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Poster location	Name	Topic	Title	Author(s)	Abstract
51	Armaan Akbar	Physical Science and Engineering	Biomimetic Small Diameter Vascular Graft	Armaan Akbar; Matteo Solazzo; Paulo Gonzalez; Daniel Jacobs; Michael Luketich; Rich Hoff, MA; Antonio D'Amore, PhD; William Wagner, PhD	Current methods utilized in coronary bypass include the use of synthetic as well as biologic tissue derived small diameter vascular grafts; while relatively effective on the short term, these scaffolds are affected by a number of issues such as: inadequate mechanics or mechanical mismatch, re-stenosis due to intimal hyperplasia or thrombosis. This study aims to introduce a novel processing technique for small-diameter tissue-engineered vascular graft (TEVG) mimicking the three-layer native vessel structure and mechanics. The current prototype combines the synthetic and biologic graft approach with a three-layer structure of anatomically distinct components designed to duplicate native tissue heterogeneity. The three graft layers are processed with electrospinning (ES), thermal induced phase separation (TIPS) of polyester urethane urea, and decellularized small intestinal submucosa tissue gel (SIS-ECM). The grafts are designed so that the ECM facilitates cell recruitment and tissue growth within the tunica media, while the dry ES layer prevents cell infiltration from the tunica intima. Compliance and suture retention forces of the graft have shown to be comparable to native porcine coronary arteries. SEM and histological analyses have indicated that microstructural and macrostructural dimensions of the graft are comparable with those of native tissue.
1	Cheryl L. Bell, PhD, MS	Basic Life Science	Fluorescence Recovery after Photobleaching Reveals Impaired Gap Junction-Mediated Communication in the Presence of Dynasore	Cheryl L. Bell, PhD; Deborah O. Osakue; Sandra A. Murray, PhD	A key step in regulating gap junction-mediated communication is the scissoring of gap junction buds from the plasma membrane by dynamin, a mechanoenzyme. Inhibiting dynamin with the dynamin GTPase inhibitor, dynasore, decreases its ability to clip invaginated gap junction plaque membrane from the cell surface. We performed fluorescence recovery after photobleaching (FRAP), live-cell imaging, and transmission electron microscopy (TEM) to investigate whether gap junction-mediated cell communication is altered following dynasore treatment. In the treated populations, fewer annular gap junction vesicles were released into the cytoplasm while the number and size suspended from the gap junction plaques increased. Ultrastructural analysis revealed large numbers of invaginated gap junction structures with atypical morphology, consistent with undocking of the gap junction channels that compose the gap junction plaque. FRAP analysis demonstrated that control cells rapidly recovered fluorescence after photobleaching, while dynasore treated cells did not recover communication. This observation is consistent with the atypical gap junction morphology seen with TEM. Based on these findings, dynasore treatment, in addition to altering the scissoring and release of buds into the cytoplasm, impaired the capacity for gap junction-mediated dye communication. The effects of dynasore may be important considerations needed in interpreting outcomes of dynamin-dependent intercellular communication studies.
33	Iman Benbourenane	New Research Tools and Techniques	Comparative Analysis of Photogrammetry Versus Laser-based Methods of Measuring the Physical Dimensions of Objects	Iman L. Benbourenane; Deanna Easley; Maurice Kotz; Steven Abramowitch, PhD	Photogrammetry presents a novel, low cost, non-contact alternative to measuring the physical dimensions of materials in 3-D that makes no assumptions about shape. While it has been proven accurate for use in some applications, the approach presents some challenges for many soft tissues, as their reflective and repeating pattern nature make them difficult to 3D render via photogrammetry. As a first step in exploring the feasibility of this approach, this study aims to use photogrammetry for making measurements of the cross-sectional area of objects with known geometric shapes to those obtained with laser sensors (both bounce back and collimated). It is hypothesized that the photogrammetric approach will provide the same level of accuracy and repeatability as laser-based measurements. We found that photogrammetric data yielded lower percent error, and thus higher accuracy in cross-sectional area measurements than both laser measurements. There was, however, approximately an order of magnitude greater variability within photogrammetric data. Yet, one standard deviation above and below the averaged photogrammetry result still yields comparable, and in some cases superior, readings to laser-based measurements.
52	Bryn Brazile, PhD	Physical Science and Engineering	Undulating around the Globe: Patterns of Collagen Crimp in the Eye	Bryn L. Brazile, PhD; Danielle Hu, BS; Ning-Jiun Jan, BS; Alexandra Gogola, MS; Andrew P. Voorhees, PhD; Ian A. Sigal, PhD	Biomechanical properties of soft-tissues are determined largely by collagen fiber crimp. The purpose of this study was to characterize collagen crimp across different regions of the eye. Axial longitudinal cryosections (30 µm) of three sheep eyes, were imaged using polarized light microscopy to quantify local collagen crimp in 7 regions: peripapillary sclera, posterior sclera, posterior equatorial sclera, equatorial sclera, anterior equatorial sclera, limbus, cornea. Five characteristics of collagen crimp were measured in 8,216 locations: amplitude, waviness, and tortuosity which are associated with the nonlinear biomechanical properties of tissues, and period and conformity which are associated with the structural organization of tissues. Cornea had the shortest average period, 14.92 µm, and largest average conformity, tortuosity, and waviness: 18.63 µm, 1.03, and 0.31°, respectively. Anterior equator had the largest average period, 33.92 µm, and smallest average conformity, 12.57 µm. Equator had the smallest average amplitude, waviness, and tortuosity: 0.28 µm, 0.10°, and 1.00, respectively. Posterior sclera had the largest average amplitude, 0.85 µm. All parameters varied significantly across the globe. All regions differed significantly from one another on at least one parameter. Our results show specific spatial patterns in crimp characteristics, which reflect variations in the local biomechanical properties across the eye.

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2	Elizabeth Caves	Basic Life Science	Testing Epithelial Cell's EBV Lytic Activation Using the Air Liquid Interface Method	Elizabeth Caves, Sarah Cook, Laura Wasil, Kathy Shair	The Epstein-Barr virus (EBV) is a herpes virus that's found in approximately 90% of the adult population. EBV typically causes lytic infection in epithelial cells. Yet, in abnormal cases, EBV has been able to remain latent in epithelial cells for an extended time period. When EBV remains persistent within epithelial cells, it's been shown to cause cancers such as nasopharyngeal carcinoma – a head and neck cancer. The current monolayer culturing of epithelial cells has no natural lytic reactivation in infected cells, limiting this method's validity in testing latency and lytic activation. The Shair lab is currently testing a method to allow lytic virus activation in a tissue culture model, called Air Liquid Interface (ALI). ALI culturing creates an apical/basal-polarized system that mimics in-vivo infection. Over a three-week period, HK1 cells (epithelial cancer cells) and HK1 EBV infected cells were cultured using the ALI culture method. Through protein, RNA, and viral infectivity assays, we seek to prove the validity of the ALI method to test EBV lytic activation. With the use of ALI culturing to activate lytic phase, the EBV field will have a more accurate system to test if genes such as LMP1 impact EBV's ability for lytic activation.
64	Bharesh Chauhan, PhD	Translational Life Science	Pyramidal Cataracts, Completely Intact Irides, and Nystagmus from Three Novel PAX6 Mutations	Bharesh K. Chauhan, PhD; Anagha Medsinge, MD; Matthew P. Baumgartner, PhD; Hannah L. Scanga, MS; Smaragda Kamakari, PhD; Eva Gajdosova, MD, PhD; Carlos J. Camacho, PhD; Ken K. Nischal, MD	To examine the association between novel mutations in PAX6 to the unusual intact iris and bilateral anterior pyramidal congenital cataracts (APCC) phenotype through functional and modeling analyses. Four patients underwent ophthalmic exams to obtain ocular phenotypes. Each were then screened for mutations in PAX6. Resulting mutations were created in Pax6 isoforms by site-directed mutagenesis and employed with PAX6 and PAX6-5a reporters in transactivation dual-luciferase-type assays. 3D-modeling of the PAX6 mutations was conducted using AMBER 14. Ophthalmic exams diagnosed three of the patients with intact iris and APCC. Genetic screening revealed these three patients have novel mutations in PAX6. The fourth patient had typical aniridia and anterior polar cataracts due to a frame-shift mutation in PAX6. These mutations were generated in PAX6 and PAX6-5a isoforms by site-directed mutagenesis and luciferase-based transactivation assays showed abnormal transactivation for all PAX6 isoform mutants that segregate with the cataract phenotype in all patients, and significant reduction in the 5a-form that segregate with the aniridia phenotype. 3D-modeling confirmed that DNA-binding and stability was not significantly affected in the intact iris PAX6 mutants. The abnormal DNA-binding and activation of the novel mutations in the PAX6 isoforms partly explains the APCC phenotype with intact iris.
3	Amin Cheikhi, PhD	Basic Life Science	Mitochondrial Architecture Underlies Transmission of Cellular Memory	Amin Cheikhi, PhD; Callen Wallace, BS; Claudette St. Croix, PhD; Charles Cohen, BS; Wan-Yee Tang, PhD; Peter Wipf, PhD; Fabrisia Ambrosio, PhD, MPT; Aaron Barchowsky, PhD	It is recognized that cell state transitions require remodeling of mitochondria, yet the function of mitochondrial morphology in maintaining the state of the cell remains undefined. Given that alterations in mitochondrial structure affect their function and, consequently, the cell's behavior, we hypothesized that rules of cell-fate decisions must be codified within the mitochondrial architecture. Using in vitro studies in stemlike myogenic cells, we show that dynamic modulation of mitochondrial networks topology enables heterogeneous cell state and behavior at the cell population level. We elucidated architectural principles constraining the dynamics of mitochondrial networks, revealed their small-world properties, and uncovered statistical scaling signatures that link mitochondrial and cell population heterogeneity. We found that the architecture of perinuclear mitochondrial subnetworks endow a distinct subpopulation of cells with transmissible memory. This is achieved through histone modification and DNA methylation, which are driven, at least in part, by mitochondrial hyperpolarization and ROS generation. Taken together, these studies implicate perinuclear mitochondrial architecture as a novel regulator of cellular memory and heterogeneity.
53	Maria Cohen, MD	Physical Science and Engineering	Single Nucleotide Polymorphisms Associated with Propofol Biotransformation are Associated with Altered inflammation and Clinical Outcomes in Trauma Patients	Maria Cohen, MD; Lukas Shimunek, MD; Rami A. Namas, PhD; Haley Lindberg; Fayten el-Dehaibi; A. Murat Kaynar, MD, MPH; Timothy, R. Billiar, MD; Yoram Vodovotz, PhD	Propofol is an intravenous anesthetic with a varied individual response that may be influenced by individual genetic variation in the form of single nucleotide polymorphisms (SNPs). Prior research in humans has found high individual susceptibility to the anesthetic propofol in SNP rs6313 in the serotonin gene, associated with effect-site concentration (Cep) and onset time of induction. Also, SNP rs6746030 in the sodium channel was linked to a varied bispectral index (BIS) which is a measure of depth of anesthesia. In this study, we studied 453 trauma patients' blood samples and analyzed the impact of SNPs rs6313 and rs6746030 on propofol biotransformation, and modulation of the immune system and effects on clinical outcomes. We found that patients with rs6313 AA major allele had elevated systemic levels of multiple inflammatory mediators compared to BB genotypes. In rs6746030, patients with the minor allele had reduced systemic levels of multiple inflammatory mediators. Clinical outcomes were measured by need and length of mechanical ventilation, ICU length of stay, total length of stay in hospital and multiple organ dysfunction score (MOD score). Our study found no significant findings in clinical outcomes in rs6313 and rs6746030, suggesting an association between propofol susceptibility and variance in immune modulation.
65	Aria Eppinger	Translational Life Science	Serum Marker of Dietary Glyphosate Exposure and Oral Microbiome Diversity	Aria Eppinger; Alison Morris, MD	Background: Oral dysbiosis is associated with periodontal, cancer and other diseases. Smoking is one cause of oral dysbiosis. Identifying other causes represents an important public health research area. Glyphosate, the active ingredient in herbicides like Roundup, is found on food and in human urine, likely from diet. Glyphosate is linked to decreased beneficial gut bacteria. It is unknown whether eating foods with glyphosate residue leads to oral dysbiosis. We determined, for the first time, the association between the oral microbiome and serum glyphosate levels. Methods: Using a competitive ELISA, we analyzed serum glyphosate concentrations from 46 HIV-negative men (27 never-smokers) with 16S rRNA oral microbiome data. Using QIIME, Virtualbox Microbiome Helper, and MicrobiomeAnalyst, microbiome diversity was compared among serum glyphosate quartiles. Results: Measures of diversity were not significantly different among all participants. When restricted to never smokers, higher glyphosate levels were associated with lower alpha diversity (Chao1, p=0.19) and lower levels of phyla Cyanobacteria (p=0.005), Spirochaetes (p=0.04), TM7 (p=0.09) and Synergistetes (p=0.12) Conclusion: The association between serum glyphosate levels and oral microbiome diversity appears limited to never smokers. Future work is needed with larger numbers of healthy, never-smokers to understand the association between glyphosate exposure and the oral microbiome.

54	Xiaonan Fan	Physical Science and Engineering	lncRNA-MFDL: Identification of Human Long Non-coding RNAs by Fusing Multiple Features and Using Deep Learning	Xiaonan Fan, MS; Shaowu Zhang, PhD	Long noncoding RNAs (lncRNAs) are emerging as a novel class of noncoding RNAs and potent gene regulators, which play an important and varied role in cellular functions. lncRNAs are closely related with the occurrence and development of some diseases. High-throughput RNA-sequencing techniques combined with de novo assembly have identified a large number of novel transcripts. The discovery of large and 'hidden' transcriptomes urgently requires the development of effective computational methods that can rapidly distinguish between coding and long noncoding RNAs. In this study, we developed a powerful predictor (named as lncRNA-MFDL) to identify lncRNAs by fusing multiple features of the open reading frame, k-mer, the secondary structure and the most-like coding domain sequence and using deep learning classification algorithms. Using the same human training dataset and a 10-fold cross validation test, lncRNA-MFDL can achieve 97.1% prediction accuracy which is 5.7, 3.7, and 3.4% higher than that of CPC, CNCI and lncRNA-FMFSVM predictors, respectively. Compared with CPC and CNCI predictors in other species (e.g., anole lizard, zebrafish, chicken, gorilla, macaque, mouse, lamprey, orangutan, xenopus and C. elegans) testing datasets, the new lncRNA-MFDL predictor is also much more effective and robust.
55	Adelle Fernando	Physical Science and Engineering	A Machine Learning Approach to Classifying Acute Pain Using Time Scale Decomposition of EDA Signals	Adelle Fernando; Busra Susam, MS; Murat Akcakaya, PhD	Currently, methods of pain evaluation and diagnosis in the clinical setting are subjective and incoherent. The objective of this project is to classify acute pain in adolescents through the combination of electrodermal activity signals (EDA) and a feature extraction technique called time scale decomposition (TSD) for use in machine learning algorithms. EDA data was used for its connection to the sympathetic nervous system and pain response. Signals were collected from fifteen post-appendectomy patients during three visits, with Visit 1 and Visit 3 representing pain and no pain, respectively. The signal data was then downsampled, filtered and normalized and converted into TSD matrices for feature extraction. Mean, standard deviation, and entropy were selected as features and dimensionality reduction was performed on the TSD matrices using k-means clustering. After compiling all patient features, the reduced matrices were used in linear discriminant analysis (LDA), a machine learning classifier, which was able to classify acute pain of the tested patients. To extend this project, other classifiers including quadratic discriminant analysis and support vector machines could be used alongside LDA to provide a more in-depth classification. In the future, this system could be implemented in a clinical setting to diagnose pain with less subjectivity.
4	Paine Fleisher	Basic Life Science	Induction of Deubiquitinating Enzyme USP50 during Erythropoiesis	Paine R. Fleisher, BA; Junting Cai, PhD; Jianxin Wei, PhD; Valerie Schrott, MS; Jing Zhao MD, PhD; Mark Gladwin, MD; Grant Bullock, MD, PhD; Yutong Zhao, MD, PhD	Anemia is the most common hematologic disorder worldwide resulting from the loss of blood, or the reduced production or increased destruction of red blood cells (RBCs). Protein degradation, which plays a crucial role in erythropoiesis, the complex process of RBC differentiation and maturation, can be regulated by protein ubiquitination, which in turn can be reversed by deubiquitinating enzymes (DUBs); however, the role of DUBs in erythropoiesis have not been well studied. We examined the expression of DUBs during erythropoiesis using an ex vivo human CD34+ hematopoietic progenitor cell culture system. Here we show that ubiquitin-specific protease 50 (USP50) levels are increased during erythropoiesis. USP50 mRNA levels are significantly increased on Day 3 and protein levels are elevated on Day 9 of erythroid differentiation. Co-immunoprecipitation and proteomics analysis reveal that Ku70, a DNA binding protein, is associated with USP50. Over-expression of USP50 has no effect on Ku70 mRNA levels, while it reduces Ku70 protein levels, suggesting that USP50 may indirectly regulate Ku70 protein stability. USP50 protein is also not stable and its degradation is independent of the proteasomal and the lysosomal degradation systems. This study suggests that DUBs like USP50 may regulate protein stability during erythropoiesis, however, more investigation is needed.
56	Maria Giovanna Francipane, PhD	Physical Science and Engineering	Bioengineering a Kidney in Secondary Lymphoid Tissues: The Importance of the Lymphotoxin Beta Receptor Pathway in Tuning Host-derived Vascularization	Maria Giovanna Francipane, PhD; Bing Han, MD, PhD; Leif Oxburgh, DVM, PhD; Sunder Sims-Lucas, PhD; Carlton Bates, MD; Eric Lagasse, PharmD, PhD	We previously demonstrated that the mouse lymph node (LN) can support the maturation of mouse metanephroi into nephrons with glomerular and tubular functions. Recently, we found that the LN can also foster the maturation of human fetal kidney as well as kidney organoid cultures generated from mouse nephron progenitors or human iPSCs. Signaling through the lymphotoxin-beta receptor (LTβR) is critical for LN development and homeostasis, and we hypothesized it might also support ectopic kidney organogenesis. To confirm our hypothesis, mice bearing LN kidney grafts were treated with LTβR-Fc fusion protein. LTβR-/- mice were also used to confirm LTβR ablation negatively affects ectopic kidney organogenesis by impairing the function of LN-resident stromal cells. LTβR-/- mice do not have LNs, therefore omentum was used as an alternative secondary lymphoid organ for transplantation. LTβR pathway blockade resulted in reduced kidney graft growth and vascularization, indicating its pivotal role in kidney organogenesis within secondary lymphoid organs. Thus, within the LN, a complex scaffold of stromal cells not only physically supports the developing graft, but also initiates a cascade of molecular events that ultimately allows the transplanted tissue to be vascularly integrated, grow, and functionally mature.
66	Lily Francis, MBBS, MPhil	Translational Life Science	Neuropathology of POLG-related Mitochondrial Diseases in Patient-derived iPSC-neurons	Lily Francis, Jason Callio, Simon Watkins, Brett Kaufman, Leonard D'Aiuto, Donna Stolz, Vishwajit L. Nimgaonkar, Alejandro Soto-Gutierrez, Amy Goldstein, Charleen T. Chu	DNA polymerase gamma (Polg) is responsible for mitochondrial DNA (mtDNA) replication and repair. Mutations in POLG, the gene encoding the catalytic subunit of Polg, result in a set of clinical syndromes characterized by mtDNA depletion in affected tissues, with variable organ involvement and severity. Treatment for POLG-related disorders remains mostly supportive, with the majority of patients progressing to severe disability and death within a few years of diagnosis. Therefore, a better understanding of disease mechanisms in the affected cell types is needed to illuminate new therapeutic options. Most patients with POLG mutations are compound heterozygotes. This is our work studying cortical neurons differentiated from two patient-derived models of POLG-related mitochondrial diseases (PgATWS, PgATLX). Fibroblasts were reprogrammed into induced pluripotent stem cells (iPSCs), and mutation status confirmed by DNA sequencing. While the patient-derived iPSCs did not show mtDNA depletion relative to control iPSCs, both PgATWS and PgATLX failed to undergo the dramatic increase in mtDNA content observed in control neurons. Neurons differentiated from patient iPSCs exhibited shortening of the neuritic arbor, with abnormal neuritic swellings. PgATWS and PgATLX also exhibited abnormal mitochondrial ultrastructure by electron microscopy. Ongoing studies are aimed at characterizing mitochondrial function and dynamics in somatic and neuritic compartments.

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34	Madhavi Ganapathiraju, PhD	New Research Tools and Techniques	Pitt Antibody Exchange: a Web Portal about Who-donates or Who-needs Protein Antibodies	Sandeep Subramanian, MS; Madhavi Ganapathiraju, PhD	Background: Biologists depend on commercial vendors to buy crucial biological resources such as antibodies or cell lines, being unaware that a colleague in close proximity may be willing to share these reagents. We analyzed 'acknowledgements' sections in scientific articles, and found that occasionally scientists benefit from donation of antibodies from other scientists. However, these donor/acceptor relations seem to be through personal communication, as there is currently no information hub that facilitates such exchange. Methods: We built a web-portal called Antibody Exchange (AbX), especially for Pitt scientists, where they may post information that they are either in need or are able to donate antibodies, or even cell lines, DNA constructs or other such resources. Availability: https://tonks.dbmi.pitt.edu/brx/ Key Features: Scientists can login using Pitt passport or LinkedIn or Facebook credentials. Once logged in, the website shows posts from others either requesting or announcing willingness to donate a resource. Any user would be able to post that they are requesting or are willing to donate such resources. Posting information is not a binding that the exchange actually takes place. AbX could serve as Pitt's central resource to share information about who-has-what about bioresources for experimental biology.
5	Gabrielle Gentile	Basic Life Science	Defense and Counter-Defense Mechanisms Employed by Phage-Host Dynamics	Gabrielle M. Gentile; Rebekah M. Dedrick, PhD; Rebecca A. Garlena; Daniel A. Russell; Deborah Jacobs-Sera; Graham F. Hatfull, PhD	Microbial warfare between prokaryotes and their viruses has been waging for billions of years with continual evolution and selection of the bacteria and the viruses that infect them. Previous research has shown that temperate phages confer prophage-mediated viral defense during lysogeny through the expression of genes that prevent viral superinfection. Little is known about the mechanisms by which temperate phages defend in order to maintain microbial success; therefore, I proposed to study the interaction interface of representative phages on the five Cluster I lysogens. Sensitivity assays revealed several defense escape mutants on the Sbash lysogen. Five members of Cluster Q and phage Crossroads (L2) were extensively investigated. Illumina sequencing of the Cluster Q mutants identified mutations falling within the same gene homolog (Pham6023). RNA-Seq analysis of the Sbash lysogen reveals ten candidate genes to be involved in defense. Individual knockouts have been designed for these genes, and eight plasmids were constructed each containing a different operon. Screening on these constructs implicated Sbash genes 30-31 in defense against Crossroads through an unprecedented system hypothesized to involve restricted phage growth and modification. Currently, we are elucidating the basis for these systems to understand the ongoing evolutionary battle between phages and their hosts.
35	Marie Gerges	New Research Tools and Techniques	The Dose Utility Explorer	Roger Day, ScD; Marie Gerges	The Dose Utility Explorer (DUE) is an interactive website that allows clinical investigators to assess different doses for implementation in Phase I clinical trials. The DUE assumes that every patient has two distinct dose "thresholds": response and toxicity. A dose that exceeds one or both of the thresholds will cause a patient to either respond or experience toxicity upon treatment. Using preclinical data, users input values pertaining to their patients' median thresholds of response and toxicity. The DUE generates a joint bivariate lognormal mixture that divides patients into quadrants that correspond to the four possible outcomes of treatment. The DUE integrates each quadrant of the mixture to calculate the probability of the outcome. Users then select one of four treatment strategies, represented by buttons labeled 'Additive,' 'Simple,' 'Cautious,' and 'Aggressive'. Finally, an "expected utility" function combines the probabilities with the treatment strategies to determine an optimal dose. Because of the sparse amount of information available prior to Phase I trials, clinical investigators will benefit most from the DUE by treating the website as a "thought tool," or mode of risk-free experimentation. The model has the capacity to answer questions regarding the relationship between patient heterogeneity, treatment strategy, and optimal dose.
6	John Goté	Basic Life Science	How Does Eye Morphology Change across Development in the Jumping Spider *Phidippus audax* ?	John Goté; Patrick Butler; Annette Stowasser, PhD; Daniel Zurek, PhD; Elke Buschbeck, PhD; Nathan Morehouse, PhD	Light provides an enormous amount of information for guiding behavior, and eyes have evolved repeatedly across the animal kingdom to address this valuable opportunity. However, as a result of their diminutive size, jumping spider eyes face extreme trade-offs between resolution and sensitivity. As adults, their eyes operate at the physical limits for vision. Yet juveniles face even more severe size constraints during development. Little is known about how their eyes cope with these constraints. We studied developing *Phidippus audax* spiders to understand how these animals address the difficulties associated with sensory miniaturization while maintaining remarkable visual capacities. Previously, we determined that the spiders ameliorate (to some extent) the issues associated with tiny eyes by building proportionally larger eyes during early development. Our current research aims to address how the retina adapts to the size constraints of early development. Using ophthalmoscopic techniques, we investigated how the density of photoreceptors changes across development. We constructed retinal maps of the anterior lateral eyes to determine the total photoreceptor number per individual. Our data indicate that photoreceptor numbers may remain constant throughout development, suggesting that a developmental constraint may impose severe challenges to visual acuity and sensitivity during early developmental stages.

67	Michael Granovetter	Translational Life Science	Norepinephrine's Role in Statistical Learning of Speech	Michael C. Granovetter; Lori L. Holt	When perceiving speech, individuals rely on select statistical dimensions of the auditory input learned from previous environmental exposure. If the characteristics of speech input are inconsistent with long-term representations of speech acquired a priori, however, listeners are able to reweight their attention to different stimulus features. The neural processes involved in the utilization of long-term statistical features of speech--and the reweighting of attention to these features during novel stimulus encounters--remains to be elucidated. One candidate mechanism is that norepinephrine (NE), which is thought to globally increase the signal-to-noise ratio, or neural gain, of cortical circuits, could be released at lower tonic concentrations when a listener is required to adapt to stimulus characteristics that are inconsistent with statistics acquired a priori. In this study, native English speakers performed a speech discrimination task while being primed with stimuli containing features either consistent or inconsistent with native English statistics, while we recorded task-evoked pupil dilations, an established correlate of cortical NE release. Our preliminary results explore whether NE concentrations are lower when listeners must learn from novel speech input, in comparison to when they subsequently are exposed to speech with canonical stimulus features.
36	Mark Greenhalgh	New Research Tools and Techniques	The Use of Mobile Health in Treatment for Post-Traumatic Stress Disorder	Mark Greenhalgh, BS; Josh Marino, MS; Rory Cooper, PhD	Post-Traumatic Stress Disorder (PTSD) affects witnesses and survivors to a life-threatening event and are defined by distressing hyper-vigilance, re-experiencing, avoidance, and emotional numbing. Frustrations regarding costs, waitlists, and stigmatization dissuade half of this population from seeking professional treatment. Untreated symptoms create problems with cardiovascular disease, drug abuse, and suicide. Smartphone applications are potential complimentary tools for health care. The purpose of this research was to identify mobile health tools for PTSD and check their validity as tools for users with PTSD symptoms. Researchers conducted a thorough review of the literature, targeting personal feedback and symptom effects. Results presented three smartphone applications (PTSD Coach, T2 Mood Tracker, and RELAX) and two unnamed Ecological Momentary Assessments (EMA) (one Android programmed and one computer based) show efficacy in populations susceptible to PTSD symptoms. Users reported compliance, positive ratings, reduced symptoms, or increased confidence in sharing their experiences. This is promising for mobile health based PTSD treatments and interventions. The researchers of this study can use the information to develop a novel complimentary intervention for PTSD. Specifically, through smartphone application development and a Machine Learning (ML) utility, the product can predict PTSD “trigger” contexts, allowing for symptom management before a stressful situation.
7	Aditi Gurkar, PhD	Basic Life Science	Endogenous DNA Damage Contributes to Congestive Heart Failure and Dilated Cardiomyopathy	Aditi U. Gurkar PhD; Rebecca Vanderpool, PhD; Sara McGowan; Mark Ross, PhD; Charles McTiernan, PhD; Claudette St. Croix, PhD; Simon Watkins, PhD; John Gorcsan III MD; Ana Mora, MD; Laura J. Niedernhofer, MD, PhD	With aging, muscle degeneration is universal, affecting both motor and cardiac function. This drives two of the most common aging-related diseases: cardiovascular and musculoskeletal disease. The etiology of age-related decline in myocyte function is not well-defined. Here, we asked if endogenous, nuclear DNA damage is a contributing factor. Bulky DNA lesions block transcription and thus can negatively impact virtually all other cellular processes. Therefore post-mitotic cells are anticipated to be particularly vulnerable to damage to the nuclear genomes. We knocked-out ERCC1-XPF, a DNA repair endonuclease required for nucleotide excision repair of bulky lesions, in differentiated myocytes of mice to increase the burden of endogenous DNA damage and determined the impact on muscle function. Loss of DNA repair caused sudden death by 6 months due to myocardial disease. Surprisingly, skeletal muscle integrity and function were not appreciably affected by the DNA repair defect. In contrast, deletion of ERCC1-XPF in cardiomyocytes led to thinning of the left ventricular wall and impaired cardiac function, hallmarks of dilated cardiomyopathy. These data support a role for endogenous DNA damage in cardiomyocyte dysfunction and congestive heart failure and define a novel murine model of this age-related degenerative disease for rapidly testing therapeutic interventions.
8	William Holliday	Basic Life Science	A Putative Electrophysiological Biomarker of Auditory Sensory Memory Encoding is Sensitive to Pharmacological Alterations of E/I Balance	William B. Holliday, Kate Gurnsey, Robert A. Sweet, Tobias Teichert	Background: The amplitude of the auditory evoked N1 component that can be derived from non-invasive electroencephalographic recordings increases as a function of time between subsequent tones. N1 amplitudes in schizophrenia (SZ) saturate at a lower asymptote. Reduced N1 dynamic range is a putative electrophysiological biomarker of altered sensory memory function. Here we test the hypothesis that reduced N1 dynamic range results from a shift in excitatory/inhibitory (E/I) balance towards an excitation-deficient or inhibition-dominant state. Methods: Auditory evoked potentials (AEP) were recorded while four macaques passively listened to sequences of sounds of random pitch and stimulus-onset asynchrony (SOA). The effect of the NMDA receptor channel blockers ketamine and MK-801, as well as the GABAA receptor positive allosteric modulator midazolam on N1 dynamic range was tested. Results: Ketamine, MK-801 and Midazolam reduced peak N1 amplitudes for the longest SOAs. Other AEP components were also affected but revealed distinct patterns of susceptibility that point towards quantitative differences in the circuitry maintaining E/I balance of different components. Conclusions: N1 dynamic range may be a marker of altered E/I balance. Reduced N1 dynamic range in SZ may indicate that the auditory cortex is in an excitation-deficient/ inhibition-dominant state.

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37	Debby Hollingshead, MSIS	New Research Tools and Techniques	Evaluation of Clariom D Transcriptome Profiling with Degraded RNA Samples	Deborah J. Hollingshead, MSIS; Liane D. Fairfull, BS; Erica Fong, BS	The Affymetrix (ThermoFisher) WT pico assay produces labeled cRNA for use with whole transcriptome arrays from a wide range of RNA quality, including FFPE derived RNA. This study assesses the impact of RNA degradation on differential RNA expression data. Starting with the MicroArray Quality Control (MAQC) samples (Universal human reference (UHR) and Human Brain RNA (HBR)) we created degraded/intact pairs of identical RNA and analyzed each in triplicate using Clariom D arrays. Following hybridization to Clariom D microarrays, analysis was performed between UHR and HBR at both the gene and transcript level for intact and degraded input. Degradation has a minor impact on signal reproducibility between replicates but degraded samples contained approximately 60% as many detectable genes as intact samples resulting in identification of fewer differentially expressed genes. Ten percent of genes found to be differentially expressed in intact samples, were also identified in degraded samples. Ten percent of differentially expressed genes identified in degraded RNA were not identified using intact samples. RNA degradation leads to reduced assay sensitivity and loss of information. Although the Clariom WT pico assay measures RNA expression levels in degraded/FFPE derived RNA, degradation reduces the assays effectiveness in detecting expression changes and may confound results.
9	Megan Hudnall	Basic Life Science	Stimulation of Adult Limb and Tail Regeneration with Lizard Spinal Cord Implants	Megan L. Hudnall, Thomas P. Lozito, Rocky S. Tuan	Unlike salamanders, lizards are unable to regrow lost limbs, distinguishing lizards as the only vertebrates to combine regenerative tissues (i.e. tail) and non-regenerative tissues (i.e. limbs). We have identified the lizard spinal cord as the critical source of signals responsible for patterning regenerated tails of lizards. We hypothesize that (1) lizard tail regeneration is induced by signals originating from the spinal cord, and (2) transplanting spinal cord pieces into amputated limbs improves healing. Spinal cords were removed and/or added to the stumps of amputated lizard tails. Spinal cord removal resulted in the complete loss of regeneration in amputated lizard tails, and transplantation of exogenous spinal cord pieces to tail stumps lacking endogenous spinal cords restored tail regeneration. Similarly, exogenous spinal cord pieces implanted as autografts within dorsal muscles of original tail portions induced normally structured ectopic regenerates at implantation sites, resulting in multi-pronged “forked” tails. Finally, exogenous spinal cord pieces implanted into the normally non-regenerative amputated hind limbs of lizards induced enhanced, yet tail-like, regenerates. Formation of ectopic tails was significantly diminished by co-treatment with the hedgehog inhibitor cyclopamine. This study has identified the lizard spinal cord as necessary and sufficient for inducing regeneration in a process involving hedgehog signaling.
10	Kerry Iles	Basic Life Science	Isolation and Characterization of Floral Phages	Kerry Iles, Andrea Fetters, Debora Jacobs-Sera, Rebecca A. Garlena, Daniel A. Russell, Graham F. Hatfull, Tia-Lynn Ashman	Human land use is changing the earth’s ecosystems at an exponential rate. One major transition has been the conversion of native vegetation to urban landscapes. Urbanization affects ecological communities by changing abiotic conditions as well as modifying existing biotic interactions and creating new ones. However, the consequences of urbanization for species interactions is just beginning to be understood. Two key interactions for plant success involve pollinators and soil microbes, and the effects of urbanization on these have received some attention. The microbial communities within flowers have been studied less and whether they host bacteriophages is unknown. As a first step to understanding this tri-trophic interaction, we sought to characterize bacteriophage infection of Actinobacteria living in flowers in an urban environment. Flowers from eleven cosmopolitan plant species common to Pittsburgh were collected along an urban to peri-urban transect. Floral samples were enriched using nutrient-rich broth with a variety of Actinobacteria hosts. Each enrichment was sampled daily for one week to assess phage lysis. One phage isolated from Trifolium pratense was found to infect Gordonia terrae. This G. terrae phage, Gustav, has a genome 44,408 nucleotides in length which contains an estimated 69 genes and has a GC content of 67.9%.
57	Daniel Jacobs	Physical Science and Engineering	Computational Quantification of Enhanced de novo Extracellular Matrix Elaboration in an Elastomeric Scaffold Model with Engineered Micro-Architecture	Daniel Jacobs; Dima Denisenko; Samuel Luketich; Richard Hoff; Xinzhu Gu, PhD; William R. Wagner, PhD; Antonio D’Amore, PhD	Elastomeric biodegradable scaffolds have been utilized as viable tissue surrogates in a broad spectrum of applications: cardiac patches, vascular grafts, and heart valves. Similarly, mechanical conditioning regimens are widely recognized as effective methods to facilitate extracellular matrix (ECM) accretion and to improve engineered constructs mechanical properties. However, the understanding of the underlying cells-matrix interaction mechanisms remains rather limited. In an effort to reduce this gap in knowledge this study utilized cells seeded elastomeric scaffolds to investigate on how mechanical strain and micro-architecture impact ECM formation and elaboration. We hypothesized that specific levels of strain and micro-architectures can be identified to enhance ECM production in quantity and quality. In this study, vascular smooth muscle cell-seeded polyurethane scaffolds having different micro-structure, have been dynamically cultured using a uniaxial stretch bioreactor for 21 days at fixed 30% strain, 1 Hz. A Matlab code was developed that separated and quantified the amount of ECM, cells, and scaffold in each sample, showing the existence of specific micro-architectures able to maximize ECM elaboration given a specific imposed macroscopic mechanical load. The improved understanding of the complex process of ECM formation might lead to a more effective engineering of tissues surrogates operating under demanding mechanical in-vivo environments.

68	Gabrielle Kaplan	Translational Life Science	Mitochondrial Alterations in a Mouse Model of Bipolar Mania	Gabbie N. Kaplan; Yinna Wang, PhD; Sruti S. Shiva, PhD; Ryan W. Logan, PhD; Colleen A. McClung, PhD	A confluence of evidence points towards an underlying dysfunction of mitochondria in bipolar disorder (BD) which may lead to an increase in oxidative stress and inflammation. The Clock mutant mouse, which has been shown to display a behavioral repertoire similar to bipolar mania, serves as a model in which we can investigate neuronal mitochondrial dysfunction in the prefrontal cortex, a critical structure known to regulate mood and decision making in the brain. Frontal cortex mitochondrial isolate was used to compare mitochondrial subunit expression as well as respiratory measures. For protein expression analysis, mitochondrial protein lysates were run on a gel and blotted using an antibody cocktail of against critical subunits of the OXPHOS complexes. RNA isolated from PFC tissue sections were also used for quantitative PCR for genes related to OXPHOS and mitochondrial biogenesis. Human postmortem studies conducted in the PFC of patients with BD have shown a decrease in mitochondrial integrity. Our data shows a similar decrease in respiratory rate but with differing alterations to protein and gene levels specific to mitochondria and its upstream targets, particularly an increase in mitochondrial biogenesis. Future studies will investigate the links between circadian clock machinery, cellular metabolism, and mitochondrial respiration.
69	Elizabeth Kenny	Translational Life Science	Graphical Calculation of Estimated Energy Expenditure in Burn Patients	Francesco M. Egro, MBChB, MSc, MRCS; Elizabeth M. Kenny, BS; Ernest C. Manders, MD; Ernest K. Manders, MD	Introduction: Estimated energy expenditure (EEE) equations overestimate the caloric support necessary for burn patients and remain challenging to apply in clinical settings given the difficult mathematics involved. This study aims to introduce a graphical calculation of EEE in burn patients that can be easily utilized in the clinical setting. Methods: Two equations for EEE, derived from multivariate logistic regression by Ireton-Jones et al., were rearranged into linear equations. By choosing an energy expenditure and the age of the subject, the weight was calculated. The endpoints were then calculated and a graph was mapped using Adobe FrameMaker. Results: A graphical representation of Ireton-Jones et al. equations was obtained by plotting weight (kg) on the y-axis, age (years) on the x-axis, and EEE in burn patients as a series of parallel lines. Two graphs were plotted: one for ventilator-dependent patients and one for spontaneously breathing patients. Correction factors for gender, the presence of additional trauma, and obesity are indicated on the graphical calculators. Conclusion: We propose a graphical tool to calculate caloric requirements in a fast, simple, and portable manner. The graphical calculator can be useful to predict caloric requirements and effectively manage patients with severe traumatic burns.
70	Elizabeth Kenny	Translational Life Science	A Nomogram for Rapid Prediction of Hematocrit Following Blood Loss and Fluid Shifts	Elizabeth M. Kenny, BS; Francesco M. Egro, MBChB, MSc; Ernest C. Manders, MD; Ernest K. Manders, MD	Introduction: There is often a need for a simple means of predicting hematocrit (Hct) – the volume of red blood cells in the blood – following blood loss, administration of intravenous fluids, or fluid shifts without cumbersome calculation or costly clinical testing. This study aims to introduce a nomogram for rapid prediction of Hct in a number of common clinical scenarios. Methods: Assuming a constant blood volume (BV) (75 ml/kg), a nomogram for prediction of Hct was created using the following variables: 1) BV determined from body weight, 2) estimated blood loss, and 3) initial Hct. Results: Two nomograms were generated for prediction of Hct after blood loss, administration of intravenous fluids, or fluid shifts in 1) neonates, infants, and children, and 2) adults. Using the nomogram, we demonstrated its utility in prediction of Hct after fluid or blood loss, fluid administration, or a combination of the two. The nomogram allows adjustment for measured and insensible fluid losses and fluid administration. Alternatively, fluid loss or blood loss can be back-calculated if Hct is known. Conclusion: It is possible to use the in's and out's of fluid balance to calculate resultant Hct. A nomogram makes this task fast, simple, and cost-effective.
11	Katherine Kerr	Basic Life Science	Changes in the Secretome of Stem Cells over Multiple Passages	Katherine E. Kerr; Katherine L. Lorentz, MS; David A. Vorp, PhD; Justin S. Weinbaum, PhD	Changes in the Secretome of Stem Cells Over Multiple Passages Introduction: Current methods of coronary artery revascularization have a failure rate upwards of 70%. Tissue-engineered vascular grafts (TEVGs) could provide a solution; previous studies from our group indicate that stem cell-seeded scaffolds remodel into a patent, remodeled, TEVG after 8 weeks in vivo. Paracrine signaling by the seeded cells is thought to be key to the remodeling response. Hypothesis: Secretion of paracrine signals decreases as stem cells are passaged prior to seeding. Materials and Methods: Human mesenchymal stem cells (RoosterBio, passage 1-4) were cultured to 80% confluence. New media was applied and collected after 48 hours. Non-conditioned media served as a negative control. The concentration of two molecules in the conditioned media - vascular endothelial growth factor (VEGF) and hepatocyte growth factor (HGF) – was then quantified. Results and Discussion: VEGF levels decreased significantly (from 3917 to 1157 pg/ml) between passage 1 and passage 3 while HGF levels remained constant (~1110 pg/ml). Conclusions: The significant decrease in VEGF between passage 1 and passage 3 supports the hypothesis. In contrast, the persistent HGF levels suggest different regulation of these two paracrine signals.
12	Solomon Klombers	Basic Life Science	Assessing CFTR'S Tolerance for Nonsense Mutation Correction in NBD1	Solomon Klombers; Patrick Thibodeau, PhD	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 resulting in protein degradation and loss of function. Our project will focus on two CFTR nonsense mutations: G550X and S489X. Both are located in nucleotide binding domain 1 (NBD1) and result in nonfunctional CFTR. Current therapeutics targeting nonsense mutations are imprecise and do not provide specific replacement of the native amino acid. As such, specific nonsense mutations will likely show differential efficiencies in correction. We will therefore generate missense mutations at positions G550 and S489 to test for the possibility of therapeutic correction. Using site-directed mutagenesis, we will assess the impact of substitutions at these loci on folding of NBD1 and full-length CFTR. Our preliminary data suggest S489 is tolerant of correction; the S489A and S489R replacements demonstrate folding comparable to wild type NBD1, while the S489E replacements fold at 70% of WT NBD1. We will continue to evaluate the S489 locus with additional replacements, to assess the potential efficacy of small molecule read-through therapeutics.

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71	Anisha Konanur	Translational Life Science	Effects of Pre-, Peri-, and Post-mortem Factors on Brain Ultrastructure Quality in Human Dorsolateral Prefrontal Cortex	Konanur Anisha; Lewis David, MD; Glausier Jill, PhD	Electron microscopy (EM) studies of postmortem human brain tissue provide a level of resolution key for analyzing the human brain in normal and disease states. However, biochemical processes associated with death can impair the cellular and organelle ultrastructural preservation required for rigorous EM studies. Although postmortem interval (PMI), the time between death and preservation of tissue, is proposed to be the most influential factor of ultrastructural quality, numerous factors may influence ultrastructural preservation. The goal of the present study is to assess the effects of a priori defined factors on multiple components of ultrastructural preservation in the postmortem human dorsolateral prefrontal cortex. Tissue samples from 30 subjects (PMI range: 5.9-24.3 hours) were processed using standard EM histochemistry. The primary dependent measure was percentage of neuronal profiles identified and secondary measures included presence of mitochondria and synapses. As expected, shorter PMIs predicted larger primary and secondary measures. However, some neuronal profiles and all secondary measures could be identified with PMIs up to 24 hours. Higher pH values also predicted larger primary and secondary measures, with an interaction of PMI and pH in low-PMI subjects. These studies indicate that PMI and pH can affect multiple aspects of brain ultrastructural preservation.
38	Erik Koppes, PhD	New Research Tools and Techniques	Droplet Digital PCR Provides Quantitative DNA Analyses of Genome-edited Deletion Alleles, Mosaicism, and Copy Number Variation	Erik Koppes, PhD; Marie. A. Johnson, BS; Dale W. Lewis, BS; Susanne M. Gollin, PhD; Patrizia Luppi, MD; Bethany K. Redel, PhD; Randall S. Prather, PhD; Jerry Vockley, MD, PhD; Robert D. Nicholls, DPhil	Droplet digital PCR (ddPCR) utilizes PCR chemistry contained within immersion droplets such that each droplet either contains or lacks the template giving a binary output for 20,000 droplets per reaction for precise nucleic acid quantification. We assessed genomic copy number of targeted loci in our novel pig models of phenylketonuria (PKU) and Prader-Willi syndrome (PWS) generated by CRISPR/Cas9 genome-editing. In an affected PKU animal ddPCR detected compound heterozygous PAH null alleles with alternative deletion breakpoints. Next, we quantified cellular mosaicism in a pig harboring a deletion of the PWS imprinting-center with 50% each of wildtype and heterozygous null cells. Similarly, in an in vitro model of insulin production in PWS, we estimated the presence of 1% cells with wildtype alleles in clonal lines predominantly having homozygous deletion of the PWS-imprinted domain and validated these findings by fluorescence in situ hybridization (FISH). Finally, we estimated haploid copy number of the imprinted macrosatellite SNORD116 to be in the range of 70-150 and 25-35 for SNORD116a and SNORD116b subfamilies in the pig, with 50 and 100 copies of SNORD116 in the ferret and cat genomes, respectively. In conclusion, ddPCR is a powerful technology to accurately characterize complex natural and genome-edited genetic sequence variation.
75	Katherine Kruckenberg	Translational Life Science	Stress, Personal Growth and Outcomes after Liver Transplantation	Andrea DiMartini MD; Christopher Hughes MD; Katherine Kruckenberg	Introduction: Alcoholic Liver Disease (ALD) is the most common cause of liver disease in the US and a common reason for liver transplantation (LT). Post transplant factors such as stress, worse health on self report, pain, loss of vitality, etc. reported by patients correlate positively with potential for relapse in those with preexisting alcohol use disorders. This suggests that some patients have gone through a traumatic event (transplant), and cope through returning to old patterns of stress management with alcohol consumption. Specific aims: 1) Identify useful criteria to group high relapse risk individuals in the ALD LT population together with the highest risk periods post transplant. 2) Explore the frequency of post traumatic growth in the ALD LT population. 3) Understand the nature of the relationship (if one exists), between Post Traumatic Growth and relapse in patients transplanted for for alcoholic liver disease. Methods: A Cross Sectional Survey will be utilized looking at ALD recipients one-year post LT, with a single administration. This will give us correlational data. Analyses will be performed between measures and alcohol use outcomes, with specific interest in the association between PTG and alcohol use. A scoring algorithm will be used to achieve this.
13	Zachary Lakkis	Basic Life Science	Glycolysis Linked Regulation of Cytokine Production in T Lymphocytes	Zachary I. Lakkis; Ashley V. Menk; Greg M. Delgoffe, PhD	Cytokine production by T lymphocytes is vital to mounting an immune response. Cytokine production, however, is suppressed in the tumor microenvironment (TME), allowing tumors to evade the immune system. The mechanism by which this occurs is not fully understood. We propose that the hypoglycemic TME inhibits cytokine production by limiting glycolysis, freeing lactate dehydrogenase (LDH), which then binds to interferon gamma (IFNG) mRNA and blocks its translation to IFNG protein in T cells. To test this hypothesis, we used ELISA to quantify IFNG production by T cells in the presence or absence of dichloroacetic acid (DCA), an indirect inhibitor of glycolysis. We found that T cells activated by anti-CD3 and anti-CD28 had a significant decrease in IFNG production when treated with DCA. qPCR showed that DCA did not reduce IFNG mRNA despite reduction in IFNG protein. These findings support our hypothesis that cytokine translation and not transcription is inhibited by limited T cell glycolysis in the TME.
59	Olivia Lanes	Physical Science and Engineering	4th Order Cancellation	O.Lanes, T.Chien, X.Cao, P.Lv, G.Liu, M.Hatridge	Microwave parametric amplifiers based on Josephson junctions have become a key component of many quantum information experiments. In previous work, higher-order Hamiltonian terms inherent to the Josephson Junctions have been neglected. We have recently shown in our new paper that these Kerr terms not only hinder the performance of the amplifier more then previously thought, but we also present a new theory and experiment showing that it is possible to be free from these terms. We also present a new methodology for optimizing device performance in the presence of Kerr nonlinearities while retaining device tunability and point to the necessity of controlling higher-order Hamiltonian terms to make further improvements in parametric devices.

76	Sarah Lazzaro	Translational Life Science	Developmental Switch Cost in Task-switching Paradigm	Sarah K. Lazzaro, Bart Larsen, Beatriz Luna	Cognitive abilities continue to mature across development from adolescence to adulthood, leading to more effective cognitive control of behavior. A key component of adolescent cognitive development is improvements in cognitive flexibility. The present study examined the development of cognitive flexibility in 81 individuals aged 14-32 years using a task-switching paradigm. Specifically, we assessed individuals' accuracy and reaction time when they switched between tasks that taxed working memory and inhibitory control. Task-switching led to significant increases in reaction time and reductions in accuracy across the entire sample, with switches to inhibitory control showing most pronounced developmental improvements. Our findings revealed a decreasing switch cost from adolescence to adulthood, with adults showing greater accuracy over adolescents while switching into the inhibitory control task; this effect was only apparent in conditions with high cognitive demand. These results suggest that a key aspect of cognitive maturation into adulthood is the ability to flexibly switch between cognitive tasks with limited cost to performance or speed.
15	Jiyoung Lee, PhD	Basic Life Science	Dynamics and Druggability of Intact γ-Secretase	Ji Young Lee, PhD; Zhiwei Feng, PhD; Xiang-Qun (Sean) Xie, PhD; Ivet Bahar, PhD	γ-secretase is an attractive target for developing pharmaceutical compounds against Alzheimer's disease (AD) because of its central role in the cleavage of amyloid precursor protein (APP) into amyloid-beta (Aβ) peptides, the aggregation of which is the hallmark of AD. The recent elucidation of the intact structure of γ-secretase opens the way to a full-atomic scale characterization of the structural dynamics of this complex using computational models and methods at multiple scales. We analyzed the motions of the intact structure using membrane-coupled anisotropic network model (membrANM) recently implemented in DynOmics. Our study shows a strong coupling between the motions of the extracellular (EC) domain and those of the transmembrane (TM) domain, consolidated by the concerted dynamics of the lipid bilayer. These motions are proposed to be essential for controlling and mediating substrate entry and cleavage. Our druggability simulations further reveal several sites that are druggable, apart from the catalytic pocket, which provide new glimpses into potential mechanisms of allosterically controlling the APP-cleavage function of γ-secretase.
16	Donna Lee	Basic Life Science	The Role of ABL1 in the Therapeutic Response of GIST Cells to Imatinib Mesylate	Donna M. Lee, Li Liu, Jessica L. Rausch, Sergei V. Boichuk, Areej A. Ali, Sneha Patil, Matthew F. Brown, Kathleen R. Makielski, Ying Liu, Takahiro Taguchi, Shih-Fan Kuan, Anette Duensing	Most gastrointestinal stromal tumors (GISTs) are caused by activating mutations of the KIT receptor tyrosine kinase. The small molecule inhibitor imatinib mesylate was developed to target the constitutively activated BCR-ABL1 kinase in chronic myeloid leukemia. However, imatinib also effectively inhibits KIT and is hence successfully used to treat GISTs. Although KIT inhibition clearly has a major role in the therapeutic response of GIST cells to imatinib, the contribution of concomitant inhibition of native ABL1 in this context has never been explored. We show here that ABL1 is expressed in the majority of GISTs. Using siRNA-mediated knockdown, we demonstrate that depletion of KIT in conjunction with ABL1 –mimicking imatinib treatment – leads to reduced apoptosis induction and attenuated inhibition of cellular proliferation when compared to depletion of KIT alone. These results are explained by an increased activity of the AKT survival kinase in this context, which is mediated by the cyclin-dependent kinase CDK2, likely through direct phosphorylation. Our results highlight that distinct inhibitory properties of targeted agents can impede antitumor effects and provide insights for rational drug development. Novel KIT-targeted agents to treat GIST should therefore comprise an increased specificity for KIT while simultaneously displaying a reduced ability to inhibit ABL1.
17	Hongchun Li, PhD	Basic Life Science	Dynamic Modulation of Binding as a Mechanism for Regulating Interferon Signaling	Hongchun Li, PhD; Nanaocha Sharma, PhD; Ignacio J. General, PhD; Gideon Schreiber, PhD; Joseph M. Salvino, PhD; Ivet Bahar, PhD	We focused on interferon (IFN) signaling. IFNα2, a Type-I interferon, forms a ternary complex with two receptors, IFNAR1 and IFNAR2. We have shown that the binding affinity of IFNα2 to these receptors, as well as downstream signaling strength, can be modulated by altering the dynamics of the IFNAR1. The global motions of the IFNAR1-IFNα2-IFNAR2 ternary complex were predicted using the membrANM in which the lipid environment is included in the model and simulations. IFNα2 associated immune responses were shown to be modulated by introducing Cys-Cys double mutants which form cross-links between different subdomains of IFNAR1. The downstream activities (gene expression) and binding affinity experiments carried out with mutants selected based on our computations, showed the changes in binding and activity consistent with the predictions. Druggability simulations identified multiple druggable sites of IFNAR1. We have constructed the corresponding pharmacophore models which are currently screened against libraries of small compounds to identify hit compounds that may be developed into modulators of IFNAR1 activity, in collaboration with the Weizmann Institute (Israel) and Wistar Institute (USA).
18	Ebru Lider	Basic Life Science	In Vitro Testing of Inhibitors of the Mitogen Activated Protein Kinase Phosphatase DUSP6/MKP-3 Identified by Virtual Screening	Ebru Lider; Tamar Skaist; David Koes, PhD; Andreas Vogt, PhD	The mitogen activated protein kinase (MAPK) pathway is responsible for cell proliferation, death, and survival. While these kinases are being extensively studied, mitogen activated protein kinase phosphatases (MKP) are less studied. These MKPs negatively regulate and terminate MAPKs signaling via dephosphorylation. MKPs are upregulated in many cancers. Genetic deletion of MKPs in cancer cells causes cell death, loss of motility, invasiveness, and tumorigenicity. Therefore, MKPs have the potential to become anticancer drug targets. This project aimed to test inhibitors of the phosphatase DUSP6/MKP-3 predicted from computational studies. It was hypothesized that compounds that bind to DUSP6/MKP-3 would cause ERK hyperphosphorylation if such binding resulted in MKP inhibition. To test this hypothesis, MDA-MB-231 cancer cells were plated, treated with different concentrations of compounds, fixed, and stained onto 384-well plates, and an ArrayScan-II measured ERK phosphorylation and toxicity. Data are consistent with the hypothesis that compounds predicted to bind to MKP-3 could cause ERK hyperphosphorylation through MKP inhibition. The project also explored toxicity of the compounds and found that ERK phosphorylation correlated with cell loss. Eventually, a Western blot should be conducted to directly show that compounds interact with MKP-3, and these compounds should be tested for their anticancer activity in mice.

19	Jr-Jiun Liou	Basic Life Science	Application of Platelet Rich Plasma in Combination with Cell Based Therapy for Cartilage Repair	Jr-Jiun J. Liou, MEng; Benjamin B. Rothrauff, PhD; Peter G. Alexander, PhD; Rocky S. Tuan, PhD	Autologous cell-based repair of cartilage injury is limited by donor site morbidity and ex vivo expansion. Mesenchymal stem cells (MSCs), which are more accessible and have extensive expansion and chondrogenic potential, represent an alternative cell type for cartilage repair. Platelet-rich plasma (PRP), a popular biologic treatment for injured articular joint, has been shown to promote stem cell proliferation and tissue healing. To test the effect of PRP on MSC chondrogenesis, MSCs were isolated from arthroplasty donors and PRP was collected from human whole blood. Our results showed that increasing duration of PRP exposure corresponded to decreased gene expression of collagen type II and aggrecan and decreased deposition of cartilage-specific extracellular matrix in pellet cultures. Similar results were observed in three-dimensional hydrogel cultures. As vascular endothelial growth factor (VEGF), a growth factor found in PRP, has been suggested to impair chondrogenesis and cartilage repair, its involvement in PRP action was tested here. Our results showed aggrecan gene expression decreased in the PRP group but addition of anti-VEGF antibody ablated this reduction. Taken together, PRP may not enhance cartilage formation, due to the adverse effect of VEGF on chondrogenic differentiation. Our findings provide information on the application of PRP for cartilage repair.
77	Chia-Hsin Liu, MD	Translational Life Science	Toll-like Receptor 2 Deficiency Enhances Kras-driven Lung Cancer	Chia-Hsin Liu, MD; Y. Peter Di, PhD	Toll-like receptor 2 (TLR2) is essential for inflammatory responses, and has been reported to play either pro-tumorigenesis or tumor-suppressive role. However, the role of TLR2 in KRAS-mutant lung tumorigenesis remains unknown. We analyzed human lung adenocarcinoma cohort (TCGA RNAseq dataset), and result showed that KRAS-mutant lung tumor showed lower TLR2 mRNA expression than paired normal adjacent lung tissue. In survival analysis, patients who have adenocarcinoma with lower TLR2 expression showed worse survival. To functionally test the role of TLR2 during KRAS-driven lung cancer, we generated a mouse model of lung adenocarcinoma mutated for K-ras (K-rasLA2), with and without TLR2 inactivation (K-rasLA2 TLR2-/- and K-rasLA2TLR2+/+, respectively). Surprisingly, the tumor number and tumor area significantly increased in K-rasLA2 TLR2-/- mice compared to K-rasLA2TLR2+/+ mice. In addition, the inflammatory cells in bronchoalveolar lavage fluid (BALF) significantly increased in K-rasLA2 TLR2-/- mice. Gene expression of K-rasLA2 TLR2-/- lung tumors showed higher inflammatory chemokines and cytokines (Ccl1, Ccl2, Cxcl1, Cxcl2, Cxcl5, Csf1, IL-6, Tnfa) than K-rasLA2TLR2+/+. BALF were analyzed using Luminex assays and CXCL1 is significantly higher in K-rasLA2 TLR2-/-. Our results suggest that TLR2 deficiency may promote Kras-mutant lung tumorigenesis through increased cancer-related inflammation and the lower TLR2 expression is associated with worse survival.
20	Sarel Loewus	Basic Life Science	Using *Caenorhabditis elegans* to Investigate Mechanisms that Coordinate Organism-wide Responses to Cellular Stress	Sarel J. Loewus; Todd Lamitina, PhD	Recent work has revealed that cell autonomous responses to cellular stress are also controlled at the organismal level. Defining these organismal control mechanisms will provide insights into stress response pathways and conditions associated with elevated cellular stress, such as ageing. Osmotic challenge is one type of stress that cells universally must respond to in order to maintain a water and solute balance. When *C. elegans* are exposed to conditions of hypertonicity, they upregulate the expression of a glycerol-producing enzyme, GPDH-1, in the intestine and hypodermis. *C. elegans* also evokes behavioral responses to hypertonicity via the activity of at least two neuronal circuits. We hypothesize that these neuronal circuits are critical for the non-neuronal expression of gpdh-1in response to hypertonicity. We also hypothesize that the physiological response to hypertonicity elicits changes in the sensory neuronal circuits that modify behavior to facilitate adaptation. We will use genetic screens to identify the signaling proteins required for gpdh-1 expression. Additionally, we will use existing mutants that alter sensory neuron function to test the signaling between neuronal and non-neuronal cells during hypertonic stress. Our studies will characterize the signaling pathways required to execute and integrate the physiological and behavioral response of *C. elegans* to hypertonicity.
21	Ricardo Londono, MD, PhD	Basic Life Science	Cellular Origins of Regenerated Lizard Tail Musculoskeletal Tissues	Ricardo Londono, Wei Wenzhong, Bing Wang, Rocky S. Tuan, Thomas P. Lozito	Following tail amputation lizards form a blastema, a structure that gives rise to the regenerated tail. According to one hypothesis, stump cells de-differentiate and then re-differentiate to form regenerated tissues. An alternate hypothesis posits that reserve stem/progenitor cells residing within stump tissues differentiate directly into cells of regenerated tails. The goals of this study are to investigate the cellular origins of regenerated tail tissues and to test the roles of cell identity and differentiation on cell fate. We use the parthenogenetic lizard species Lepidodactylus lugubris to show that cells pre-labeled with fluorescent markers and injected into the stumps of amputated tails contribute to regenerated tail tissues. We tested the ability of various populations of cells to contribute to regenerated cartilage and muscle tissues. Labeled muscle, cartilage, and fibroblast (control) cells implanted into tail stumps contributed to regenerated tail blastemas. Labeled cells re-extracted from tail blastemas exhibited the abilities to differentiate into cartilage and muscle cells in vitro. All three cell types were also detected in both regenerated cartilage and muscle tissues after 3 weeks of regrowth. These results indicate there is differentiation plasticity during lizard regeneration, and that regenerated tissues are formed from de-differentiated stump cells rather than stem cells.

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78	Ashwinee Manivannan	Translational Life Science	Linking Working Memory Activation with Duration of Untreated Psychosis in Patients with First Episode Psychosis	Ashwinee Manivannan; Maria Jalbrzikowski, PhD; Vishnu P. Murty, PhD; Will Foran; Beatriz Luna, PhD; Deepak Sarpal, MD	A longer duration of untreated psychosis (DUP) has been linked with worsened response to antipsychotic treatment and variation in corticostriatal functional connectivity in areas in the central executive network. The following fMRI study examined the link between DUP and working memory (WM) activation in corticostriatal nodes in 29 first episode psychosis (FEP) patients. Patients underwent fMRI scanning while performing a visual WM task. At the single subject level, task conditions were modeled, and at the group level, each condition was examined along with DUP. We observed that activation in a region of the right putamen during WM maintenance negatively correlated to length of DUP. Analysis of key prefrontal WM nodes revealed varied left dorsolateral prefrontal cortex activation during maintenance with increasing WM load: during a lower load, DUP positively correlated with activation (R2=0.1453, p=0.034); with higher load, DUP negatively correlated with activation (R2=-0.1265, p=0.05) These results suggest that a longer DUP is associated with impairments in prefrontal efficiency and sheds light on potential neural mechanisms associated with untreated psychosis.
60	Beatrice Milnes	Physical Science and Engineering	Macrophages are Required for Adult Mourning Gecko (*Lepidodactylus lugubris*) Tail Regeneration	Beatrice Milnes; Thomas Lozito, PhD	Lizards are the closest relatives of mammals that exhibit enhanced healing or regenerative capabilities as adults. Infiltrating immune cells have been shown to play a major role in mammalian wound repair and are critical to limb regeneration in the axolotl salamander (*Ambystoma mexicanum*). Here we investigated the immune response during lizard tail regeneration, and revealed a temporally defined requirement of macrophage infiltration in the regenerative process. Mourning Gecko (*Lepidodactylus lugubris*) tails were regrown to regenerative landmarks then immunostained for macrophage and neutrophil markers. Systemic macrophage depletion during lizard tail regeneration was achieved via clodronate liposomes. Treated tails were collected and compared in length, as well as expression of macrophage and neutrophil markers. Successful macrophage depletion showed a direct correlation to regenerative ability and reduced macrophage marker expression. Taken together, these results confirm the recruitment of immune cells at various stages of lizard tail regeneration, and indicate a dependency on macrophage infiltration for progression of normal tail regrowth. Future work will determine the roles of other immune cells, such as T-lymphocytes, in lizard tail regeneration, as well as comparisons to mammalian immune responses to injury in the hopes of enhancing tissue regeneration in humans.
39	Al-Walid Mohsen, PhD	New Research Tools and Techniques	Inhibitor-induced In Situ-Chaperone Therapy: A Novel Drug Targeting Strategy for Treating Metabolic Disorders	Al-Walid Mohsen; Anuradha Karunanidhi; Bianca Seminotti, PhD; Guilhian Leipnitz; Catherine Kochersperger; Lina Ghaloul-Gonzalez; Shrabani Basu; Jerry Vockley	Metabolic disorders resulting from missense mutations often lead to protein instability. Protein stability is improved by ligand binding. In this study, we tested the use of inhibitory drugs of downstream pathway to accumulate intermediates that may bind to the unstable variant enzyme(s) and confer stability, improve its function, and provide clinical benefit. Three pathways were targeted: fatty acid □-oxidation, and the Phe and Leu catabolic pathways. Patient fibroblasts deficient in enzymes of these pathways were cultured in the presence of downstream reaction inhibitors, trimetazidine, nitisinone (NTBC), and epigallocatechin gallate (EGCG), respectively. Immunostaining and western blotting indicated that the VLCAD variant presence in cultured patients' fibroblasts improved in a dose dependent fashion with the trimetazidine treatment while enzyme activity increased comparably. Phenylalanine hydroxylase and tyrosine aminotransferase presence increased up to two fold in cells with PKU when NTBC was present. Improvements varied with the severity of the variants' stability. EGCG improved the protein signal in IVD, MCCC, and HMGCL in IVD deficient cells. Treatment of metabolic genetic disorders with inhibitors of downstream reactions improved the presence of enzyme variants catalyzing upstream reactions, providing proof of concept for the efficacy of such drugs and the validity of this novel drug targeting approach.
22	Ian Moran	Basic Life Science	The Development of a Mg Ring for the Regeneration of a Torn ACL for Human Application	Ian Moran, Jonquil Mau, Savio L-Y. Woo	We have developed and tested a promising new technique for healing the ACL by combining mechanical and biological augmentation strategies. Using literature values for finding the geometry of the human ACL showed that it was necessary to have three sizes for the Mg ring to fit a human ACL, which can vary substantially in size. They were modeled in SolidWorks (Waltham, MA) and then printed using PLA plastics. The smallest ring was appropriate for three humans, and the largest ring was appropriate for one larger leg. FEBio was used to Stest the rings structural properties. A force of 40 N was applied to each of the fixation suture holes where sutures would contact the ring. An inward force of 20 N directed towards the central axis was also applied to the space between the edge of the ring and the suture holes in order to simulate the conditions during surgery. The results showed, the range of the effective stress was 108 to 188 MPa when the Mg ring was loaded as previously described, with the highest effective stress being the largest ringe. The yield strength of the ring was lower than then the largest observed effective stress.
40	Adam Moritz	New Research Tools and Techniques	Material Viscosity Prediction under Normal Swallowing Conditions via High Resolution Cervical Auscultation	Adam Moritz; Ervin Sejdic, PhD; Yassin Khalifa	Introduction: Dysphagia is a medical condition associated with difficulty swallowing foods and liquids. The current standard for diagnosis is to use x-ray monitoring while the patient swallows different barium-coated materials. This test is fairly invasive and smaller clinics might not have access to the equipment necessary. One of the key factors affecting swallowing is the viscosity of the swallowed materials. If an algorithm were able to identify the viscosity of the swallowed material, it may suggest that a similar algorithm could identify dysphagic swallows. Methods: A total of 507 swallows performed by 147 patients served as the dataset. Features were extracted directly from the signals using standard statistical properties as well as using analysis of wavelet signal decompositions. With these features, multiple machine learning classifiers were trained. Results: The Support Vector Machine with a Gaussian Kernel was able to differentiate between thin and thick swallows with a 90% accuracy using 10-fold cross validation. Discussion: From this study, we have confirmed that swallowing accelerometry can be used to identify characteristics of individual swallows. The end goal for this research is for an algorithm to be developed that is able to determine whether the patient is dysphagic or not.

23	Jennifer Naciri	Basic Life Science	Generation of Three-dimensional Human Neuronal Cultures for Modeling CNS Viral Infections	JN. Naciri, Leonardo D'Aiuto, Nicholas Radio, Sesha Tekur, Dennis Clayton, Gerard Apodaca, Roberto Di Maio, Yun Zhi, Peter Dimitrion, Paolo Piazza, Matt Demers, Joel Wood, Robert Yolken, James McNulty, Paul Kinchington, David Bloom, VL Nimgaonkar	Neurotropic viral infections can cause structural and functional changes in the central nervous system (CNS), resulting in long-term neurological sequelae. An improved understanding of the pathogenesis of neurotropic viruses is important for the development of efficacious antiviral interventions, but the investigation of CNS infections in humans has been hampered by the absence of satisfactory human neuronal cell models. Human induced pluripotent stem cells (hiPSCs), offer the unprecedented opportunity of generating limitless amounts of different CNS cell types, as well as the possibility of generating three-dimensional (3D) neuronal cultures which can recapitulate aspect of tissue architecture more accurately than 2D cultures. Herein, we describe a prototype of scaffold-free human iPSC-based 3D human neuronal platforms in 96-well plates. To test their suitability for drug screening, 3D neuronal cultures were infected with Herpes Simplex Virus, type 1 (HSV-1) with/without acyclovir. The IC50 of acyclovir, determined using both flow cytometry (FC) and the CX7 High Content Screening (HCS) platform (Thermo Fisher Scientific, Inc) were 3.14 ?M and 3.12?M, respectively, and differed from earlier estimate using 2D cultures. Our 3D human neuronal cultures, along with a novel confocal-based HCS platform (CX7) provide an unprecedented opportunity for drug screening programs for new therapies for CNS infections.
61	Sead Niksic	Physical Science and Engineering	Eye Tracking Integration in Medical Data Visualization for Area of Interest Prediction	Sead Niksic; Kayhan Batmangelich, PhD; Andrew King, MS	Frequently, radiologists do not possess enough time to complete all their necessary duties. Spending hours manually parsing through scans from the previous day is costly, inefficient, and results in reduced accuracy of diagnoses. Machine Learning (ML) can automate part of this process and reduce their workload. However, most ML algorithms focus on constructing task specific predictions that require many expert annotations. Our research over the summer has the long term goal of predicting areas of interest (AOI) in medical scans, to improve the efficiency and accuracy of patient diagnoses. This will be accomplished by two systems. Firstly, a web application, to visualize medical image data in browser, will record eye tracking fixations (places your gaze holds) on the medical image. Secondly, these fixations will be ranked by importance (length of time) and fed into a neural network, which will assess doctors' logs and focus to predict AOI in future images. We are still developing the first system, focusing on improving the accuracy of our eye-tracking code in browser. To visualize medical images in browser, we use a JavaScript toolkit called AMI. Our eye-tracking data is obtained from a Tobii EyeX eye-tracker.
79	Rema Padman, PhD	Translational Life Science	The Wunderlich Project: Assessing the Risk of Postoperative Complications from Group-based Trajectory Modeling of Temperatures	Rema Padman, PhD; Jennifer Grant, MD; Moira McNulty, MD; Ari Robicsek, MD; Krista Kinnard, MS; Pravin Rao, MS; Daniel Nagin, PhD; Nirav Shah, MD, MPH	Fever is common in the postoperative setting and is frequently a normal physiologic response not indicative of an infection. Despite this, diagnostic evaluations are performed in more than half of febrile patients but reveal an infection in less than 20% of these patients. Postoperative fevers result in increased diagnostic testing, antibiotic usage and length of stay. These evaluations are significant and can result in decreased patient satisfaction, increased antimicrobial resistance, higher healthcare utilization and increased morbidity and mortality. This study investigates the application of group-based trajectory modeling to generate temperature curves of postoperative patients following similar progression of temperatures and potentially delineate patients at high risk of postoperative complications. We evaluated 5,494 unique patients who had elective knee arthroplasty between January 1, 2007, and December 31, 2013. Results indicate three distinct trajectories of post-operative temperatures that result in different rates of overall and specific complications. Complications were also found to cluster at different time points. With roughly 50 million inpatient surgeries in 2010 in the United States, improving clinicians' ability to target only those patients at highest risk of complications has the potential to improve patient safety, quality of care and value on a large scale.
41	Krithika Pennathur	New Research Tools and Techniques	Outcomes Following Surgical Resection for Large Cell Neuroendocrine Carcinoma of the Lung	Krithika Pennathur; Arjun Pennathur, MD; Omar Awais, DO; Neil A. Christie, MD; Ryan M. Levy, MD; Rodney J. Landreneau, MD; James D. Luketich, MD; Matthew J. Schuchert, MD	Introduction: Neuroendocrine carcinoma constitutes 15-17% of non-small cell lung cancers and exhibits a more aggressive biology characterized by increased local and distant recurrence rates. The primary aims for this study were to evaluate recurrence patterns following resection and to elucidate factors associated with recurrence risk. Methods: We performed a retrospective analysis evaluating recurrence patterns and survival rates in patients undergoing resection for clinical stage 1 pulmonary neuroendocrine carcinoma. The primary outcome variables included overall recurrence rates, recurrence-free survival, and overall survival. Survival estimates were performed utilizing the Kaplan-Meier method. Multivariate analysis was conducted via COX proportional hazards modeling. Results: Overall recurrence rates for lobectomy, segmentectomy and wedge resection were 18.2%, 26.1%, and 53.8%. Overall 5-year survival was 66%, 69%, and 30%, respectively. Wedge resection was associated with significantly worse recurrence-free survival compared to lobectomy (p=0.03) and segmentectomy (p=0.05). Multivariate analysis revealed that wedge resection was an independent predictor of increased recurrence risk (HR= 3.60; CI: 1.31, 9.82; p=0.01). Conclusions: Non-anatomic wedge resection is associated with increased recurrence rates following surgical resection of clinical stage I neuroendocrine carcinoma. This study supports the use of anatomic lung resection (lobectomy or segmentectomy) when resecting neuroendocrine lung tumors.
24	Vanessa Perez Silos, MSc	Basic Life Science	Evaluation of a Xeno-free Culture System for Differentiation of Human Adipose Derived Mesenchymal Stem Cells	Vanessa Perez, MSc; Hang Lin, PhD; Rocky S Tuan, PhD; Alberto Camacho, PhD; Lizeth A Fuentes, PhD	Human adipose derived mesenchymal stem cells (hADMSCs) are multipotent cells with the capacity to differentiate into multiple cell lineages, and represent a promising cell source for regenerative medicine. In vitro cell expansion is often required to achieve workable cell number and fetal bovine serum (FBS) is commonly used. However, the use of xenogeneic serum is associated risk of transmitting infectious agents and immunogenic effects. Recently, human serum (hSu) has been suggested as an alternative to replace the FBS, due to its availability and possibility for human pathogens testing before use. This study evaluated the effect of hSu in supporting the proliferation and differentiation of hADMSCs. hADMSCs were isolated from clinical lipoaspirate. We compared the effects of hSu and FBS on the proliferative and differentiation activities of hADMSCs, in vitro. Our results showed that hSu improves the in vitro proliferation and osteogenic differentiation of hADMSCs. The results suggest that hSu may represent a more supportive culture supplement for adult MSCs for culture expansion and maintenance of differentiation potential.

42	Luca Ponzoni, PhD	New Research Tools and Techniques	Structural Dynamics is a Determinant of the Functional Significance of Missense Variants	Luca Ponzoni, PhD; Ivet Bahar, PhD	Accurate evaluation of the effect of point mutations on protein function is essential to assessing the genesis and prognosis of many inherited diseases and cancer types. Currently, a wealth of computational tools has been developed for pathogenicity prediction of non-synonymous single-nucleotide polymorphisms (nsSNPs). Two major types of data are used to this aim: sequence conservation/evolution and structural properties. Here, we demonstrate in a systematic way that another determinant of the functional impact of missense variants is the protein's structural dynamics. Measurable improvement is shown in the predictive ability of pathogenicity analyses by taking into consideration the dynamical context and implications of the mutation. Our study suggests that the newly introduced class of descriptors may be used in conjunction with existing features to not only increase the prediction accuracy of the impact of variants on biological function, but also gain insights into the physical basis of the effect of missense variants.
80	Alina Quach	Translational Life Science	Neurocognitive Development of Error Monitoring and Risk for Substance Use	Alina Quach; Brenden Tervo-Clemmens; Tammy Chung, PhD; Beatriz Luna, PhD; Duncan B. Clark, MD, PhD	Previous research indicates that poor response inhibition and lower levels of brain activity supporting cognitive control are risk factors for substance use. In normative development, inhibitory control functions undergo progressive refinement through adolescence into adulthood. However, the relationship between neurocognitive development of response inhibition and risk factors for substance use has not been definitively determined. As part of the National Consortium on Adolescent Neurodevelopment and Alcohol study, an antisaccade task was administered during functional Magnetic Resonance Imaging acquisition at baseline (N= 125), two subsequent annual follow ups for healthy controls (CON, n = 61) and adolescents at risk for problematic alcohol use (n = 64), based on family substance use disorder history, externalizing symptoms (EXT, n = 34), or internalizing symptoms. The sample spanned adolescence and adulthood (mean age =16.94, sd = 2.61). We will present main effects and interactions regarding the relationships between age, antisaccade performance and blood oxygen level dependent activity in regions of interests supporting inhibitory control. Results suggest that inhibitory control impairments may be uniquely associated with externalizing risk. Specifically, externalizing symptoms in early adolescence may confer limitations in inhibitory control due to abnormalities in cognitive control brain systems that normalize with maturity.
81	Vineet Raghu	Translational Life Science	Scalable Causal Discovery of Latent Variable Models on Categorical and Continuous Data	Vineet K. Raghu; Joseph D. Ramsey, PhD; Alison Morris, MD, MS; Dimitrios V. Manatakis, PhD; Peter Spirtes, PhD; Panos K. Chrysanthis, PhD; Clark Glymour, PhD; Panayiotis V. Benos, PhD	Modern technologies allow large, complex biomedical datasets to be collected from patient cohorts. These datasets have both continuous and categorical data ("Mixed Data") and essential variables may be unobserved due to the complex nature of biomedical phenomena. Causal inference algorithms can identify important relationships from biomedical data; however, scalable causal inference over mixed data with unmeasured confounders is still an open problem. Despite recent advances into causal discovery strategies; no study exists that comprehensively compares these approaches in this setting. Here, we present a comparative study that compares the accuracy and efficiency of different strategies in large, mixed datasets with latent confounders. We experiment with two extensions of the Fast-Causal Inference (FCI) algorithm: a maximum probability search procedure we recently developed to identify causal orientations more accurately, and a strategy which quickly eliminates unlikely adjacencies to achieve scalability to high dimensional data. We demonstrate that these methods significantly outperform the state of the art in the field in achieving both accurate edge orientations and tractable run-time in simulation experiments on datasets with up to 500 variables. Finally, we demonstrate the usability of the best performing approach on real data by applying it to a biomedical dataset of HIV infected individuals.
82	Vijaya Priya Rama Vijayasarathy, MSHCPM	Translational Life Science	Statistical Modeling and Analysis of Chronic Disease Progression Using Electronic Health Record Data (EHR)	Vijaya Priya Rama Vijayasarathy; Rema Padman, PhD	According to the Centers for Disease Control and Prevention, chronic diseases account for approximately 75% of the aggregate healthcare spending per year in the US. Among the most complex, costly, and high mortality chronic illnesses, Chronic Kidney Disease (CKD) poses significant concerns in disease monitoring and management for both patients and providers. Tracking disease progression and identifying high-risk patients is a serious challenge that needs to be addressed for improving care delivery for this population. Leveraging the availability of a rich and unique 22-year clinical dataset extracted from the Electronic Health Record (EHR) of a community nephrology practice, we develop innovative, data-driven, statistical approaches to identify risk groups and analyze their CKD progression over many years. Early results using group-based trajectory models, applied to a key clinical marker of the disease, indicate five distinct trajectories of disease progression in this population, enabling risk stratification for targeted interventions. Furthermore, we extend the analysis using additional laboratory markers of multiple comorbidities and complications of CKD, adjusting for nonrandom attrition across the different groups, to profile important group characteristics and predict critical outcomes. These insights may empower patients and clinicians to better manage CKD progression, reduce costs, and improve quality of care delivery.
25	Patrick Rimple	Basic Life Science	40 Sequenced Bacteriophages Isolated on Arthrobacter Hosts	Patrick Rimple; Audrey Jonas; Gabrielle Giglietti; Megan Ulbrich; Johnathon Schiebel; Daniel Russell; Rebecca Garlena; Deborah Jacobs-Sera; Graham Hatfull, PhD	As the most abundant biological particles on earth, bacteriophages, viruses that infect bacteria, constitute a diverse and ever-changing population. Phage genomes are mosaic due to illegitimate recombination of genomic elements from other phages and hosts. Isolating and characterizing phages of different bacterial hosts expands our knowledge of phage diversity and evolution through genomic analysis. This work builds on data published by Klyczek, et. al. that described 46 Arthrobacter phages isolated on Arthrobacter sp. 21022, none of which infected any of 14 other Arthrobacter hosts. In this investigation, 71 phages were isolated from environmental samples on *A. globiformis* , *A. atrocyaneus* , and *A. sulfureus* . Plaque and virion morphologies, phage host range, and restriction enzyme digests revealed similarities and differences between the phages. So far, 33 phages display probable temperate phenotypes, producing turbid plaques due to phage DNA integration into the host genome, while 51 were found to infect at least one other Arthrobacter host. Preliminary genome annotation through bioinformatic analyses of nucleotide similarity and protein structure predictions will advance our understanding of the global phage population, creating opportunities for mechanistic application and genetic discovery.

43	Pierangeli Rodriguez	New Research Tools and Techniques	Binder Jet Additive Manufacturing of Dental Material from Cobalt-Chrome Alloy	Pierangeli Rodríguez; Amir Mostafaei; Markus Chmielus, PhD	Binder jet printing (BJP) holds distinctive promises among Additive manufacturing technologies due to its fast, low-cost manufacturing; stress-free structures with complex geometries. Interest in Co-Cr-Mo, as a biocompatible alloy with high specific strength, corrosion and heat resistance, rises to replace Ni-Cr dental materials that release toxic Ni-ions. The objective of this research was to understand how different sintering temperatures affect the porosity of BJP Co-Cr-Mo parts to improve microstructure and mechanical properties. Coupons were printed from gas-atomized Co-Cr-Mo powder using X1-Lab printer. After curing, parts were sintered at temperatures ranging from 1240 °C to 1380 °C with 20 °C increments for 2 h. Samples were cross-sectioned, mounted, grounded and polished for optical observations. Density and dimension changes were measured using Archimedes principle and ImageJ analysis of optical micrographs. Results showed that nearly fully-densified part (~ 99%) was achieved at 1380 °C, as practically no pores remained and grain boundaries were filled with precipitate. Pore interconnection decreased when sintered from higher that 1340 °C, and pore size increased at 1360 °C due to pore coarsening. Vickers microhardness tests on the cross-section of sample revealed an increasing trend as the sintering temperature increased, reaching a maximum of 295.2 HV0.1 at 1380 °C.
26	Paige Rudich	Basic Life Science	Dissecting the Toxic Effects of Peptide Byproducts of Repeat Expansions in Neurodegenerative Diseases	Paige Rudich, Carley Snoznik, Todd Lamitina, PhD	Expanded GC-rich repeats cause many age-onset neurodegenerative diseases. These repeats can be translated without a start codon in all three reading frames, sense and antisense, through Repeat Associated non-ATG (RAN) Translation. RAN translation occurs in the C9orf72 repeat expansion, the most common genetic cause of Amyotrophic Lateral Sclerosis (ALS), and in mutations like the CAG repeat expansion in Huntington's Disease (HD). We created peptide-only models in *C. elegans* for both repeat expansions to better understand the mechanisms of RAN peptide toxicity in each disease. The two C9orf72 arginine-containing RAN dipeptides, Pro-Arg (PR) and Gly-Arg (GR), were toxic when expressed in muscle or motor neurons. Age-onset toxicity from PR (but not GR) could be delayed or quickened through genetic regulation of the insulin-ageing pathway. An RNAi screen of the worm genome found inhibition of proteasomal components suppressed PR toxicity. The HD RAN peptides (polyLeu/polyCys/polySer) were individually expressed in *C. elegans* muscles and neurons, and formed puncta. PolyLeu was toxic in both cell types. PolyCys and polySer aggregated and colocalized. None of the HD RAN products colocalized with polyGln aggregates. Understanding how the different RAN peptides interact and contribute to HD and ALS is vital for developing treatments for these diseases.
83	Johnathon Schiebel	Translational Life Science	Investigating Tumor Immune Microenvironment in Esophageal Adenocarcinoma Progression	Johnathon Schiebel; Derek Nancarrow, PhD; Kiran Lagisetty, MD; David Beer, PhD	Esophageal adenocarcinoma (EAC) is among the most rapidly increasing types of cancer in the United States despite new therapies. There is a distinct pathological progression from the tissue metaplasia Barrett's Esophagus (BE) to low-grade dysplasia, high-grade dysplasia and finally EAC. Immune blockade therapies represent a novel method to potentially treat EAC, however, little is known about the tumor immune cell microenvironment and the immune profile of BE-EAC tissue progression. In this study, RNA sequencing data from BE-EAC tissue progression and EAC tumors was used to determine expression levels of immune checkpoint pathway markers PD-1, PD-L1, CTLA-4, and TIGIT. This data was also used to predict immune cell composition in both progression and tumor tissue using the bioinformatic program XCell. Results show increases in immune checkpoint pathway markers throughout BE progression to EAC tumors, as well as a predicted increase in suppressive T regulatory lymphocytes. Tissue microarrays of EACs were immunohistochemically stained to verify the presence of immune checkpoint pathway markers and determine their location in the tumor microenvironment. In many samples, the tumor cells in addition to immune cells displayed one or more of the checkpoint markers, suggesting a subset of EAC patients may benefit from immune blockade therapy.
27	Lukas Schimunek	Basic Life Science	Novel Single Nucleotide Polymorphisms (SNPS) Associated with Clinical Complications and Altered TH17 Responses in High-severity Blunt Trauma	Lukas Schimunek, Rami A. Namas, Dongmei Liu, Jinling Yin, Ruben Zamora, Timothy R. Billiar, Yoram Vodovotz	Background: Trauma is a leading cause of morbidity and mortality. Genomic differences have been associated with varying post-trauma outcomes. The ability of SNPs to predict outcomes is undefined. We hypothesized that specific SNP haplotypes could prognosticate patient outcomes; a genome-wide analysis was conducted by comparing SNPs of trauma survivors (S) vs. non-survivors (NS). Methods: 397 obtained patient genomic DNA samples were examined for 551,839 SNPs. Of these, 13 patients were NS. They were matched algorithmically (SPSS) for injury severity score (ISS), age, and gender ratio with 13S. Homozygous and heterozygous allele frequencies for each SNP genotype were compared between matched groups. SNPs in NS were further compared to SNPs in 371S. Results: The comparison yielded a final total of 7 SNPs that distinguished survivors from non-survivors. Severely injured survivors with the same seven SNPs as non-survivor exhibited distinct inflammatory responses from similarly injured survivors without those SNPs, and specifically had evidence of altered Th17 phenotypes. High-severity MPPED2 AA patients exhibited clinical complications compared to high-severity MPPED2 AB+BB patients. Conclusions: We suggest an interaction between genetic polymorphism, injury severity, and initial inflammatory responses in driving trauma outcomes. Especially the AA genotype of MPPED2 may predispose high-severity trauma patients to poor outcomes.

THURSDAY, 1 P.M. SESSION
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45	Samantha Schloder	New Research Tools and Techniques	Density Variation in Additively Manufactured TI-6AL-4V	Samantha Schloder; Erica Stevens; David Schmidt, PhD; Markus Chmielus, PhD	Powder bed binder jet printing is a metal additive manufacturing process where a three-dimensionally modeled design can be made by adding a binder to the powder of each stacked layer, thus, producing a green part in a complex shape. This process makes a part that is loosely held together by the binder and requires further processing to increase strength and density. How a green part is bound together before post-processing will greatly affect the microstructure of the finished product and, thus, the mechanical properties as well. In this research study, Ti-6Al-4V, was 3D-printed using powder bed binder jet printing then sintered in post-processing. The uniformity of the densification was examined. There are two clear trends seen that result from powder bed binder jet printing and affect the density of the final part. The first is the less dense area along the outside edges while the second is how the curve is relatively denser than the rest of the sample. There are three potential reasons for this variation in density: a variation in sintering temperature and, therefore, densification kinetics during sintering, variations in the powder spreading, and variation in the binder density.
62	Catherine Smith	Physical Science and Engineering	Biomaterial Repair of the Rat Supraspinatus Tendon Enthesis	Catherine Smith, BS; Gerald Ferrer, BS; Joao Novaretti, MD; Benjamin Rothrauff, MS; Rocky Tuan, PhD; Volker Musahl, MD; Richard Debski, PhD	Though surgical repair of small rotator cuff tears has been clinically successful, there is up to a 94% re-tear rate with larger tears. Re-tear rates may result from poor healing capacity of the rotator cuff enthesis. This study assessed effects of different biomaterials (fibrin, GelMA, ADSCs and TGFβ) alone and in combination on the tensile properties of healing rat supraspinatus tendons. Rat humeri (following full-thickness transection of the supraspinatus and infraspinatus post 4 weeks healing) were mounted in a materials testing machine. The experimental protocol consisted of a preload, preconditioning and load-to-failure tests. Structural properties were determined from the load-elongation curve. Treatment groups utilizing GelMA had a failure rate at the enthesis of 43.2% while groups using fibrin failed at the enthesis 23.4% of the time. No differences between treatment groups were found for any structural properties. Fibrin may strengthen the enthesis better than GelMA due to its lower enthesis failure rate. Chronic tears were weaker than acute tears in terms of having a lower ultimate load. The results indicate that the biomaterials used can restore the site of injury to a similar degree.
84	Lindsey Snyder, PhD	Translational Life Science	LifeX: An Accelerator and Investment Fund to Drive Public Health Impact	Lindsey Snyder, PhD; Donald Burke, MD; Dietrich A. Stephan, PhD	The Graduate School of Public Health has decided that part of its mission is to positively impact the health and wellness of the global population by bringing its innovation to market. To do so, a new infrastructure, expertise and capital sources has been developed and will launch in late 2017. This includes an accelerator which can incubate new companies that have spun off from the University that have identified large unmet public health needs, and have promising technology that have the potential to make a large impact in extending the healthy lifespan. The accelerator will provide wet and dry lab space with equipment that is accessible to accelerator companies so they can build value in a capital efficient manner. In addition, the accelerator will have resident experts who can provide management expertise to each company – filing a major operational gap. The accelerator will also have a Seed Fund that can provide up to $500,000 in equity financing to approximately 10 companies per year. Finally, over the next 18-24 months, LifeX plans to raise a biotechnology venture fund scoped at $250m, to make up to 25 investments in population and consumer health companies and also biopharmaceuticals, diagnostics, and devices.
31	Stanley Tsou	Basic Life Science	Examining Compounds that Inhibit Reactive Oxygen Species-mediated Damage Repair at Transcriptionally Active Sites	Stanley Tsou; Hao Chen; Li Lan, MD, PhD	Generated by endogenous metabolism and exogenous factors, reactive oxygen species (ROS) can cause multiple forms of DNA damage including single-strand breaks (SSBs), double-strand breaks (DSBs), and damages on nucleotide bases. In particular, transcriptionally active sites are more susceptible to ROS damage, resulting in instability at coding regions, and further leading to potential mutations and tumorigenesis. In previous studies, we have developed a DNA Damage At RNA Transcription sites (DART) system by fusing KillerRed (KR), a light-stimulated ROS-inducer, to a transcription activator (TA). With this system, we are able to screen the factors that are specifically recruited to DNA damage at actively transcribed sites. Our objective is to evaluate the effects of different compounds in inhibiting the damage response of the target protein using DART assay and fluorescent microscopy. We examined seven chemically synthesized inhibitors designed for our target protein and identified that N2-58-R1 exhibited a significant inhibiting effect. In addition, based on the cell viability assay, its cell toxicity is low relative to other screened compounds. These results provide us a new approach to assess the effects of inhibitors for their targets and may be used for early stage tests for drug selections with potential clinical applications in the future.
46	Fuchiang Tsui, PhD	New Research Tools and Techniques	Detection of Twitter Users with Depression	Fuchiang Tsui, PhD; Pei-Han Kuan, MS; Ling-Yun Shi, MS	Background: Depression is a critical mental disorder in the U.S., which affects 80 million people and costs $70+ billion annually. With 328 million monthly active users generating 500 million tweets per day in 2017, Twitter provides a potential channel for depression surveillance. We applied machine learning algorithms in a pilot study to identify Twitter users with depression. Methods: We collected 764,208 total tweets from randomely selected 610 twitter users between March 23, 2015 and October 1, 2016. Collected data included tweet text, tweet location, user profiles, and time-specific weather data. We defined a depression case as a user who reported his/her clinical depression in a tweet. The dataset comprised 373,746 tweets from 232 cases and 390,462 tweets from 378 controls within a year. We identified 3 categories of features: (1) tweet statistics, e.g., total number of tweets, average weekday tweets, nighttime tweet ratios, (2) sentiment statistics; and (3) weather data. We used 10-fold cross-validation to compare nine machine learning algorithms. Results We found that random forest had the best performance: area under ROC curve of 0.86 and accuracy of 81.6%. Conclusion: We demonstrated machine learning and sentiment analysis can be applied to Twitter data to successfully detect users with depression.

85	Andrew Warburton	Translational Life Science	A Guilt-by-Association Model to Determine lncRNA Expression in METABRIC from TCGA and Patient Survivability	Andrew Warburton; David Boone, PhD	An increasing number of long noncoding RNAs (lncRNAs) have been found to play key roles and provide new biomarkers in mammary tumor development. Testing one lncRNA is extremely laborious and expensive. We aimed to design in-silico guilt-by-association (GBA) model using two datasets: the TCGA data and the METABRIC dataset. The TCGA dataset provides excellent genomic data, but only short-term follow-up on patients whereas the METABRIC dataset provides poor genomic data but excellent long-term clinical data. We used logistical regression of known protein-coding genes (ERBB2, ESR1, etc.) to calibrate our GBA model and contract correlational matrices of TCGA and METABRIC datasets. To build relative survivability models and Kaplan-Meier curves, ssGSEA projections were used to find correlational patterns between lncRNAs and protein-coding genes. Various correlational cutoffs and gene minimum cutoffs were set. Over 120,000 permutations were analyzed using the HTC cluster. Higher gene cutoffs over higher correlational cutoffs seem to yield more accurate results with fewer false positives. Once an optimal correlational and gene minimum cutoff is found, the most significantly correlated lncRNAs will be tested in the lab to verify the in-silico model in-vitro.
86	Li Wen	Translational Life Science	Novel Calcineurin Inhibitor Strategies to Prevent Radiocontrast-induced Organ Injury Using the Pancreas as a Prototypic Organ	Li Wen, MD, PhD; Tanveer Javed, MSc; Sohail Husain, MD	Radiocontrast agents are used in a multitude of imaging procedures. However, a major problem is that radiocontrast exposure can induce debilitating end organ injury. The goal of our studies is to devise effective preventatives for radiocontrast injury. In the current work, we focused on pancreatitis resulting from radiocontrast exposure to the pancreas during ERCP. In further preliminary studies, we extended the work to studying radiocontrast-induced nephropathy. A recent proof-of-concept discovery from our laboratory is that radiocontrast exposure in models of post-ERCP pancreatitis (PEP) induces the activation of the calcium-activated phosphatase calcineurin, specifically within the pancreatic acinar cell. To further translate this finding, we first examined whether co-administration of calcineurin inhibitors with the ERCP radiocontrast could effectively target pancreatic calcineurin. In a mouse model of PEP, we found that a novel combination of the calcineurin inhibitor FK506 (1 μM), along with the radiocontrast iohexol, prevented post-ERCP pancreatitis by 61% ($P < 0.05$; n=5). We also examined whether the calcineurin inhibitors could prevent radiocontrast-induced nephropathy and found that FK506 pretreatment prevented early radiocontrast-induced inflammatory change in tubular kidney cell lines. Overall, we believe that ongoing optimization to target calcineurin will yield novel and effective strategies for preventing the problem of radiocontrast-induced injury.
47	Maribeth Wesesky	Basic Life Science	Asymptomatic HSV-1 Infection is Associated with Dysfunctional Emotion Discrimination and it Improves with Valacyclovir Treatment	Maribeth Wesesky, Triptish Bhatia, Joel Wood, Satish Iyengar, Sreelatha Narayanan, Konasale Prasad, Kehui Chen, Robert Yolken, Faith Dickerson, Ruben Gur, Raquel Gur, Smita Deshpande, Vishwajit Nimgaonkar	Background: In the vast majority, herpes simplex virus, type 1 (HSV-1) is asymptomatic, with lifelong latent infection in neurons; it rarely causes encephalitis. HSV-1 infected individuals have greater cognitive dysfunction than uninfected individuals, particularly persons with schizophrenia – without encephalitis. We investigated whether HSV-1 related cognitive dysfunction is progressive or remediable. Methods: In a prospective naturalistic follow up sample (PNFU), temporal changes in cognitive functions were analyzed in relation to baseline HSV-1 infection in persons with/without schizophrenia (N=226). In a randomized controlled trial (RCT), HSV-1 infected, clinically stabilized SZ outpatients received Valacyclovir (VAL) or placebo (PLA) added to standard antipsychotic treatment (N=67). HSV-1 infection (seropositivity) was estimated using serum IgG antibodies. Clinical evaluations were blinded to HSV-1 or treatment status. Results: PNFU: At baseline, HSV-1 infected participants had significantly lower accuracy scores for Emotion Identification and Discrimination (EMOD), Spatial memory and Spatial ability, regardless of SZ diagnosis (p=0.025, 0.029, 0.046, respectively). They also had significantly steeper temporal worsening for EMOD (p=0.03). RCT: EMOD improved in VAL-treated patients (p=0.048, Cohen's d=0.43). Conclusions: Dysfunction in emotion discrimination is attributable to HSV-1 infection. HSV-1 infection could contribute to age related decline in emotion discrimination in the population.
32	Nan Wu	Basic Life Science	Computational Chemogenomics and Systems Pharmacology for Capaton Addiction	Nan Wu, Zhiwei Feng, Lirong Wang, Xiang-Qun (Sean) Xie	Captagon, a war drug with addiction, fuels the Syrian conflict! Captagon, also known as fenethylline in its generic name, is easy to be synthesized and has a larger CNS simulating effect than its metabolite, amphetamine. Terrorists used this drug to control their soldiers not to feel pain and be more aggressive. Moreover, it can generate revenues of millions of dollars, some of which was almost certainly used to fund weapons. However, the underlying mechanism of Captagon is still undisclosed. In the present work, we systematically analyzed the mechanism of addiction for Captagon and its metabolites (amphetamine and theophylline) using the system pharmacology methods. First, we found that amphetamine mainly targeted at several GPCRs, including TAAR1, dopamine receptor 1 (D1R) or dopamine receptor 2 (D2R), while theophylline is reported to be an antagonist of the Adenosine receptor. We reported the detailed interactions between amphetamine/theophylline and their targets. After analyzing the signaling pathway of these two metabolites, we found that Amphetamine will be the main cause of Captagon addiction. However, theophylline, an A2a antagonist, can attenuate the behavioral sensitization caused by Amphetamine. Meanwhile, we found that amphetamine can intentionally slow down theophylline's metabolism and elimination. Finally, we also carried out the off-targets prediction for amphetamine using our in-house tools (HTDocking and TargetHunter), which is related to the side effects such as hallucination of Captagon. All these results will help us better understanding of Captagon addiction and future drug abuse prevention.

48	Wenting Xie	Basic Life Science	Mitochondrial-Telomere ROS Cross-Talk in Parkinson's Disease	Wenting Xie; Qing Bai, PhD; April Dukes, PhD; Patricia Opresko, PhD; Bennet Van Houten, PhD; Marcel Bruchez, PhD; Edward A. Burton, DPhil	Mitochondrial reactive oxygen species (ROS) are regarded central to Parkinson's disease (PD) pathogenesis; however, the role of mitochondrial oxidative damage to telomeres is unknown. Recent evidence suggests that telomeric dysfunction can result in mitochondrial defects. We hypothesize that ROS cross-talk induced a self-perpetuating cycles of damage between telomeres and mitochondria that underlies neurodegeneration in PD. To test this, we generated transgenic zebrafish models in which we can uncouple telomeric and mitochondrial damage, in the relevant disease-susceptible dopaminergic neurons in vivo, using a novel chemoptogenetic ablation method. The method allows regulated generation of singlet oxygen in specific cellular locations. Since the effective range of the short-lived singlet oxygen is extremely small, this results in oxidative damage to surrounding cellular components with a remarkable organelle-level degree of spatial resolution, and with graded severity dictated by light dose. This new technology will enable us to test our hypothesis by inducing selective damage at mitochondria or telomeres, while measuring ROS flux and dysfunction at both sites. Our initial data provide proof of concept that we can induce both functional and morphological changes, both acutely and chronically, in mitochondria targeted by our novel chemoptogenetic approach in zebrafish neurons in vivo, resulting in neurological phenotypes.
49	Jiuyang Xu	Basic Life Science	Differential Pathogenesis of Human Metapneumovirus Clinical Isolates in Mouse Models	Jiuyang Xu; Yu Zhang, PhD; Sharon J. Tollefson; Saumendra N. Sardar, PhD; John F. Alcorn, PhD; Jieru Wang, MD, PhD; John V. Williams, MD	Human metapneumovirus (HMPV) is one of the leading causes of respiratory tract infection worldwide. The disease outcome ranges from asymptomatic infection to fatal pneumonia. HMPV has 4 genetic subgroups (A1, A2, B1, and B2) and multiple HMPV strains often co-circulate in a given season. The contribution of viral genetic diversity to pathogenesis is poorly understood. Currently, most published HMPV studies are limited to a few laboratory-adapted strains, mostly of a single subgroup. Here, we tested eight HMPV clinical isolates from different genetic subgroups in comparison to a laboratory reference strain TN/94-49 (A2) in an established C57BL/6 mouse model. Among them, the clinical isolates 1501 (A1), C2-202 (B1), and TN/91-320 (B2) induced significant weight loss and more severe lung histopathology compared to the laboratory strain. The high virulence was confirmed in BALB/c and DBA/2 mice. However, the amount of viral replication in mouse lungs did not correlate with disease severity. Significant higher pro-inflammatory cytokine production in lungs was associated with more severe disease. Our observations indicate that the severe disease caused by HMPV clinical isolates was due to exuberant immune response, which led to immuno-pathologic tissue damage. These data suggest that different HMPV strains engage with host immune mediators differently.
50	Chenxuan Yang	Basic Life Science	Notch Signaling Pathway Plays a Protective Role in Spleen against Apoptosis during Endotoxemia via TLR4/Myd88/iNOS/NO/TACE Pathway	Chenxuan Yang; Meihong Deng, MD; Melanie Scott, MD, PhD; Timothy R. Billiar, MD	Notch is a conserved transmembrane receptor well-known to regulate cell fate decisions. Recently, Notch signaling has been implicated in inflammation, yet its regulation and roles in sepsis are unknown. TNFα-converting enzyme (TACE/ADAM17) participates in cleavage and activation of Notch. We have previously shown that TACE is activated via the TLR4/MyD88/iNOS/NO pathway in hepatocytes. We hypothesized that Notch signaling is regulated by TLR4/Myd88/iNOS/NO/TACE pathway in spleen during endotoxemia. Notch signaling was activated in the spleen and in splenocytes by LPS in a time-dependent manner, indicated by increased notch intracellular domain (NICD) in western. The NICD levels peaked at 8 hours and 4 hours after LPS in spleen and in splenocytes, respectively. Inhibition of Notch activation using DAPT (5 mg/kg), 3 hours prior to LPS injection, resulted in a significantly increased level of cleaved-caspase-3, indicating more apoptosis. LPS-induced Notch activation was significantly lower in Myd88-/- and TLR4-/- mice as well as iNOS-/- after LPS challenge and this we associated with increased levels of cleaved-caspase3. Similar results were obtained in splenocytes treated with an iNOS inhibitor 1400w (2 uM) and TACE inhibitor. Notch activation was induced in splenocytes by SNAP (200 uM) as NO donor or directly by the cGMP analog 8-pCPT-cGMP(400 uM).
63	Yicheng Zhou	Physical Science and Engineering	Tuning Gold Nanoparticle Assemblies with a Family of Azobenzene Peptide Conjugates	Yicheng Zhou, Andrea D. Merg, Nathaniel L. Rosi	Azobenzene-incorporated peptide conjugates have been used to control the reversible assembly of gold nanoparticles. A series of peptide conjugates, Azo-(CH2)m-An-PEPAu (m = 1-3, n = 0-2), with varied hydrophobic and beta-sheet interactions were designed to systematically tune the assembly structure and control the reversibility behavior. By increasing the aliphatic spacer or alanine residues between azobenzene moiety and peptide section, gold nanoparticle assembly shifts from spherical to linear, and become less responsive to UV or visible light irradiation. The results provide new methods on dynamically control nanoparticle assembly via photo stimulus.