classical polymers. Tuning the structure of the small molecule building blocks allows for control over the properties of the SMP. Using protein-based monomers takes advantage of the self-assembly and highly specific molecular recognition properties encodable in polypeptide sequences to rationally design SMP architectures. The central hypothesis underlying our work is that α-helical coiled coils, a well-studied protein quaternary folding motif, are well-suited to SMP design through the addition of synthetic linkers at solvent-exposed sites. Through small changes in the structures of the cross-links and/or peptide sequence, we are able to control both the nanoscale organization and the macroscopic properties of the SMPs. Using metal chelation we are able to design crystals of metal peptide frameworks (MPFs). Likewise, isomeric changes to the hydrophobic core of the peptide greatly alter rigidity and dimensionality of the SMPs from linear chains to nets. Biophysical, spectroscopic, and crystallographic evidence combined with computational modeling for the underlying structural causes of these observations will be presented.
Michael Washington	62	Physical Science and Engineering	The Impact of Monomer Sequence and Stereochemistry on the Physico-Chemical	Poly(lactic-co-glycolic acid) (PLGA)-based biodegradable materials have attracted considerable interest in the field of bioengineering due to its biocompatibility, FDA approval and tunable physico-chemical properties. However, the current methods for tuning the properties of PLGAs for a specific therapeutic application are limited to changing the monomeric ratio and stereochemistry of cyclic esters prior to ring-opening polymerization (ROP), resulting in an unsequenced, random copolymer.

			Properties of Biodegradable Materials Composed of Poly(lactic-co-glycolic acid)	This study focuses on evaluating the properties of a new set of precisely sequenced PLGAs prepared via segmer assembly polymerization (SAP). PLGAs synthesized by SAP contain exact repeating sequences whose components are interchangeable, which allows for a directed synthesis of sequences tailored for a specific application. Changes in sequence, stereochemistry and monomeric ratios were shown to have a profound effect on such properties as in vitro erosion, swelling, acidic microclimate distribution and compressive modulus. Devices fabricated with sequenced PLGAs were shown to have enhanced stability both in vitro and in vivo. These results emphasize the importance of using monomeric sequence to control the hydrolysis kinetics of a copolymer which contains a variety of hydrolyzable linkages.
Laura Beth Fulton	87	Physical Science and Engineering	Improvement of Rosetta Biocomputing Software for Canonical Antibody CDR Loop Prediction	Computational modeling of protein structures and protein-protein interactions is increasingly important for molecular biophysics research as well as for applied drug design. Antibodies, with their high affinity and specificity to target antigens, are of particular interest as therapeutics for the prevention and treatment of infectious diseases. Experimental antibody prediction is labor intensive and costly, involving X-ray crystallography and NMR. At Johns Hopkins University, the Gray laboratory is developing computational tools for protein prediction as part of Rosetta biocomputing software. This research focuses on improving accuracy of antibody complementarity determining region (CDR) loop prediction. Previous research in the Gray laboratory indicates template selection of antibody crystal structures based on sequence similarity is inconsistent with predicting lowest energies as assessed by Rosetta score functions. It was hypothesized that selection of CDR median conformations as templates for the non-H3 CDR loops will yield lower energy structures. To improve selection, median CDR conformations were incorporated into the antibody prediction algorithm, a python script was written to parse PDB clusters, and C++ code filtered prolines for CDR loops. This research contributes to improved prediction of antigen binding sites highly relevant for antibody docking applications and design strategies based on homology models.
TRANSLATIONAL LIFE SCIENCE				
Junting Cai	63	Translational Life Science	An Antagonist of Lysophosphatidic Acid Receptor 1, AM966, Increases Pulmonary Lung Endothelial Permeability through Pho Signaling Pathway and VE-Cadherin Phosphorylation	Maintenance of pulmonary endothelial barrier integrity is important for reducing severity of lung injury. Lysophosphatidic acid (LPA) is a bioactive lysophospholipid which regulates cell motility, cytoskeletal change and survival. LPA has been shown to increase lung epithelial barrier integrity. But it reduces endothelial barrier function, which plays a role in the development of pulmonary fibrosis diseases. AM966 is an LPA receptor 1 antagonist exhibiting an anti-fibrotic property. However, the effect of AM966 on pulmonary endothelial barrier integrity has not been well studied. To investigate cell junction integrity, an electric cell-substrate sensing (ECIS) system was used to measure permeability in human lung microvascular endothelial cells (HLMVECs). Similar to the effect of LPA, AM966 increases endothelial permeability immediately in a dose dependent manner. VE-cadherin and f-actin

				double immunostaining reveals that AM966 induces gap formation and stress fibers, as well as dissociation between VE-cadherin and f-actin. Through LPA1-Gα12/13 pathway. AM966 activated RhoA and increased phosphorylation of myosin light chain (MLC) at T18/S19. Meanwhile, phosphorylation of VE-cadherin at Y658 is also increased through the same pathway. This study reveals that AM966 induces lung endothelial barrier dysfunction, which is regulated by activation of the RhoA and phosphorylation of VE-cadherin.
Rohan Chalasani	64	Translational Life Science	Development of Novel PET Imaging Agents for PD-L1	Introduction: To clarify the role of PD-L1, which has been implicated in cancer immune evasion for some cancers, we are developing minibodies (Mb) for molecular imaging of PD-L1 in preclinical models. Mbs, engineered antibody scFv-CH3 homodimers, offer great potential as PET imaging agents due to their high affinity, high stability, and short circulation times. Methods: A highly diverse scFv phage library was screened using biopanning and surface plasmon resonance (SPR) to identify scFv's with high affinities for PD-L1. Mbs derived from the high-affinity scFv's were produced through transient transfection and confirmed with immunoblots and SDS-PAGE gels. Mb purification was performed through IMAC and purity was assessed with gels. Lastly, in vitro assessment of the Mbs was performed by SPR and immunofluorescence microscopy. Results: Based on screening results, three scFv's were selected for subsequent Mb production. Transient transfection was shown to successfully produce Mbs and subsequent purification produced relatively pure Mb samples in good yields. In vitro analysis of the Mbs indicated that the Mbs are functionally folded and have the ability to bind PD-L1 natively presented on cells. Conclusions: Results indicate that the Mbs have high potential as PET imaging for PD-L1, subject to confirmation by in vivo imaging studies.
Rahul Deshpande	66	Translational Life Science	Global Lipid Changes in Primary Human Alveolar Macrophages Treated with Conjugated Linoleic Acid and Nitro-Conjugated Linoleic Acid	Lipids play a key role in cell, tissue and organ physiology. Lipid metabolism involving cholesterol, free fatty acids and other lipid species has been shown to directly impact inflammatory pathways. NO2-conjugated linoleic acid (NO2-cLA) and conjugated linoleic acid (cLA) have been shown to have anti-inflammatory and tissue-protective actions and they are presently being evaluated for their effects on inflammation and airway hyperresponsiveness in the obese asthmatic pathology. Therefore, we sought to investigate their impact on global lipid metabolism in alveolar macrophages taken from obese asthmatic subjects at the time of bronchoscopy. Rapid and high throughput analysis of multiple lipid species is challenging due to the diversity in physical and chemical properties in the lipidome and the presence of isomeric and isobaric species also complicates the identification. For this analysis, we developed a liquid chromatography data dependent MS/MS method using high resolution, accurate mass spectrometry. Data was analyzed using LipidSearch (Thermo Fisher Scientific) software to identify and relatively quantify lipid species. This methodology was able to differentiate the

				effect of NO2-cLA and cLA on the lipid profile of primary human alveolar macrophages compared to vehicle treated cells at both 4 and 24 hr.
Jill Glausier	67	Translational Life Science	Characterization of Inhibitory and Excitatory Parvalbumin Synapses in Human Prefrontal Cortex	Background: Altered synapses of local prefrontal cortex (PFC) GABA neurons containing parvalbumin (PV), and from PV glutamatergic thalamocortical projections, are implicated in PFC dysfunction in schizophrenia. Interpretations of PV synaptic alterations in schizophrenia can be robustly informed by studies in monkeys. Previous electron microscopy (EM) studies in monkey demonstrated that PV thalamocortical synapses are restricted to middle cortical layers and preferentially target spines. To determine if PV innervation of monkey PFC is comparable to human, we performed quantitative electron microscopy (EM) studies in human PFC. Methods: Human brain tissue was obtained from subjects without psychiatric or neurological disorders from the Allegheny County Medical Examiner's Office (Pittsburgh, PA), and the Maryland Brain Collection. For EM studies, PV axon terminals were analyzed in the superficial and middle layers of PFC area 9. Results: In contrast to monkey, thalamocortical PV synapses in human are present in both superficial and middle PFC layers, and target both spines and dendrites. Conclusions: These studies demonstrate differences between monkey and human in the innervation zone and postsynaptic target of PV thalamocortical synapses. These data provide interpretative value for future studies in schizophrenia, and the applicability of monkey experimental and anatomical studies to the human PFC.
Christina Grogan	68	Translational Life Science	Analyzing Predicted Native Asaia SP. SF2.1 Secretion Signals for Use in Malaria Control Strategies	Plasmodium sp., the parasite that causes malaria, is transmitted by the Anopheles sp. mosquito vector. The symbiotic bacteria within the mosquito midgut can be transgenically modified to affect the mosquito's phenotype, a strategy known as paratransgenesis; the bacteria can be engineered to secrete anti-malarial molecules into the midgut to combat the parasite. One candidate, Asaia sp., a gram-negative bacteria, has been shown to colonize the midgut, ovaries, and salivary glands within the Anopheles mosquito. Common secretion signals, such as the E. coli Type II OmpA and TolB leader peptides, and signals from closely-related species do not function in Asaia. A genetic library screen found only one native secretion signal that provided sufficient secretion of protein into the supernatant. Therefore, the Asaia sp. SF2.1 genome was sequenced and used to predict Type II secreted proteins. Leader signals were identified and cloned into the plasmid pNB92, containing the PnptII constitutive promoter and the c-terminal domain of alkaline phosphatase lacking a secretion signal. These were transformed into the Asaia sp. SF2.1 lab strain. Positive colonies were grown to log phase and separated into the supernatant, lysate, and cell-surface fractions. The abundance of protein in the different fractions was tested using an ELISA assay.
Adriana Johnson	69	Translational Life Science	Identifying Risk Factors for Morbidity and	Background: We sought to identify risk factors predictive of morbidity and mortality for pediatric congenital heart disease (CHD) patients treated in an intensive care unit (ICU) setting. Outcomes of interest were cardiac arrest, extracorporeal membrane

			Mortality in the Pediatric Cardiac Intensive Care Unit	oxygenation (ECMO), reintubation, and hospital mortality. Methods: A targeted PubMed search was performed and literature was screened to identify papers that provided outcome rates for pediatric cardiac patients in an ICU setting. Inclusion criteria required a pediatric CHD patient population, ICU setting, outcomes of interest, and significance of $p < .01$. Results: Six hundred and thirty four abstracts were screened, resulting in the inclusion of 28 articles and 39 predictive variables: 6 predicting cardiac arrest, 4 predicting ECMO, 5 predicting reintubation, and 24 predicting mortality. Discussion: The majority of variables found using this literature search predict mortality in a pediatric cardiac ICU setting. The next step is to use these variables in a predictive Bayesian Network model and test it using clinical data from Children's Hospital of Pittsburgh.
Erin Kirschmann	70	Translational Life Science	Effects of Age of Initiation on Cannabinoid Self-Administration and Corresponding Cognitive Consequences in Male Sprague-Dawley Rats	Marijuana (Cannabis sativa) is the most commonly used illicit drug in the US. Retrospective clinical studies suggest that initiating cannabinoid use in adolescence, relative to adult initiation, increases risk for negative outcomes. We examined abuse potential, and long-term effects on cognitive performance, after self-administration (SA) of the selective, potent, cannabinoid receptor agonist WIN55,212-2 (WIN) in adolescent vs. adult male rats. Adolescent and adult rats self-administered WIN, were tested for cue-induced reinstatement of WIN-seeking during abstinence, and then were trained/tested on a delayed-match-to-sample working memory (WM) task (drug-free conditions). An additional group of adults was trained on WM before WIN SA initiation. Rats acquired WIN SA and displayed stable levels of intake during the last days of training. While all adolescents met acquisition criteria, only a subset of adults acquired. Adolescents (tested as adults) increased WIN-seeking in prolonged abstinence, suggesting an “incubation of craving,” whereas adults did not exhibit an incubation effect. With abstinence in adulthood, adolescent-, but not adult-onset, WIN SA resulted in improved WM performance. Adult WIN SA acutely impaired WM performance, relative to baseline. Our findings suggest that use of cannabinoids can produce addiction-like effects, particularly in adolescents, and that continued use in adulthood can impair cognitive performance.
Donna Lee	75	Translational Life Science	The Protein Translation Inhibitor Homoharringtonine is a Promising New Agent for the Treatment of Gastrointestinal Stromal Tumors (GISTs)	Although KIT/PDGFRA-mutant GISTs can be effectively treated with imatinib mesylate (IM), many patients develop resistance to IM as well as second- and third-line tyrosine kinase inhibitors. Resistance mainly involves secondary mutations in the KIT/PDGFRA kinases, on which these tumors are still highly dependent. New therapeutic strategies targeting KIT/PDGFRA through different mechanism are therefore highly intriguing. Homoharringtonine (HHT, omacetaxine) is an inhibitor of protein translation that has recently been FDA-approved for IM-resistant chronic myeloid leukemia (CML). HHT was also active in KIT-mutant mastocytosis models. We hypothesize that HHT could be effective in GIST through downregulation of KIT expression, abolishing KIT activation. Studies were performed in IM-sensitive and IM-resistant GIST cells as well as BCR-ABL-positive CML cells (K562). HHT was highly

				effective in GIST cells, irrespective of IM sensitivity. IC50s were 18-76 nM (48 nM in K562). HHT led to complete abolishment of KIT activation/expression at this concentration while mRNA levels were minimally affected. Molecularly, the response involved PARP/caspase 3 cleavage and reduction of cyclin A levels. Inhibition of protein translation seems a promising strategy to overcome IM resistance in GIST. Further preclinical studies dissecting the precise mechanism of action of HHT and testing the compound in vivo are ongoing.
Chunlei Li	76	Translational Life Science	Immune Suppressive Effects of Human Alpha-Fetoprotein on Human Dendritic Cells	Alpha-fetoprotein (AFP) is produced by over 50% of hepatocellular carcinomas (HCC), and its secretion by tumors is usually correlated with poorer patient outcomes, increased tumor growth, and tumor stem cell-like properties. Our recent studies have shown that tumor-derived AFP (tAFP) can interfere with dendritic cells (DC) and impair their T cell stimulatory activity. Our lab also observed that the expression pattern of lipid metabolism and lipid antigen presentation genes (CD1 family) are changed in AFP treated DCs. Surface CD1a, CD1b, CD1c and CD1d are greatly reduced and are known to be critical for NKT cell activation. We hypothesized that AFP might impair the ability of DC to stimulate human NKT cells. We pulsed DC groups with the NKT cell activating antigen alpha-GalCer, and co-cultured the DC and NKT cells. Intracellular staining was carried out to identify the cytokine producing cells. Alpha-GalCer is a strong stimulus that may overwhelm any effect of AFP protein, as no significant difference was observed. We are now testing other known lipid antigens to determine if less strong stimulus will allow us to detect AFP-mediated downregulation of CD1d effects on NKT cell function.
Jenna Parrish	77	Translational Life Science	Estradiol Modulation of the Renin Angiotensin System and the Regulation of Fear Extinction	Low estradiol during fear extinction impairs extinction consolidation, resulting in increased fear during extinction recall in females. However, the mechanism is unknown. Estrogen modulates the renin angiotensin system (RAS) by downregulating angiotensin II type I receptors (AT1R). We found that systemic administration of AT1R antagonist losartan before fear extinction enhances extinction consolidation and reduces fear during extinction recall in female rats with low estradiol. We investigated mechanisms by which estradiol interacts with the RAS to enhance extinction consolidation. Female rats received injections of a hormonal contraceptive (HC) that lowers estradiol, or vehicle, for 5 days. Serum estradiol and angiotensin II (AngII) levels were measured, and brain AT1R expression and protein levels were analyzed. Another cohort of rats received fear conditioning training. AngII or vehicle was administered systemically before/after extinction in females with high estradiol. HC-treated females had decreased estradiol and increased AngII in serum versus vehicle-treated females. No differences in AT1R expression or binding were detected. Pre-extinction treatment with AngII non-significantly increased freezing during extinction recall. AngII was increased in rats with low estradiol levels, but no differences were found at the receptor level. Thus, extinction consolidation deficits in rats with low estradiol may be due to increased AngII.

Sneha Patil	78	Translational Life Science	Second-Generation Inhibitors of the Proteasome as Novel Treatment Options for Gastrointestinal Stromal Tumors (GISTs)	KIT/PDGFRA-mutant GISTs can be effectively treated with imatinib mesylate. However, many patients develop resistance to imatinib and the second- and third-line tyrosine kinase inhibitors sunitinib and regorafenib. Because the main mechanism of resistance involves secondary mutations in KIT/PDGFRA, strategies that do not target these kinases are intriguing. We have shown that the FDA-approved proteasome inhibitor bortezomib is highly effective in GIST cells through transcriptional downregulation of KIT and upregulation of the pro-apoptotic histone H2AX. We now tested proteasome inhibitors (carfilzomib, ixazomib, delanzomib) with better pharmacologic properties and compounds that inhibit regulators of the proteasomal degradation process, such as UCH37/USP14 (b-AP15) and the NEDD8-activating enzyme (MLN4924). Carfilzomib, ixazomib and delanzomib proved highly effective in all cell lines independently of their imatinib sensitivity. Apoptosis and reduced cell viability was seen at 10nM. Action was rapid, within less than 8h. Timing coincided with a massive increase in ubiquitylated proteins, loss of KIT expression/phosphorylation and H2AX induction. b-AP15 only induced apoptosis at a concentration of 1µM and higher. MLN4924 had a mostly cytostatic effect. Targeting the ubiquitin-proteasome machinery is a promising strategy to overcome resistance in GIST, although inhibition of regulators of proteasomal degradation appears less favorable. Preclinical in vivo testing is currently ongoing.
Matthew Rich	79	Translational Life Science	Cocaine-Cue Memory Extinction is Associated with Depotentiation at Amygdala Synapses.	Extinction of memories associated with cocaine use may help reduce relapse. The BLA is a locus for cocaine-cue memory extinction. Depotentiation of excitatory synapses in the BLA has been proposed as a cellular mechanism for fear extinction, but it is unclear if this mechanism explains the extinction of drug-associated memories. We tested if cocaine self-administration potentiates excitatory synapses in the BLA, and if cocaine-cue extinction causes depotentiation. Rats self-administered cocaine or saline, paired with an audiovisual cue (CS), for ≥10 days. 24 hours after the last training day, were returned to operant chambers and received either 0, 60, or 120 noncontingent presentations of the CS in the absence of reinforcer. The next day, rats were euthanized and brains processed for whole-cell recordings of BLA principal neurons. Neurons were voltage-clamped at -70 mV. Thalamic afferents were stimulated and EPSCs were recorded. Cocaine training potentiated BLA synapses, as shown by an increased EPSC amplitude relative to saline-trained controls. Cocaine-cue extinction depotentiated the synapse dose-dependently, as 120 CS presentations fully reversed the potentiation caused by cocaine self-administration. Therefore, excitatory synapses in the BLA seem to encode cocaine-associated memories, and depotentiation at these synapses may be important for relapse prevention.
Samuel Rosko	80	Translational Life Science	Toward Shareable Individualized Drug Interaction Alerts	Drug-drug interactions (DDIs) are becoming increasingly more common in modern medicine and many tools have been developed to help clinicians stay aware of DDIs. Despite the effort put into developing these tools, override rates for potential drug-

				drug interaction (PDDI) alerts remain around 70-90%, largely due to the problem of alert fatigue. One of the problems contributing to alert fatigue is that alert acceptance heavily depends on the patient themselves. Therefore, one approach to addressing alert fatigue is to contextualize PDDI alerts using patient-specific data instead of simply firing alerts on the co-prescription of drug pairs. To do this, data was collected at the University of Arizona Medical Center (UAMC) to determine which drug pairs resulted in the PDDI alerts that were overridden most frequently. These drug pairs were studied by a group of pharmacists, who developed decision trees for each pair that indicated when and when not to fire an alert, along with evidential support and an explanation of the decision. These decision trees are currently being modeled using the JBoss Drools production rule system. Once these rules are implemented, their firing rates will be compared to raw firing rates to measure the effect that contextualization has on firing rates.
Jackie Shane	82	Translational Life Science	A Paratrangenic Approach to Inducing Anti-Malarial Genes Using the Mosquito Blood Meal	Paratransgenesis is the process of genetically modifying symbiotic bacteria to affect their host's phenotype. In this study, bacteria colonizing the Anopheles mosquito midgut, Asaia sp. SF2.1, have been engineered to secrete anti-malarial effector molecules into the mosquito midgut, hindering its ability to carry Plasmodium. However, the constitutive overexpression of effectors causes a fitness disadvantage to the Asaia that carry them. Therefore, it is desirable to express them only when Plasmodium is present in the midgut, namely during a blood-meal. Possible conditional promoters were discovered through RNA-seq, library screening, and evaluating conditional homologous genes. Promoters were cloned into the plasmid pGLFR1, which has dual reporters GFP and lux, then transformed into Asaia and plated on inducing media. GFP fluorescent colonies were screened both in-vitro and in-vivo, inside the mosquito midgut, to isolate the promoters that were only induced when blood meal conditions were present. To evaluate the conditionality in-vivo, the transformed bacteria were introduced through a sugar meal and mosquitoes were separated for blood feeding. Both blood-fed and sugar-fed mosquitoes were dissected and conditional fluorescence of their midguts was evaluated. Quantification of promoter strength is currently underway using various methods to collect both transcriptional and translational differences in expression.
Josh Tarantino	83	Translational Life Science	Assessing the Host Inflammatory Response to Acellular Lung Scaffolds	Chronic respiratory disease is one of the leading causes of death in the United States. However, there are not enough available lungs to meet the demands of patients on the transplant list. Repopulating decelluarized lung tissues with cells from the patient is a promising approach to the development of transplantable lung tissue. This method is promising because it replaces the cells from the donor tissue with cells from the patient while leaving connective structures intact, allowing a new lung to be created. Ideally, this new tissue will not trigger an adverse immune response after implantation. For this study, four different decellularized lung scaffolds were used for implantation in a primate model. The biopsies of the

				scaffolds were then analyzed using different staining techniques at 2, 4, and 10 weeks. Images of each stain were taken for every sample. These images were used to establish cell counts for different types of immune cells to characterize the immune response. Scaffolds that saw a marked infiltration of host immune cells after week 2 indicated a strong inflammatory response, while scaffolds that saw an overall decline in host cells were considered indicative of successful integration with the host lung.
Jingjing Wang	84	Translational Life Science	Over-Expression of Melatonin Synthesis Enzymes Arylalkylamine N-Acetlytransferase and Aromatic L-Amino Acid Decarboxylase for Treatment of Huntington's Disease	Huntington's disease is an autosomal-dominant chronic neurodegenerative disease that is universally fatal and lacks effective treatment. Melatonin, a naturally occurring pineal hormone, is a potent endogenous antioxidant and G-protein coupled receptor ligand and through these mechanisms it protects neurons from death caused by stress, in neurodegenerative diseases such as HD. Published data show that HD patients show a gradual decrease of serum melatonin, and data from our laboratory indicate that Arylalkylamine N-Acetyltransferase (AANAT), the rate-limiting enzyme in the pathway of melatonin synthesis decreases in HD patient brains as compared with controls. Our hypothesis is that correcting the deficient neuronal melatonin synthesis pathway in HD will increase survival of the striatal median spiny neurons, which are the most affected neurons in HD. Specifically, we will use genetically modified herpes simplex virus (HSV) vectors to over-express two enzymes involved in the synthesis of melatonin: Arylalkylamine N-Acetyltransferase (AANAT), and Aromatic L-amino Acid Decarboxylase (AADC). We will then evaluate the protective effect of the constructed HSV in cellular and animal models of HD. Our research thus investigates a potential new treatment for HD, through the use of gene therapy. If successful, this strategy may also be applied to many other neurodegenerative diseases as well.
Wenjing Wei	85	Translational Life Science	Increased Cerebral Blood Flow in Dorsal Default Mode Network (dDMN) is Associated with Improvement in Depression Severity in a Longitudinal Treatment Trial of Late-Life Depression	Due to an aging population, depression, affecting 10% of older adults, is becoming an increasing public health issue. Regional cerebral blood flow (CBF) has been shown to be associated with depression as well as antidepressant therapy. Treatment of late-life depression (LLD) often requires long trials which are associated with increased risk of negative health outcomes. In this study we used arterial spin labelling to investigate CBF changes in the brain in a sample of LLD patients at baseline, following a placebo, following a single dose of venlafaxine, a week after starting treatment, and at the end of the trial. LLD patients (N=46, 29 female) were enrolled into a 12-week treatment trial and underwent five MRI scans. Montgomery–Asberg Depression Rating Scale (MADRS) was used to evaluate depression and treatment outcome. Increased CBF between baseline and end of trial was significantly associated with improvement in depression severity in the dorsal default mode network (dDMN). Previous studies have shown that LLD patients have lower CBF compared to healthy elderly participants in dDMN that increase after treatment. We found that dDMN increased in CBF, and we further

				demonstrate that there may be an early marker of treatment outcome within a week of treatment.
Jue Wu	86	Translational Life Science	Improvements of Brain Development After Stem Cell Transplantation in Krabbe Disease	Background: Krabbe disease is a rare but severe neurodegenerative disorder mainly affecting infants. Hematopoietic stem-cell transplantation (HSCT) is the only treatment available for this quickly progressing and demyelinating metabolic disease. We investigate the change in cerebral myelination by diffusion MRI and propose a more sensitive and objective tool to access the effects of the transplant treatment and compare them with the natural course of the disease. Method: Diffusion tensor imaging (DTI) was obtained to assess white matter integrity of the brain. We longitudinally scanned 55 Krabbe patients with early infantile onset, of which 14 were treated with HSCT. Alignment of the patient image to an age-matched normal atlas was made such that specific white matter tracts could be delineated. Fractional anisotropy (FA) was derived from DTI as a measure of the organizational quality of the corticospinal tracts, responsible for motor control. Results and Conclusion: Patients that were not treated with HSCT started with compromised white matter integrity (lower than normal FA) and the FA decreased significantly within two years, which indicated fast disease progression. Patients treated with HSCT mostly followed the normal developmental trajectory of the corticospinal tract, which indicated that the white matter quality was preserved over time.