MARVELLOUS AKINLOTAN

The Impact of a Nurse Practitioner-led Home Visit Program on Emergency Department Super-Utilization: A Quality Improvement Project

Background
Low income, uninsured and Medicaid beneficiaries utilize the emergency department (ED) for ambulatory care sensitive chronic conditions at high rates. This quality improvement program evaluated the impact of a nurse practitioner-led home visit program on the reduction of avoidable ED visits for ambulatory care sensitive chronic conditions.

Objective of Quality Improvement Project
To reduce ED super-utilization for ambulatory care sensitive chronic conditions to from 5.47% to < 5.12 percent within a year among uninsured, low-income or Medicaid patients who visit a local hospital in Central Texas.

Methods
The value-based innovative home visit program was developed to address social determinants of health for the underserved population who are high utilizers for ambulatory care sensitive chronic conditions. Descriptive statistics were calculated for demographic characteristics, insurance status, chronic conditions, and ED visits. A paired sample T-test was conducted to compare the average number of monthly ED visits among participants in the year before enrollment in the home visit program with the monthly number of ED visits after enrollment (n=69).

Results
Sixty-nine patients were enrolled in the nurse practitioner designed and directed Home Visit Program by December 31st 2019. The nurse practitioner-led home visit program reduced ED utilization for ambulatory care sensitive chronic conditions in the target population to 5.04 percent by the completion of 2019, exceeding the program's goal metric. Patients enrolled in the program for approximately 3 months experienced the highest reduction in ED visits per month (pre-post difference=-0.52, 95% CI -0.79,-0.25). This was followed by those enrolled for about 2 months (pre-post difference -0.29, 95% CI -0.46, -0.12).

Conclusions
A nurse practitioner designed and directed home visit program was successful in reducing the percentage of ED visits related to ambulatory care sensitive conditions. Reducing avoidable ED utilization is a contribution nurse practitioners can make to improve the health of communities.

UMAIRBIN ASIM

Modeling the non-classical crystallographic slip in nanolayered ternary carbides

A family of ternary carbides and nitrides with nanolayered hexagonal crystal structure referred to as MAX phases, exhibit unique set of properties needed for high temperature applications. They are lightweight, stiff, thermodynamically stable and refractory, like ceramics, but damage tolerant, pseudo-ductile and machinable, like metals. Micropillar compression tests of select MAX phases have shown that these materials undergo non-classical crystallographic slip i.e. they violate the classical Schmid's law. Herein, we have developed a constitutive model within the continuum crystal plasticity framework to predict the non-classical crystallographic slip observed in the micropillar compression tests of MAX phases. The presentation will focus on the model and the results of the crystal plasticity finite element calculations elucidating the effect of non-classical crystallographic slip on the plastic deformation of MAX phases.

GAURAV BARANWAL

Impact of genetically augmented renal lymphangiogenesis in acute kidney injury

Acute kidney injury (AKI) is characterized by reduced renal function and increases the risk towards chronic kidney disease (CKD) progression. Not only the degree of the initial AKI inflammatory response, but also how well it resolves - both in time and in function - are likely factors dictating the potential for future CKD progression. Lymphatic vessels, and inflammation-associated lymphangiogenesis LAG, help to restore homeostasis following tissue injury. Any roles of lymphangiogenesis in AKI recovery/CKD progression are largely unknown. Our lab has recently characterized transgenic mice that overexpress the potently lymphangiogenic signal VEGF-D only in the kidney upon doxycycline administration. These conditional "KidVD" mice exhibit marked lymphangiogenesis throughout the kidney. To test if a kidney-specific increase in lymphatic density was protective in AKI we utilized KidVD mice in the well-characterized kidney bilateral ischemia reperfusion (I/R) model. We also crossed KidVD mice to the POD-ATTAC mouse line, a model of inducible podocyte apoptosis and proteinuria. When renal lymphangiogenesis was first induced on the KidVD mouse kidneys prior to injury, we found reduced expression of inflammatory cytokines and matrix fibrosis at 7 days post insult in both models. POD-ATTAC x KidVD mice demonstrated reduced interstitial fibrosis and reduced immune cell numbers 28 days following podocyte loss. Furthermore, KidVD mice demonstrate improved renal function measured by both glomerulus filtration rate (GFR) and urinary protein:creatinine ratios. Identifying the mechanisms by which renal lymphatics protect kidney function following injury, therefore, remains a continuing goal for identifying post-AKI risk and helping patients avoid AKI-to-CKD transition.

KELLY ANN CHURION

Staphylococcus aureus Fibronectin binding protein A (FnBPA) possesses more than one binding site in the minimal binding domain for human fibrinogen

The opportunistic pathogen Staphylococcus aureus (S. aureus) is highly human adaptive and has evolved to exploit host proteins to establish infections for survival. It is a highly versatile bacterium that is capable of causing a wide spectrum of diseases ranging from relatively benign skin infections to life threatening diseases including endocarditis, pneumonia and sepsis (Kristinsson, 1989; Lowy, 1998). In addition, it is also a major cause of infections associated with in dwelling medical devices, such as catheters and prostheses. The emergence of antibiotic-resistant strains presents significant therapeutic challenges and no vaccine is yet available to treat any of these types of infections. The development and establishment of disease relies on interactions between S. aureus proteins and host proteins. S. aureus produces a variety of microbial surface component recognizing adhesive matrix molecules (MSCRAMMs) such as fibronectin binding protein A (FnBPA) that enable the bacteria to colonize and multiply within the host. Host protein fibrinogen (Fg) is one of the major targets of S. aureus FnBPA given that this protein is found in abundance in blood plasma and is usually targeted for tissue adherence inititation, host cell invasion, and attachment to implanted materials. The site between FnBPA regions N2 and N3 located in the A domain (Foster 1995, Ganesh 2008), also termed trench binding region, interacts in particular to the C-terminal residues of the fibrinogen γ gamma chain via a dock-lock-latch like mechanism common to all Fg binding MSCRAMMs. Recently, it was found that in addition to its originally identified FgγC trench binding site, MSCRAMM ClfA A domain binds to another distinct site in fibrinogen. Since ClfA and FnBPA are structurally and functionally related MSCRAMMs, it is likely that FnBPA binding to Fg also involves a two-site mechanism. Using techniques such as surface plasma resonance (SPR) and isothermal titration calorimetry (ITC), we were able to determine that FnBPA possesses more than one binding site but different interacting residues when compared to ClfA. Due to the importance of FnBPA as a virulence factor, understanding the molecular mechanism of interaction with an important host protein [fibrinogen], is crucial to potentially explore vaccine candidate development.

JUGAL DAS

Improving the function of chimeric antigen receptor-modified T cells in cancer immunotherapy

Adoptive immunotherapy with chimeric antigen receptor-modified T (CAR-T) cells have heralded a new era in the treatment of difficult malignancies. However, a number of challenges still remain and limit the successful adoption of CAR-T based adoptive anti-cancer immunotherapy. Therefore, our research aims to identify effective strategies to augment the anti-cancer cytotoxicity and intra-tumoral persistence of the CAR-T cells.

Eukaryotic elongation factor-2 kinase (eEF-2K) is a conserved protein kinase, which associates multiple upstream signals with protein synthesis and cellular metabolism. eEF-2K is a highly unusual protein kinase that regulates protein

synthesis, and its expression/activity is up-regulated in inflammatory immune cells. It is crucial for the survival of stressed immune cells. For in-vivo adoptive immunotherapy, WT C57BL6 (B6) congenic Thy 1.1+ mice were subcutaneously injected with 1 x 106 MC32 tumor cells (carcinoembryonic antigen/CEA+) in the right flank followed by intravenous injection of WT anti-CEA CD8+CAR-T cells or eEF-2K KO anti-CEA CD8+CAR-T cells (Thy1.2+). All the mice were monitored for changes in tumor size and mortality until Day 28 post onset of tumor. The tumor infiltrating Thy1.2+ CD8+ lymphocytes were also quantified on Day 28. The functionality and mechanism of action of the Thy1.2+ CD8+ CAR-T cells were investigated, including their activation (CD69), cytokine production (IL-2, TNF- α, IL-6, IL-21, IL-7, IFN-γ) memory and effector T cell formation (CD62L).

Our results indicated that the loss of eEF-2K in murine CD8+ T cells significantly increases their early proliferation and metabolism, driving them towards premature senescence. The Thy1.2+ anti-CEA CD8+ CAR-T cells lacking eEF-2K had significantly lower IL-2, TNF- α and IFN-γ while having higher PD-1 expression.
Taken together, our results indicate that eEF-2K plays a crucial role in the activity of CAR-T cells in vivo; overexpression of eEF-2K in CAR-T cells could be explored as an effective anti-cancer vaccine strategy, which would improve CAR-T cell mediated anti-cancer efficacy.

JIACHEN DING

Modeling the optical properties of graupel, hailstone and snowflake with varied shapes and density

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Graupel, hailstone and snowflake are naturally formed in the terrestrial atmosphere. The microphysical properties (i.e., morphology) of these particles are determined by ice nucleation mechanism. The microphysical properties of these particles determine their optical properties. An accurate modeling of the graupel, hailstone and snowflake optical properties is fundamental to remote sensing of their microphysical properties as well as evaluation of their potential effect on the radiation budget involved in climate study. In this study, we use the state-of-the-art light scattering computational capabilities to model the optical properties of graupel, hailstone and snowflake with various particle shapes and bulk mass densities. The graupel, hailstone and snowflake have complicated shapes and morphologies. Their bulk mass densities usually vary from 0.05 g/cm3-0.89 g/cm3. We develop an algorithm to generate aggregate particles with a varying bulk mass density along with the bulk shapes based on in situ observations.

SHINSUKE FUJII

Tasting RNA as a nutrient -the conserved ability in the insect world

Many insects, especially in the order diptera, grow rapidly during the larval stage. We previously showed that ribonucleosides and RNA, in addition to proteins, carbohydrates and fat are essential macronutrients during this fast growth phase of fruit fly Drosophila melanogaster. Like other nutrients, RNA is detected by specific Gustatory receptors (Grs) in the taste organs of larvae, and we showed that a small Gr gene cluster, DmeGr28, is necessary and sufficient for RNA/ribonucleosides detection in D. melanogaster larvae. Interestingly, the six DmeGr28 genes are among the most conserved taste receptor genes in insects, homologues of which are found in genomes of mosquitos, ants, bees, beetles, cockroaches, fleas and termites.

Here, we demonstrate that larvae of blow flies and mosquitoes can sense and are attracted to RNA/ribonucleosides. Moreover, we show that the DmeGr28 homologues of the Yellow fever mosquito Aedes aegypti, AaeGr19a, when expressed in taste neurons of D. melanogaster larvae lacking the DmeGr28 gene cluster, can restore the appetitive taste behavior of larvae to RNA. These results indicate that the appetitive taste response to RNA/ribonucleosides is a conserved behavior in dipteran insects and is mediated by conserved Gr28 like receptors.

Flies and mosquitoes are transmitters of microbes that cause deadly human diseases, killing close to a million people each year and sickening hundreds of millions more. Likewise, many other insect species are agricultural pests, consuming crops and fruits and leading to famine in many parts of the world. Our findings provide a unique molecular target for the design of a novel class of pesticides to control the spread and growth of pest insect larvae.

DON HOOD

Automated Boulder Identification on the Martian Surface with MBARS

The Martian surface is littered with meter-scale boulders due to a long history of impact cratering and very little erosion to remove and transport boulders as we see on Earth. These boulders are an extremely important hazard for spacecraft operations, and assessing their locations and sizes is an important step in selecting landing sites. In addition to a hazard, boulders are a big scientific opportunity as patterns in their sizes and distributions can be used to understand a variety of surface processes on Mars. To understand their locations and sizes, these boulders are typically measured in high-resolution images by humans due to the underlying challenge of recognizing boulders in these images. We have created a system by which these boulders can be automatically identified and measured at a speed which outpaces manual measurement. The Mars Boulder Automatic Recognition System (MBARS) is a python-based open-source toolset to enable scientists to measure large populations of boulders on the Martian surface with relatively little coding expertise and reasonable computational resources. It has been shown to perform similarly to previous automated methods with less supervision and produces results that are useful to scientific investigation. Here we discuss the operation of MBARS as well as several areas of scientific investigation where it can be applied, enhancing existing studies of boulder populations with a larger sample size.

ANARGYROS KARAKALAS

Shape Memory Alloys: Enhancing a Smarter Everyday Life Potential

Shape Memory Alloys (SMAs) constitute a unique class of materials that exhibits characteristic behavioral aspects that are attributed to the diffusionless, solid-state transformation between two crystal structures, i.e., the low symmetry, low temperature Martensite and the high symmetry, high temperature Austenite. The transition between these two phases may be activated by application of a thermal, mechanical or thermo-mechanical stimulus and the resultant response is highly non-linear and hysteretic. Except for the energy dissipation related with the aforementioned hysteresis, the endothermic and exothermic reactions that take place during phase transformation render the response thermo-mechanically coupled. All the aforementioned characteristics give rise to unique phenomena that include, but are not limited to, one-way shape memory effect, pseudo-elasticity, partial transformation memory, transformation induced plasticity, tension-compression asymmetry etc. Efficient, high fidelity and robust constitutive modeling of these phenomena could render these materials a mainstream solution for actuation, damping and sensor state-of-the-art applications.

Since these materials are lightweight (compared with conventional systems), silent, spark-free, solid state, compact, may undergo high block forces or strains and are biocompatible they are already considered in various fields of science such as aerospace, automotive, bio-mechanics and bio-medical, wind energy, sports, naval, chemical, industrial, robotics engineering, oil and gas industry and much more. Recently, 4D printing of these materials opened a new perspective for their potential. Yet, even though there have been substantial contributions on the prediction of their behavior over the past few decades, still scientific community lacks a unified numerical tool that would be used in efficient design of SMA-entailing structures or products that unlock the full extent of their capabilities. To this end, the research presented aims towards developing unified, thermodynamically consistent constitutive models for SMAs that could promote these materials as viable solutions towards environmentally friendly, highly adaptable devices that enhance human standard of living.

MATTHEW KAY

Screening for alternative splicing in lncRNA Dleu2 in the mouse liver cell line AML-12

The long non coding RNA (lncRNA) Dleu2 has recently been demonstrated to be an active player in the progression of several cancers, including hepatocellular carcinoma. Dleu2 may play a role in modulating downstream cancerous effects due to alternative splicing of its multiple exons. However, how these alternative splicings of Dleu2 exons are generated is currently unknown. To envision how Dleu2 could be affected by alternative splicing, a series of alternative splicing primer sets were designed to investigate which transcripts were preferentially activated when Dleu2 was targeted for downregulation or upregulation. A specific Dleu2 siRNA which targeted an exon upstream of the tumor suppressor microRNA (miR-) miR-15a/miR-16 site significantly knocked down Dleu2 activity across all primer sets targeting alternative splicing transcripts in the mouse liver cell line, AML-12. Likewise, an application of 50 μM Resveratrol in 0.1% EtOH in complete media led to significant upregulation of Dleu2 in most alternative splicing transcripts. These results show that mouse AML-12 Dleu2 is capable of successful modulation across screenable alternative splicing transcripts, which could potentially lead to new approaches in Dleu2 diagnostics and regulation to prevent cancer.

QIAN LI

Multifunctional peptide-conjugated non-viral gene vector for dental pulp regeneration

Dental pulp, a highly vascularized tissue situated in an inextensible environment surrounded by rigid dentinal walls, receives blood supply solely from a small apical foramen (diameter < 1 mm) of the tooth root canal. Therefore, regeneration of pulp in the full-length tooth root has long been a challenge. Herein, we designed and synthesized a novel pH-sensitive multifunctional peptide conjugated non-viral gene vector to enhance the expression of vascular endothelial growth factor (VEGF) in human dental pulp stem cells (hDPSCs), and evaluated the efficiency and bioactivity of the angiogenic transfected hDPSCs in vitro. 2,3-Dimethylmaleic anhydride (DMA) was first introduced into poly(l-lysine) (PLL) because DMA becomes chemically dissociated under mild acidic conditions (pH 5.5-6.5) such as that found in endo/lysosome, which results in the formation of a strong cationic surface due to the PLL. Then multifunctional peptide C-R9-G-NLS-W was conjugated to polylysine (PLL) using click chemistry method. The multifunctional peptide-modified PLL encapsulated pVEGF plasmid using electrostatic interaction and formed gene complexes. Next, hDPSCs were transfected using the gene complexes. The cytotoxicity was reduced by the introduction of C-R9-G-NLS-W peptide. In addition, the internalization and nucleus accumulation, as well as transfection efficiency of peptide-modified gene complexes were higher than other groups. PCR analysis indicated that VEGF expression was significantly enhanced after hDPSCs were transfected with peptide-modified gene complexes. Furthermore, the conditioned medium of peptide-modified gene complexes transfected group enhanced endothelial cell migration and vascular-like tube formation, which means the increased VEGF in secretion of transfected hDPSC. In conclusion, the pH-sensitive peptide conjugated PLL is an effective non-viral vector for gene delivery and their gene complexes increased the VEGF secretion of hDPSC to enhance endothelial cell migration and vascular-like tube formation, further enhanced the revascularization in the process of pulp regeneration.

Support: This work was supported by NIH/NIDCR (DE024979)

KATHIRESH KUMAR KUMAR MANI

Repair of Ischemic Intestinal Epithelial Stem Cells: Potential Therapy to Improve Stroke Outcomes

Women's Health in Neuroscience Program, Department of Neuroscience and Experimental Therapeutics, Texas A&M University College of Medicine, Bryan, TX, United States of America

BACKGROUND: Nearly 50% of all stroke patients experience "leaky" gut, gut hemorrhage and gut epithelium damage. Gut leakiness may increase circulating inflammatory cytokines and other gut products such as endotoxins, which can impair stroke recovery. Here we tested whether transplantation of intestinal epithelial stem cells (IESC) after stroke may stimulate repair of gut structures and improve stroke outcomes.

METHODS: Reproductive senescent female Sprague–Dawley rats (12 months of age) were used for this study and assigned to the following groups: Control (no stroke); stroke with sham transplant (vehicle); stroke with IESC transplantation. Rats were subjected to stereotaxic surgery to occlude the left middle cerebral artery by using Endothelin(ET)1. Primary IECs were isolated from young female rats to prepare organoids cultures. Dissociated organoids were labeled with PKH26 and injected through iv at 4h/24h/48h after stroke. Behavioral assays and saphenous blood draws were performed pre-stroke and at 2d/4d after stroke. Trunk blood, brain tissue and a segment of small intestine was collected at termination and processed for the expression of the intestine epithelial stem cell marker (Lgr5+), cell homeostasis proteins (Na/K ATPase-α), proliferative markers (Ki67) and tight junction proteins.

RESULTS: Significant deterioration of the gut architecture was observed after stroke, including blunted or absent villi and irregular crypts. Animals that received organoid transplantation showed labeled cells incorporated in both the villus epithelial layer and within crypts. In these animals, villus structure was normal and no different from non-stroke controls. Stroke-induced mortality and infarct volume was reduced in MCAo+transplant animals. Sensory motor function assessed by adhesive removal test on the side contralateral to the infarction was severely impaired in the stroke/no transplant animals, but attenuated in the group that received organoid transplantation.

CONCLUSION: Data suggest that transplantation of IESC after stroke promotes repair of gut villus and crypts, and improves stroke outcomes

ZIRUI MAO

Optimal control of material microstructure

Many mechanical properties of materials are governed by the microstructure morphology. While general methods for controlling the evolution of material microstructure from an unstructured state to a final well-designed morphology are not available. We create a black-box feedback controller for the processing of designer materials by exploiting massively parallel, high-performance computing algorithm in order to explore some fundamental questions regarding the controllability of materials microstructure during processing. This numerical controller lies at the intersection of control theory, material modeling, and high-performance computation. The dynamics of materials microstructure evolution is simulated with Phase-Field Method, which can be controlled by selecting proper values, based on an optimal control algorithm, for two parameters in the phase-field model. We find that the proposed controller is able to give feasible controlling policy to attain desired microstructure state even for disturbance-containing systems. Currently, the model can only handle low-resolution material models due to the massive computation load. Next, we will develop the highly-efficient parallel code in order to handle high-resol

TETSUYA MIYAMOTO

Neuronal gluconeogenesis regulates glucose homeostasis via FMRFamide neuropeptide in Drosophila

Gluconeogenesis is a well-established metabolic process whereby glucose is generated from small carbon molecules in the liver and kidney, for the purpose to maintain blood glucose levels. Expression of gluconeogenic genes has been reported in other organs of mammals and insects, where their function is not yet known. In the fruit fly Drosophila melanogaster, one of the gluconeogenic genes, Glucose-6-Phosphatase (G6P) is exclusively expressed in a small number of neurons (G6P neurons) of the central nervous system.

Using a FRET-based glucose sensor, we demonstrated that G6P neurons are capable to carry out gluconeogenesis. We then showed that G6P mutant flies develop hypoglycemia within 24 hours. This phenotype can be mimicked by silencing of G6P neurons, and rescued by experimentally controlled activation in the absence of G6P. These results indicate that neural activity of G6P neurons, but not glucose production per se, is critical for glucose homeostasis. This idea is supported by the finding that neuronal gluconeogenesis promotes anterograde neuropeptide distribution from the soma to axon terminals, suggesting that the generation of glucose facilitates neuropeptide transport by an unknown mechanisms. G6P neurons consist of a heterogenous population of neuropeptide expressing cells, and we found that those expressing FMRFamide are necessary for glucose homeostasis. Taken together, our analysis has established that neuronal gluconeogenesis regulates glucose homeostasis via FMRFamide signaling in the fruit fly CNS."

MARION NACHON

Identify microbial biosignatures in aeolian environments using XRF analyses that simulate the PIXL instrument onboard the upcoming NASA Mars rover.

The objective of the upcoming NASA Mars 2020 mission (timed for launch in July 2020 and landing in February 2021) is to look for evidence of ancient life (“biosignatures”) on Mars, using the Perseverance rover. Should life have emerged on Mars, it might have been similar to the early terrestrial forms of microbial life, and potential microbial biosignatures might have been preserved in the geological record of Mars.

What to look for and where to look for, when searching for signs that ancient microbial life once existed? On Earth, microbial biosignatures have been extensively studied in modern and ancient lakes and deltas. In contrast, aeolian environments (sand dunes) have received little attention. However, on Earth, sandy deposits belong to the oldest sediments preserved in the geological record. And on Mars, sandstones have been detected by rovers. Sandy environments such as aeolian dunes thus represent potential targets of interest for biosignatures across the Solar System, both in the ancient and the modern geological record.

In this work, we perform micro-XRF (X-ray fluorescence) analyses that are analogous to those of the PIXL instrument (Planetary Instrument for X-ray Lithochemistry) onboard the Perseverance rover. Coupled to a high-resolution imager, we examine the fine scale chemical variations of modern and ancient wet aeolian deposits (that we collected respectively in Texas and in Utah) and of the microbial mats biosignatures they contain.

NICOLA OOSTHUIZEN

Presynchronization and delayed fixed-time artificial insemination increases pregnancy rates with sex-sorted semen in replacement beef heifers

To determine effects of presynchronization and delayed fixed-time artificial insemination (TAI) on pregnancy rates to TAI (PR/AI) with sex-sorted semen, 2,855 Bos taurus beef heifers were enrolled in a completely randomized design. Within location, heifers were randomly assigned to one of eight treatments: 1 and 2), heifers were exposed to the 7-d CO-Synch+CIDR protocol wherein they received gonadotropin-releasing hormone (GnRH) and a CIDR insert on day 0, prostaglandin F2α (PGF) upon CIDR removal on day 7, and were TAI 54±2 hours later with conventional (CTRL54-CNV; n=359) or sex-sorted semen (CTRL54-SEX; n=356); 3 and 4), same as CTRL54 but were TAI at 72±2 hours with conventional (CTRL72-CNV; n=366) or sex-sorted semen (CTRL72-SEX; n=360); 5 and 6), same as CTRL54 but also received PGF 7 days prior to initial injection of GnRH (day -7) and were then TAI with conventional (PRE54-CNV; n=355) or sex-sorted semen (PRE54-SEX; n=353); 7 and 8), same as PRE54 but had TAI delayed to 72±2 hours and were inseminated with conventional (PRE72-CNV; n=351) or sex-sorted semen (PRE72-SEX; n=355). All heifers received estrus detection patches on day 7, which were evaluated for activation at TAI. Ultrasonography was performed 30-45 days after TAI to determine PR/AI. Estrus expression was greater ($P<0.01$) in the CTRL72 heifers compared to CTRL54, PRE54, and PRE72 heifers (73.0 vs 55.4, 43.4, and 65.7%, respectively). Moreover, estrus expression was greater ($P<0.01$) in PRE72 heifers compared to CTRL54 and PRE54 heifers. Within treatment pairs, PR/AI were greater ($P\leq0.04$) when conventional semen was utilized compared to sex-sorted semen. Furthermore, PR/AI were greater ($P=0.02$) in PRE72-SEX heifers than CTRL54-SEX heifers (46.1 vs. 36.9%). No difference ($P=0.20$) was determined in PR/AI between CTRL54-CNV and PRE72-SEX heifers (50.4 vs. 46.1%). In conclusion, presynchronization in combination with delayed TAI increased estrus expression and PR/AI with sex-sorted semen in replacement beef heifers.

Keywords: delayed fixed-time artificial insemination, presynchronization, beef heifers, sexed semen.

JOLENE RAMSEY

A bacterial virus uses a protein leash on explosive cell lysis

Bacteriophages, or phages, are the viruses of bacteria, and the most abundant biological entity on the planet. Phages infect specific host bacterial cells, subvert the cellular system to co-opt resources for replication, then release progeny virions in an explosive event called lysis. Lysis resulting from virulent phage infection turns over a significant proportion of earth's bacterial biomass every day, influencing important biogeochemical cycles. The visually striking and devastating escape process is carefully orchestrated and timed by the invading phage at the molecular level. Specific phage protein are dedicated to overcoming the three topological barriers between assembled particles in the cytoplasm and the extracellular milieu. Paradigms for phage lysis were developed studying a few model phages for over a half-century, which suggested that three classes of proteins, one targeting each cell layer, described the scope of lysis mechanisms. However, we here demonstrate that even among well-studied model phages of Escherichia coli, there are new insights about phage lysis control to be realized. In phage Mu, we identified all the expected proteins needed to accomplish lysis, but were surprised to discover an additional required protein acting as a molecular leash on one of the canonical essential lysis proteins. Using microscopy, molecular techniques, and bioinformatics we have probed the basis of this control mechanism, as well as its conservation among phages. This analysis challenges the leading models in the field and allows us to explore additional evolutionary relationships. Besides establishing a new type of regulation for lysis caused by phages, the Mu system could be a powerful genetic tool for studying protein-protein interactions within the energized cell membrane.

DHARMANAND RAVIRAJAN

Structural and Biochemical Investigations on Fibrinogen Binding Surface Proteins of Staphylococci

Staphylococcus aureus (S.aureus), is a commensal bacterium that resides in the anterior nares of humans. It causes opportunistic infections ranging from soft skin infections to life threatening infections such as bacteremia, sepsis and infective endocarditis. S.aureus is notorious in acquiring drug resistance against multiple antibiotics and currently there is no vaccine or antibiotics for the treatment of life threatening S.aureus infections. In the US alone about 100,000 individuals are affected by methicillin resistant S. aureus (MRSA) associated invasive infections resulting in about 20,000 deaths. Recently, the CDC estimated one in five pathogens causing hospital infections are associated with multidrug resistant strain (MDR) (22).

S. aureus has long been known to form clumps in the presence of blood plasma, mainly caused by the surface proteins called 'MSCRAMMS' that is known to interact with plasma fibrinogen (26). Of these MSCRAMM proteins, Clumping factor-A (ClfA), an MSCRAMM, as the single most important contributor for the sepsis.
Currently, the complete structural details of ClfA:Fg interactions is not available except the crystal structure of ClfA in complex with a synthetic peptide derivative that mimics a partial Fg binding site. Understanding the complete binding interface of ClfA:Fg is pivotal for developing ClfA inhibitors that potentially be useful in treatment of S.aureus infections and effective vaccine design.

In order to understand the ClfA:Fg interactions, we have successfully crystallized the N2N3 subdomain of ClfA (~36kDa) in complex with the Fragment-D of Fibrinogen, a ~86kDa. The high resolution structure clearly exposed the critical residues present in the binding interface of ClfA & FgD. Using the ClfA/FgD crystal structure, we have also observed similar Fg binding interfaces present in other staphylococcal surface proteins, like Fbl (S.lugdunensis) and SpsD (S.pseudintermedius) that share ~60% & ~40% sequence similarity to ClfA.

MARIE SOUTHERLAND

Antimicrobial activity and novel formulation of silver containing non-steroidal anti-inflammatory drugs

Cystic fibrosis (CF) patients suffer from both chronic lung infections and airway inflammation. This inflammation, which precedes and is exacerbated by the lung infections, leads to irreparable tissue damage in the lungs. Combating both infections and inflammation has become a focus in treating CF. Thus, it would be advantageous to develop a new therapeutic that can simultaneously treat these two prevalent issues. The anti-inflammatory, ibuprofen, has been transformed into an efficacious dual therapeutic for this purpose by the synthesis of its silver salt (AgIBU). After stimulating a human bronchial epithelial cell line with lipopolysaccharide, treatment with ibuprofen, silver acetate, or AgIBU demonstrated that all three compounds had anti-inflammatory activity, and that AgIBU was the most potent. The antimicrobial activity of AgIBU has been evaluated against several Pseudomonas aeruginosa isolates including multi-drug resistant (MDR) isolates from CF patients using standard CLSI protocols. AgIBU has an MIC90 of 4 μg/mL and an MBC90 of 4 μg/mL, which is comparable to the activity of standard-of-care antibiotics against sensitive isolates. In addition, silver complexes of other common non-steroidal anti-inflammatory drugs (NSAIDs), naproxen and acetylsalicylic acid, have also been synthesized and evaluated for antimicrobial activity, displaying comparable MIC and MBC values (ranging from 4-8 μg/mL and 6-8 μg/mL, respectively). All three of these derivatives are highly lipophilic, with no appreciable aqueous solubility. In order to formulate these silver complexes without the use of DMSO, the excipient 2-hydroxypropyl-β-cyclodextrin has been employed to impart water solubility. Use of this excipient provides a stable solution that does not greatly alter in vitro antimicrobial activity compared to DMSO solutions. This family of silver-NSAID complexes represents a new class of anti-inflammatory and antimicrobial therapeutic options for CF patients.

CLAIRE STENHOUSE

FGF and Klotho Phosphate Regulatory Pathways Linking Placenta and Bone

Phosphate is essential for bone development and growth however little is known regarding the mechanisms of placental phosphate transport during pregnancy. This study sought to identify whether the phosphate regulatory pathways recently uncovered in the skeleton have roles in the ovine endometrium and placenta throughout gestation. On Days 9, 12, 17, 30, 70, 90, 110 or 125 of pregnancy, ewes were euthanized and hysterectomized. On Days 9-17, the uterine horns were flushed with PBS to recover conceptuses. Sections of conceptus tissue (Day 17), placentae and endometria were frozen in liquid nitrogen or fixed in 4% paraformaldehyde. Inorganic phosphate was detected spectrophotometrically in uterine flushes, allantoic and amniotic fluid, and homogenates of placentae and endometria. Concentrations of phosphate were influenced by gestational day in all samples except for amniotic fluid ($P<0.05$). Phosphate concentration was greater in placentae than endometria on Days 30, 70 and 90 ($P<0.05$). On Day 125, phosphate concentrations in the endometria were greater than placentae ($P<0.001$). Next, expression of mRNA for sodium-dependent phosphate transporters (SLC20A1 and SLC20A2) and klotho signaling pathway mediators (FGF21, FGF23, FGFR1, KL and KLB) were quantified by qPCR. Day 17 conceptuses expressed SLC20A1, SLC20A2, KLB, FGF21, FGF23 and FGFR1 mRNAs. Endometrial expression of FGFR1 ($P<0.001$) and FGF21 ($P<0.05$) mRNAs was highest on Day 30, as was KL mRNA (Days 30 and 110; $P<0.001$). Placental expression of KLB ($P=0.06$) and FGF21 ($P<0.05$) mRNAs increased between Days 110 and 125. Placental FGF23 mRNA expression increased with stage of gestation ($P<0.01$). Placental expression of FGFR1 mRNA was lowest at Day 90 and increased by Day 125 ($P=0.05$). SLC20A1 mRNA expression peaked at Day 30, before decreasing to Day 110 ($P<0.001$). These results indicate that phosphate and its transporters have dynamic expression throughout gestation, suggesting an important role for multiple phosphate regulatory pathways throughout gestation.

THERESA CHRISTINA SUTHERLAND

Age-Related Dysfunction of CNS Mitochondria May Impact the Age-Dependent Decline in Axon Growth Potential After Spinal Cord Injury

Spinal Cord Injury (SCI) places a significant and life-long burden on patients. The past decades have shown an important shift in the demographic population effected. In America the average age at injury has increased to ~43 years old and currently ~80% of all people with SCI are ≥40 years. This places great importance on understanding SCI in middle aged and aging populations. Experimentally, SCI is extensively modelled in young adult animals. This contrasts with the aging human SCI population and hampers the translation of research to clinical application. In recent years there has been significant progress made in understanding and manipulating axon growth after injury, however, our knowledge of how aging impacts axon growth in the central nervous system (CNS) is still lacking. The dynamics of axonal growth changes with age and impacts recovery from trauma.

Understanding the underlying mechanisms of an age-dependent decline in axon growth is critical for the development of therapies to stimulate repair in an aging population. One promising target we are examining is mitochondria. Mitochondria are essential to the sprouting and growth of new axons in the CNS, as well as calcium buffering and antioxidant balance. Aging has been associated with a decline in mitochondrial activity, whereas successful axon regeneration requires an increase in energy and mitochondrial dynamics. Using western blot, flow cytometry and immunocytochemistry we have observed changes in the OXPHOS machinery, the mitochondrial membrane potential and the expression of transmembrane transporters, respectively, between young (2-4 months) and aging (12-14 months) mice. Both normal aging and traumatic injury to the CNS are highly associated with mitochondrial dysfunction and oxidative stress, this poses a great challenge for an aging SCI population as the two elements can compound one another to subsequently worsen injury outcomes.

ADRIAN TINOCO NAJERA

Risk factors for urinary bacterial growth in dogs with congenital portosystemic shunts: 68 cases (1997-2019)

Objective: To identify prevalence and risk factors for urinary bacterial growth in dogs with congenital portosystemic shunts confirmed by abdominal ultrasound or scintigraphy on which a quantitative urine culture was performed.
Materials and Methods: Sixty-eight dogs were included in this retrospective cross-sectional study. Medical records from the Texas A&M University Veterinary Teaching Hospital were reviewed from 1997 through 2019. Variables of interest included age, sex, clinical signs, previous treatment, ultrasound abnormalities, chemistry abnormalities, and urinalysis abnormalities. Univariable and multivariable analyses were performed.

Results: The median age of the dogs was 1.5 years (range: 0.2 – 11). Ultrasound abnormalities (cystic calculi and echogenic debris) were reported in 61 dogs (89.7%). Urinalysis abnormalities included, pyuria in ten dogs (15%), bacteriuria in 13 dogs (20%), and haematuria in 28 dogs (42%). The median urine specific gravity was 1.021 (range: 1.004 – 1.052). Seventeen dogs (25%) had a positive quantitative urine culture. Significantly increased odds for a positive quantitative urine culture were reported for bacteriuria (OR, 120; 95% CI, 12.806 – 1124.46; P = <.0001), pyuria (OR, 6.4091; 95% CI, 1.574 – 26.657, P = 0.0098), and a pH >7.5 (OR, 0.1302; 95% CI, 0.0382 – 0.4436; P = 0.0011) respectively.

Clinical Significance: In this group of dogs, the prevalence of urinary bacterial growth was 25%. Bacteriuria, pyuria, and a pH > 7.5 were risk factors for having a positive quantitative urine culture.

ZE YIN

Ultrastable Plasmonic Bioink for Printable Point-of-care Biosensors

Point-of-care biosensors are critically important for early disease diagnosis for timely clinical intervention in resource-limited settings. The real-world application of these biosensors requires the use of stable biological reagents and cost-effective fabrication approaches. To meet these stringent requirements, we introduce a generic encapsulation strategy to realize ultrastable plasmonic bioink by encapsulating antibodies with organosiloxane

polymer through in situ polymerization. Plasmonic nanostructures serve as sensitive nanotransducers allowing for label-free biochemical detection. The plasmonic bioink with encapsulated antibodies exhibits excellent thermal, biological and colloidal stability that are compatible with printing process. As a proof-of-concept, we demonstrate the printability of the ultrastable plasmonic bioinks on different types of substrates with direct writing techniques. The organosiloxane polymer preserves the structure and biorecognition capabilities of the biosensors under harsh conditions, including elevated temperature, exposure to chemical/biological denaturants and ultrasonic agitation. Plasmonic biochips fabricated with the ultrastable ink exhibit superior stability compared to the biochips with unencapsulated antibodies.