Annual Medical Student Research Forum 2011

Friday, August 12th
10:00 am to 2:00 pm

Room 111 and the Atrium
Lee Med Building

Sanford School of Medicine
The University of South Dakota

414 East Clark Street, Vermillion, SD

Program and Abstracts

SANFORD SCHOOL OF MEDICINE
The University of South Dakota

Program Schedule

10:00-12:00 **Oral Presentations** (Lee Med Room 111)
Medical Summer Research Program participants

10:00-10:10	**Leslie Addengast:** The exposure of human alveolar epithelial cells to influenza virus increases adherence of *Streptococcus pyogenes*
10:10-10:20	**Sigurd (Sig) Hartnett:** The Role of Rab7 in the Autophagic-Lysosomal Pathway in Mouse Hearts
10:20-10:30	**Luke Hofkamp:** Analysis of the Distribution of Suppressor of Fused [SuFu] During The Cell Cycle
10:30-10:40	**Brian A. Juber:** Evaluation of a hexavalent Group A streptococcal vaccine (HEX-GAS) as a means to prevent influenza virus:*Streptococcus pyogenes* super-infections
10:40-10:50	**Jeb List:** Assessment of Chemical Irritants on the Leech: A New Animal Model to Study Chronic Pain
10:50-11:00	**Meredith Meyer:** Comparison of various signalling and cell death pathways in wild type and *Cln1*$^{-/-}$ neurons.
11:00-11:10	**Emily Reinbold:** CRF_2 receptor distribution in the brain and anxiety states during amphetamine withdrawal
11:10-11:20	**Austin Reno:** Development of GABAergic interneurons in a mouse model of Batten disease
11:20-11:30	**Phil Schneider:** Spleen is the site for antigenic priming of diabetogenic T cells during the early stage of T1D pathogenesis.
11:30-11:40	**Maria Tracy:** Antiprogestin Mifepristone and the Epithelial Mesenchymal Transition in Cancer cells
11:40-11:50	**Miranda Tracy:** Contribution of swine influenza gene segments toward virulence of influenza viruses
11:50-12:00	**Brian Westerhuis:** Development of a Novel Mouse Medulloblastoma Model to Study Tumor Cell Migration and Metastasis.

12:00-1:00 **Lunch & Poster Session** (Lee Med Atrium)
Posters presented by:
Scholarship Pathways Program
Sanford Program for Medical Student Research

1:00-2:00 **Keynote Address** (Lee Med Room 111)
Daniel G. Petereit, MD: Addressing Cancer Disparities Among American Indians Through Innovative Technologies and Patient Navigation: The Walking Forward Experience

Medical Student Research Program Abstracts

Oral Presentation, Lee Med Building Room 111

The exposure of human alveolar epithelial cells to influenza virus increases adherence of *Streptococcus pyogenes*

Leslie Addengast, Victor Huber, Ph D, and Michael Chausee, Ph D

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Background: Primary influenza infections increase individuals' susceptibility to bacterial respiratory pathogens. These secondary bacterial infections, often referred to as superinfections, account for many, if not most, deaths attributed to influenza. In the winter of 2010-11 the occurrence of *Streptococcus pyogenes* (group A Streptococcus, GAS) invasive infections (defined as the presence of the bacteria in a normally sterile site such as the lung) increased dramatically, possibly due to unusually high seasonal influenza activity. The infectious process is complex but adherence of the pathogen to host cells is considered a critical first step. We hypothesized that influenza infection may enhance the adherence of *S. pyogenes* to respiratory cells and thereby promote the establishment of a secondary bacterial infection.

Methods: To test this idea we designed an experiment to determine if the addition of influenza virus to adenocarcinomic human alveolar basal epithelial (A549) cells would increase the adherence of *S. pyogenes.* Various types of *S. pyogenes* were tested in the assay including MGAS315, a fully sequenced and clinically relevant strain, and a mutant derivative that lacked the transcription factor Rgg (*rgg*-), which is required for the expression of the virulence factor SpeB. Influenza A of the H3N2 subtype, isolated from the Hong Kong 68 pandemic, was chosen for use due to its highly virulent characteristics and commonality prior to the recent H1N1 pandemic.

Results: Data collected from our assay indicated that the addition of influenza virus to A549 cells resulted in an increase in the number of adherent MGAS315 cells (2.864- fold increase in cocci/A549 cell, 2.810- fold increase in the number of chains of cocci /A549 cell). An increase in the adherence of the *rgg*- mutant strain was also observed (2.125- fold increase in cocci/A549, 1.926- fold increase in chains of cocci/A549).

Conclusion: The consistent and substantial increase in attachment better characterizes the potential role that bacterial adherence may play in invasive and secondary infections. The clinical significance of these implications lies in the potential development of pharmaceuticals designed to inhibit these host cell - bacterial interactions, thereby effectively decreasing the associated morbidity and mortality rates linked to superinfections.

The Role of Rab7 in the Autophagic-Lysosomal Pathway in Mouse Hearts

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Background: Dysfunctions in the autophagic-lysosomal pathway were observed in the progression of many types of heart disease to congestive heart failure and their pathogenic roles have been suggested in clinical observations and are being actively investigated in experimental studies. Macroautophagy (commonly known as autophagy), a cellular process required for maintaining homeostasis, sequesters a portion of cytoplasm, including misfolded proteins and/or defective organelles, in a membrane bound compartment for lysosomal degradation. The fusion between autophagosomes and lysosomes is a critical step in the autophagic-lysosomal pathway but how the fusion is regulated remains poorly understood. A small G-protein, Rab7, has been purported to play a critical role in the fusion. To further elucidate the role of Rab7, the lab had created multiple wild type Rab7 (Rab7WT) and dominant negative Rab7 (Rab7DN) responder transgenic (tg) mouse lines. By design, these responder lines should not express a high level of the transgene unless they are coupled with a tetracycline-suppressible activator transgene (tTA). The aim of this summer project is to characterize the baseline tg protein expression in the responder mouse hearts in the presence or absence of tTA and to preliminarily examine their effects on cardiac function.

Methods: Rab7WT, Rab7DN, and tTA genotypes were determined using polymerase chain reaction (PCR). Genomic DNA extracts from mouse tissue samples were used for the PCR. At 6 weeks of age, the M-mode echocardiography (Echo) was performed. Subsequently, cardiac tissue was collected for western blots analyses of tg proteins. The tg Rab7 proteins contain an HA epitope tag, allowing them to be differentiated from endogenous Rab7.

Results: Western blot analyses for both Rab7 and the HA-tag revealed a modest level of tg expression in the heart of all 3 tested Rab7WT responder lines but, interestingly, not in any of the 3 tested Rab7DN responder lines, in the absence of tg tTA. The level of tg Rab7WT leaky overexpression ranged from 13% to 36% of the endogenous Rab7 protein level. Specifically, Rab7WT line 716 was identified to have the highest level of baseline expression of the tg protein in absence of tg tTA. Due to time restraint, only one Rab7DN responder line was analyzed for the tTA-activated tg expression. The result proves that the tTA-activated tg Rab7DN can be achieved in at least the responder line tested. Echo analyses on additional tg mice are needed to make a definitive conclusion on the impact of Rab7WT or Rab7DN tg expression on cardiac function.

Conclusions: This study has revealed that different levels of overexpression of Rab7WT were achieved in the Rab7WT responder lines, which will aid the laboratory in selecting mice for future breeding. No leaky expression was detected in the 3 tested Rab7DN responder lines, suggesting that these responders are well suited for inducible overexpression of Rab7DN in the heart.

Analysis of the Distribution of Suppressor of Fused [SuFu] During The Cell Cycle

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Background: One of the least understood features of the cell cycle is the formation and enrichment of proteins at the midbody, also known as the intracellular bridge. Depletion of midbody localized proteins results in defective midbody formation and/or cytokinesis. Suppressor of Fused [SuFu], a member of the Hedgehog [Hh] pathway is a significant target of current research due to its function as a negative regulator of the Hh signaling pathway. While SuFu is emerging as the dominant negative regulator of the Hh pathway, its role in the etiology of disease is only beginning to be understood. SuFu is known to localize to the primary cilium, cytoplasm and nucleus, and interacts with numerous proteins within the hedgehog pathway including the Gli transcription factors.

Methods: Primary prostate epithelial and stromal cells and multiple cells lines were grown in tissue culture to examine localization of SuFu in prostate epithelium *in vitro.* Following nocodazole synchronization to the formation of the midbody the cells were fixed using 4% paraformaldehyde (PFA) and SuFu and other Hh pathway components were localized using immunofluorescence and confocal microscopy. Cells were collected for western blot and co-immunoprecipitation (Co-IP) using a cell scraper, ice cold PBS and 1% PFA. Harvested cells were disrupted in a defined buffer prior to Co-IP and proteomic analysis.

Results: We have identified a consistent pattern of enrichment of SuFu at the midbody of cultured human prostate epithelial and stromal cells. The localization of SuFu to the midbody is independent of its known Hh binding partners. We have also identified other cell lines which demonstrate both positive and negative expression patterns of SuFu at the midbody. SiRNA mediated knockdown of SuFu in prostate and brain cancer cells resulted in a significant increase in proliferation as determined by increased Ki67 expression. We are currently optimizing conditions for Co-IP.

Conclusions: We postulate that the novel finding of SuFu in the midbody may represent a unique function of SuFu that is independent of its known function within the Hh pathway.

Evaluation of a hexavalent Group A streptococcal vaccine (HEX-GAS) as a means to prevent influenza virus:*Streptococcus pyogenes* super-infections

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Background: Secondary bacterial infections contribute significantly to the mortality associated with influenza virus. One of the causes of these secondary bacterial infections, group A streptococcus (GAS) shares a common seasonality with influenza virus. Pneumonia due to influenza virus:GAS super-infection contributed to the high death toll of the 1918-19 Spanish influenza pandemic, and many of the deaths in the 2009 H1N1 pandemic were also caused by GAS pneumonia. Although GAS only causes lower respiratory complications in about 11% of all invasive GAS infections, the mortality rate of GAS pneumonia is 38%. We hypothesize that vaccine-induced protection against invasive GAS bacterial infections will limit the lethality associated with influenza virus:GAS super-infections. An experimental, hexavalent GAS vaccine (HEX-GAS) was used in this study, and this vaccine is immunogenic to six different serotypes of the bacterial M-protein, a virulence factor of *S. pyogenes.* In this study, we quantify the murine humoral immune response to HEX-GAS and demonstrate its immunological role in protection against influenza:GAS super-infections.

Methods: Mice were inoculated with HEX-GAS vaccine to define its role in protection against influenza virus:GAS super-infection. Quaternary and quinternary sera were collected after inoculation with either HEX-GAS (n=28) or Alum control (n=28). Enzyme-linked immunosorbent assay (ELISA) was used to quantify the antibody response toward the M3 peptide of the HEX-GAS vaccine. The M3 serotype matches the M protein expressed by MGAS315, which is the bacterial strain used for challenge in our super-infection model. All mice were then challenged with 0.1 LD_{50} of influenza virus and a dose of MGAS315 bacteria (10^6, 10^5, 10^4, or 10^3 CFU/mL; n=7 mice for each dose) 7 days later. Morbidity was monitored by daily weight measurements and mortality was measured based on the number of surviving mice.

Results: Previous work with this vaccine indicated that an ELISA titer of 3200 was an adequate correlate of protective immunity against challenge with the bacteria alone. The quaternary antibody titers of HEX-GAS-vaccinated mice (mean=1619, s.d.=366.7) were boosted with a fifth dose of HEX-GAS, which raised the average quinternary titer (mean=4671, s.d.=876) to a sufficient level to test GAS vaccine efficacy within our super-infection model.

Conclusions: Antibody titer results demonstrate that five doses of HEX-GAS initiated a sufficient immunological response to test efficacy using an influenza virus:GAS super-infection model. Morbidity (weight loss) and mortality (survival) will be used to define overall vaccine efficacy.

Assessment of Chemical Irritants on the Leech: A New Animal Model to Study Chronic Pain

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Background: Chronic pain is a major health problem and is the most common symptom for which patients seek medical care in the United States. It results in an estimated $61 billion of lost productivity annually. Many of the pharmacological therapies used for pain management have undesirable properties (e.g. addiction and respiratory depression), thus efforts to develop new pain management strategies have begun. Understanding the mechanisms for how nociceptive signaling is modulated would facilitate the development of anti-nociceptive therapies to treat various chronic pain conditions. Transient Receptor Potential (TRP) channels detect nociceptive levels of thermal and mechanical stimuli and the activation of these receptors by chemical irritants will be the focus of this project.

The leech central nervous system (CNS) is well characterized in terms of identity of individual neurons, their function, and their synaptic connectivity. The identity of nociceptive and non-nociceptive sensory neurons and the synaptic targets of these afferent cells in the leech CNS is known in considerable detail. Thus, the leech is useful as a model system to study the modulation of pain. However, the sensitivity of these animals to chemical irritants known to activate various TRP channels is unknown. In these experiments, the ability of various TRP agonists to elicit a defensive withdrawal response in the leech was tested.

Methods: Each leech was placed in a Petri dish filled with wet moss for one hour to adjust to the room temperature. 0.1mL of ascending concentrations of various chemical irritants were applied to the posterior sucker. The defensive withdrawal response was recorded within 30 seconds of the drop and then the irritant was washed off. A 5-minute waiting period was used between each application.

Results: Capsaicin, a TRPV1 agonist, elicits a withdrawal response in a concentration dependent manner that was partially blocked when co-applied with 500 μM SB-366791, a TRPV1 antagonist. 2-APB, a TRPV2 agonist, also elicits a withdrawal response in a concentration dependent manner. Transilast (500 μM), a TRPV2 antagonist, actually potentiated the effects of 2-APB but the TRPV1 antagonist SB-366791 did partially block the effects of 2-APB. Mustard oil, a TRPA agonist, elicits a withdrawal response in a concentration dependent manner that was partially blocked by 500 μM HC-030031 (TRPA antagonist) or 500 μM SB-366791.

Conclusion: We found that nocifensive responses can be elicited in the leech by capsaicin, 2-APB, and mustard oil. Also, that these nocifensive responses can be partially blocked by corresponding and cross-reacting certain TRP antagonists. Further research will be on how nociceptive and non-nociceptive afferents respond to these compounds and to see if these compounds can be used to induce sensitization to mechanical and thermal stimuli.

Comparison of various signalling and cell death pathways in wild type and *Cln1*$^{-/-}$ neurons.

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Background: Neuronal ceroid lipofuscinoses (NCLs), also referred to as Batten Disease, are a group of recessively inherited, fatal lysosomal storage disorders characterized by intracellular accumulation of autofluorescent lipopigment and progressive neurodegeneration. NCLs primarily affect children and are caused by mutations in one of ten genes, *CLN1-10*.

Methods: This study investigates the mechanism by which *CLN1* gene affects the function and vulnerability of neurons in the *Cln1*-knockout mouse model of infantile NCL. Primary cerebellar granule cell cultures prepared from wild type and *Cln1*-knockout mice were exposed to various toxic insults in order to compare the function of various signalling and cell death pathways. Toxic insults include NMDA, t-PDC, MPP^+, NaN_3, and $ZnCl_2$. Cultured neurons were treated with toxins on the 14th and 21st days in vitro (DIV). Various concentrations of each toxin were used. Cultures were maintained in Neurobasal medium supplemented to include 2% B-27 serum replacement, 25 mM KCl, 0.5 mM glutamine, 100 U/ml penicillin, and 100 µg/ml streptomycin. A full culture medium change occurred 24 h after plating the cells, and half medium changes occurred on DIV 4, 7, 10, 14, and 17. Identification of potential anomalies could lead to the development of new therapeutic targets for NCLs.

Results: Results will be reported once obtained.

CRF_2 receptor distribution in the brain and anxiety states during amphetamine withdrawal

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Background: Humans and rats experiencing drug withdrawal from psychostimulants such as amphetamine (AMPH), show increased anxiety-like behaviors. These anxiety behaviors are normally initiated by corticotropin-releasing factor (CRF). Past studies suggest that the anxiety-like behavior experienced during drug withdrawal may result from an increase of CRF2 receptor activity and density in the dorsal raphe nucleus (dRN). Antisauvaguine-30 (ASV) is a CRF2 receptor antagonist and has been shown to reverse anxiety like states in drug naïve rats when given globally and during AMPH withdrawal when infused directly into the dRN. However, it is not known whether these effects are specific to CRF2 receptor antagonism in the dRN during drug withdrawal. Therefore, the effects of amphetamine withdrawal on CRF2 receptor levels in other brain regions mediating anxiety were determined, and the global effects of ASV in the brain during amphetamine withdrawal were tested.

Methods: Adult male Sprague-Dawley rats were either treated with AMPH (2.5mg/kg ip) or saline for 2 weeks, or went untreated, and then went through a two-week withdrawal period. Brains were collected from some of the rats (n = 10 per treatment group) for analysis of CRF2 receptor levels in the septum, hypothalamus and amygdala, using microdissection techniques and western blots. For the other rats (n = 6-8 per treatment group), an intracranial guide cannula was implanted and directed at the lateral ventricle during the withdrawal period. Rats were then acclimated to the handling process of intraventricular infusions. On the fourteenth day of the withdrawal period, rats were infused with 2µg ASV or vehicle into the ventricle before being tested for anxiety behavior on the elevated plus maze (EPM).

Results: Amphetamine pretreated rats infused with vehicle showed an increase of anxiety-like behaviors in the EPM compared to saline rats that received vehicle. Amphetamine pretreated rats that received ASV exhibited a decrease in anxiety-like behaviors when compared to amphetamine pretreated rats that received vehicle. However, ASV administration to rats pretreated with saline induced an anxiogentic effect by increasing anxiety-like behaviors, when compared to saline pretreated vehicle infused rats. Due to this result, western blots were carried out on untreated, saline, and AMPH treated brains in order to determine the adaptations of CRF2 and CRF1 receptors in the brain during the chronic stress of treatment. Overall, results show that central administration of ASV decreases anxiety-like behaviors of rats during psychostimulant drug withdrawal, suggesting that global antagonism of CRF2 receptors in the brain may be an effective treatment for withdrawal-induced anxiety.

Supported by: NIH grant NIDA R01 DA019921. Emily Reinbold was supported by a SSOM Medical Student Summer Research Fellowship.

Development of GABAergic interneurons in a mouse model of Batten disease

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Juvenile neuronal ceroid lipofuscinosis [JNCL; or Batten Disease (BD)] results from a mutation in *Cln3*, a gene found on the 16P12 locus that encodes a transmembrane protein. The most common mutation is a 1.02kB deletion which removes exons 7-8 and, as this mutant transcript is targeted for nonsense mediated decay, results in a null mutation. Onset usually begins around 5-10 years of age with visual deterioration,and progresses to include motor dysfunction, seizures, and mental retardation. Although BD has long been considered a neurodegenerative disease, mounting evidence is pointing to an early initiation in the pathogenesis with some studies suggesting a developmental component to its progression. Therefore, special focus has recently been placed on characterizing anatomic, cellular, and behavioral changes at various stages of CNS development. Animal models of BD faithfully recapitulate many of the human disease associated pathologies, including accumulation of autofluorescent storage material, expression of autoantibodies, neuronal degeneration, glial activation, and shortened life span. More recently, several murine models of BD have been used to uncover an early disturbance in cerebellar maturation and motor dysfunction. In this study, we examine cortical development in the *Cln3*$^{-/-}$ mouse to determine whether pathological changes associate with this brain region, including interneuron reduction and cortical thinning, manifest during early developmental time points*. We hypothesize that aberrant proliferation and neuronal migration in the developing cerebral cortex contributes, in part, to the reduced cortical volume in this BD model.*

Aim: To determine if the loss of Cln3 effects the proliferation and/or migration of the various subtypes of GABAergic interneurons from the ventricular zone in the Cln3 knockout mouse model.

One hallmark of BD is a disruption in select subclasses of GABAergic interneurons in the cerebral cortex. This loss varies significantly within anatomical region and the NCL mouse model studied. Here, we examine interneuronal proliferation and placement during embryonic and early postnatal development to determine if absence of these cells in the mature cortex is a result of aberrant neurodevelopmental progression.

Subaim1: Studies have shown severe cortical thinning in many areas of the cortex, suggesting neurodegeneration. Here we will examine proliferation of neural progenitor that give rise to glutametergic projection neurons and GABAergic interneuronal, respectively. Using the thymidine analog BrdU, we will label all progenitors actively dividing during at the time of injection. By sacrificing the mice at varying times post injection, we examine changes in progenitor proliferation within the dorsal or ventral VZ or the ability of these cells to migrate away from these defined neurogenic niches.

Subaim 2: Mature *Cln3*$^{-/-}$ mice faithfully recapitulate the disease-associated loss of distinct classes of GABAergic interneurons. However it remains unclear whether these cells are selectively undergo apoptosis once they reach their final target or whether they fail to properly migrate and differentiate during developmetn. We have immune-labeled calretinin^{+}, calbindin^{+}, somatostatin^{+}, NPY^{+}, and parvalbumin^{+} interneurons at key developmental time points to observe which populations are altered in the cortex.

This project will help identify the exact time points during developing where the interneuronal subpopulations are affected. With that we can properly target research to find the root cause of the disease that leads to such a wide variety of phenotypes.

Spleen is the site for antigenic priming of diabetogenic T cells during the early stage of T1D pathogenesis.

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Type 1 Diabetes (T1D) is a devastating autoimmune disease with pediatric onset; it affects 18–22 million people worldwide. Mice of the Non Obese Diabetic (NOD) inbred strain spontaneously develop a disease closely resembling human T1D, and have been widely and successfully used as an animal model of T1D. Progression of T1D involves the activation of autoimmune T cells, consequent homing of activated lymphocytes to the pancreatic islets, and ensuing destruction of insulin-producing β-cells. The autoimmunity in NOD mice and T1D patients is associated with defects in central and peripheral tolerance. Specifically, defective central tolerance mechanisms in T1D-prone individuals and NOD mice allow naïve autoreactive T cells to escape thymic negative selection and to appear on the periphery of immune system. On the periphery, the breakdown in peripheral tolerance mechanisms that are partially controlled through the expression of peripheral tissue antigens (PTAs) by the lymphoid tissues, namely, spleen and lymph nodes, facilitates antigenic priming of naïve autoreactive T cells, allowing them to acquire their full cytotoxic diabetogenic potential. The spatial and temporal characteristic of this priming determine the progression of diabetic disease.
Surgical removal of spleens (splenectomy) performed, from NOD mice at 2-3 wks of age significantly reduced diabetes incidence and delayed its onset. However, splenectomy performed later in life did not affect diabetes development, suggesting that spleen is a site for priming of a subset of diabetogenic T cells. Spleen was not required for proper homing of diabetogenic T cells, while at the same time, mice lacking spleen, and immunized *in vivo,* showed selective diminution of the response to an insulin-derived peptide but not to other peptides. Thus, we hypothesized that spleen may serve as an early priming site for T cells of at least one of the major anti-islet specificities; and that increased expression of islet-associated PTAs by splenic stromal cells results in preferential priming of naïve diabetogenic T cells. In order to investigate the levels of expression in the lymphoid tissues of PTAs, normally present in the islets, we conducted RNA isolation and Q-PCR analysis of tissues from the spleen, thymus, pancreatic and mesenteric lymph nodes, obtained from NOD mice with ages of one through five weeks.

Analysis of the expression pattern of multiple PTAs in the spleens of young NOD mice provided confirmation to our hypothesis that spleen serves as a priming site for diabetogenic T cells early in T1D pathogenesis.

Antiprogestin Mifepristone and the Epithelial Mesenchymal Transition in Cancer cells

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Background: The mechanism of cancer metastasis is not well understood and extremely complex. In many cancers, the ability to metastasize is often accompanied with the transition of the cells from having epithelial features to having a more mesenchymal phenotype, a process known as epithelial-to-mesenchymal transition (EMT), and characterized by changes in cell morphology, loss of tight junctions, remodeling of the cytoskeleton, and acquisition of migratory and invasive capacities. We have shown previously that a prototypical antiprogestin, mifepristone (MF), can inhibit growth of ovarian, prostate, breast, and brain cancer cells. It was also noted that in response to MF the cells displayed changes in morphology, and had reduced adhesive, migratory, and invasive capabilities. Thus, in this work we hypothesized that such altered cellular biological properties in response to MF are associated to modifications in the molecular apparatus driving the EMT. We examined the effect of MF on the abundance and intracellular localization of proteins involved in EMT and focal adhesion.

Methods: *Cell Culture:* Cancer cell lines of the ovary (SK-OV-3), breast (MDA-MB-231), prostate (LNCaP), and nervous system (glioblastoma; U87MG), were plated and treated with either vehicle ethanol or the IC_{50} (concentration needed to inhibit growth by 50%) of MF for 72 h. Cells were then harvested, pelleted and quickly frozen. *Western Blot:* The cell pellets were lysed, and 50 µg of each sample was loaded into 12%, 10%, or 7.5% acrylamide gels, subjected to SDS-PAGE and transferred to PVDF membranes. The primary antibodies used were against the EMT markers vimentin, E-cadherin, vinculin, phospho-focal adhesion kinase (p-FAK), FAK, and cytokeratins of high and low molecular weight. *Immunoflorescent staining (IF):* Cells were plated in 8-well chamber slides at a density of 5,000 cells per well and treated as stated above. Cells were fixed and incubated overnight with primary antibodies against FAK, vimentin, or vinculin. After mounting, slides were viewed and imaged via fluorescent microscopy.

Results: In Western blot analysis, the epithelial marker E-cadherin was found expressed in LNCaP cells but not in SK-OV-3, MDA-MB-231 or U87MG cells, and was not modified by MF. The intermediate filament protein vimentin was found in SK-OV-3, MDA-MB-231, and U87MG cells, but not in LNCaP cells, further confirming the epithelial phenotype of the latter, and the mesenchymal phenotype of the formers. MF had a slight tendency to increase vimentin expression in SK-OV-3 and U87MG cells, whereas it altered the expression of cytokeratins in LNCaP, MDA-MB-231 and U87MG, but not in SK-OV-3 cells. Furthermore, the focal adhesion marker, vinculin, was abundantly expressed in all cell lines and was not modified by MF, whereas FAK and/or its phosphorylated form (pFAK) were down-regulated by MF in LNCaP, MDA-MB-231, and U87MG cells, but not in SK-OV-3 cells. In IF analysis, the intermediate filament protein vimentin was found abundantly expressed in the cytoplasm of all but LNCaP cells, whereas FAK and vinculin were found in the cytoplasm of all cell lines studied. Although MF altered the morphology of the cells and the cytoskeletal architecture as depicted by the intracellular distribution of β-actin, the distribution of vimentin, FAK, and vinculin were not apparently modified by the steroid.

Conclusion: Antiprogestin MF, at doses causing reduced cancer cell adhesion, migration and invasion, altered the expression of high and low molecular weight cytokeratins, and reduced the abundance and phosphorylation status of FAK, which is usually overexpressed in cancers and correlated with malignant or metastatic disease and poor patient prognosis. Thus, the anti-cancer effect of MF is not only manifested in the inhibition of cellular growth and migration, but also in the dysregulation of proteins involved in EMT and in the formation of focal adhesions.

Contribution of swine influenza gene segments toward virulence of influenza viruses

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Background: The influenza virus contains 8 negative-sense RNA segments coding 12 different proteins. The eight segments code for three polymerases (PB1, PB2, and PA), nucleoprotein (NP), hemagglutinin (HA), neuraminidase (NA), matrix (M), and non-structural (NS) genes. Based on its role in host cell binding, the HA gene is the most evaluated with regard to infection and immunity. However, the other 7 genes can make significant contributions to virulence, especially when the virus crosses between species. We recently observed that a swine-origin influenza virus (0209) induced cell death (cytopathic effect, CPE) during propagation within both a traditional influenza virus cell line (MDCK) and a novel swine cell line (IPEC-J2), while a mouse-adapted influenza virus (PR8) only induced significant CPE in the MDCK cells. We hypothesize that individual influenza genes from the two different viruses (mouse-adapted and swine-origin) will differentially regulate virulence when they are propagated in either MDCK or IPEC-J2 cells.

Methods: To test our hypothesis, we cloned individual genes for all 8 RNA segments from the 0209 virus into plasmids that can be used to create viruses by reverse genetics. We then created reassortant viruses based on the PR8 background using previously characterized plasmids containing these genes. Rescued viruses were propagated in embryonated chicken eggs, and their phenotype was compared in MDCK and IPEC-J2 cells.

Results: We successfully cloned all 8 influenza virus genes into plasmids for use in our reverse genetic system. Attempts to rescue viruses that contained a single 0209 gene and 7 PR8 genes (1:7 reassortants) yielded viruses expressing the 0209 HA, NS, NP, and M genes. Viruses expressing either the 0209 NA, PA, PB1, or PB2 genes were not rescued. Using the four 1:7 reassortant viruses, we observed that at least three of the four rescued viruses (NS-, NP-, and M-1:7 reassortants) did not induce significant CPE on the IPEC-J2 cells, while they were able to produce CPE in the MDCK cells. This phenotype was more like the mouse-adapted virus (PR8) than the swine-origin virus (0209). The HA 1:7 reassortant is currently being tested.

Conclusions: Based on these findings, we conclude that the swine-origin NS, NP, and M genes do not control the CPE in the IPEC-J2 cells. Since the three rescued viruses tested to date did not demonstrate CPE in the IPEC-J2 cells, we hypothesize that the polymerase complex (PB1, PB2, and PA) and/or the NA plays a role in this phenotype. We are most interested in the potential that a protein produced by the PB1 gene (PB1-F2) controls this phenotype, as this protein is known to play a role in apoptosis through its natural interaction with the mitochondria.

Development of a Novel Mouse Medulloblastoma Model to Study Tumor Cell Migration and Metastasis.

Brian Westerhuis, Katie Piccotte, and Haotian Zhao

Medulloblastoma, an invasive embryonal tumor of the cerebellum, is the most common malignant brain cancer in childhood. Medulloblastomas tend to disseminate to other parts of brain, the spine and even extra-neural sites. Metastasis is the primary cause for treatment failure and the most significant prognostic indicator of poor outcome. A detailed understanding of the mechanisms promoting medulloblastoma migration and metastasis will significantly impact the development of novel therapeutic strategies for preventing metastasis. Disruption of developmental pathways remains the fundamental mechanism of medulloblastoma initiation, invasion and metastasis. Constitutive activation of the Sonic Hedgehog/Patched (Shh/Ptch) pathway leads to medulloblastoma development. Proneural transcription factor *Atonal homolog 1* (*Atoh1*) plays an important role in cerebellar development. Loss of Atoh1 triggers the differentiation of granule neuron progenitors (GNPs), while overexpression of Atoh1 prevents differentiation and together with Shh signaling converts GNPs into tumor-initiating cells. To explore developmental mechanisms underlying the invasive behaviors of medulloblastoma *in vivo*, we are developing a novel mouse model in which tumor initiation can be precisely regulated by inducible Atoh1 expression in preneoplastic GNPs from *Ptch1*$^{-/+}$ mice. This model will enable us to examine the motility characteristics of tumor cells at the early stages of tumor development, reveal the dynamic subcellular structures of migrating tumor cells and examine the role of developmental signaling in tumor cell migration and metastasis. The invasive behaviors of medulloblastoma in our mouse model will closely resemble those seen in human diseases, making it a unique preclinical model to evaluate therapeutic agents targeting tumor cell migration/metastasis.

Scholarship Pathways Program

Poster Session, 12:00-1:00 pm, Lee Med Atrium

Chaltu Ayano
Development of an international clinical experience in Addis Ababa, Ethiopia

Jon Christensen
Increasing public access to the Automated External Defibrillator

Brad Julius
The role of family involvement in a nutrition and physical activity education program

Chelsea Koepsell
Perceptions of spirituality and religion in medical care

Jordan Makela
Comparison of the CNS signs used in early and late diagnosis of fetal alcohol spectrum disorders

Ryan Miller
IHI Open School: An educational model for patient safety and quality improvement

Nathaniel Paulson
Analysis of blood donor motivations

Joshua Ryan
Medical School Boot Camp: Promoting early interest in medicine

David Somsen
Globalizing Global Health: Educating tomorrow's health care leaders on the state of the world

Joel Tjarks
Correlation between saccadic eye movements and symptom scores in patients with MTBI

Erin Williams
Influence of cosmetic dermatology on dermatology residency programs

Scholarship Pathways Program Abstracts

The Scholarship Pathways Program is an elective opportunity developed to enrich the medical school experience by promoting rigorous independent scholarship and scholarly excellence as well as produce leaders in medical education, research and service. The program spans all four years and develops critical thinking and independent learning skills. At the end of their first summer in the program, students create a poster summarizing their project and progress to date. The included abstracts represent each student's work in progress.

Development of an international clinical experience in Addis Ababa, Ethiopia

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Background
A student can benefit from optional clinical rotations in countries that practice allopathic medicine differently from what is available in the United States. Hospitals in developing countries such as Ethiopia offer presentations of multiple advanced pathologies, exposure to a different healthcare setting, and the chance to practice medicine in such settings. Opportunities to observe and participate in the clinical setting of a developing country are scarce for students of Sanford School of Medicine (SSOM). Although the clinical years at SSOM allow practical learning in the clinics around South Dakota and externships elsewhere in the nation, they do not encompass an international component. This project will design an experience in global medicine at Tekur Anbessa Specialized Hospital of Addis Ababa, Ethiopia. Its goal is to offer SSOM students an elective, four-week rotation in Addis Ababa during their fourth year.

Project Description
Experience in the medical community of Addis Ababa was gained during six weeks in the surgery departments of GI, cardiothoracic, and urology. About 40 percent of each week was spent on rounds shadowing attending physicians, residents, and interns. The remaining time was spent in the OR of each unit. In addition to observing and learning from the advanced pathology, this time allowed a better understanding of the way medicine is practiced, from patient admission to procedure and discharge at the hospital. Similar opportunities will be included in the planned elective.

Outcome
The described clinical experiences would most benefit a student who has completed the basic science courses and at least some training in physical diagnosis and patient care. Ideally, the created elective would be available for students in their fourth year.

Next Steps
The following steps outline the upcoming goals of this project: a) develop a curriculum for a four-week elective rotation in Addis Ababa, Ethiopia, that includes lectures and handouts to provide students with a background on how the hospital functions and an education on the culture and customs of the country prior to travel, b) meet with the administrators of SSOM to discuss the curriculum options, c) establish contact between the administrators of Tekur Anbessa and SSOM, and d) arrange housing and transportation for students interested in the elective.

Increasing public access to the Automated External Defibrillator

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Background
Sudden cardiac arrest (SCA) is one of the leading causes of death in the United States, claiming between 250,000-500,000 lives a year. A majority of deaths occur outside the hospital where the survival rates are usually low, ranging between 1-5%. Defibrillation applied by an Automated External Defibrillator (AED) has been recognized as the most important intervention for someone suffering from SCA. In addition, early defibrillation is vital to resuscitation, as research has found that someone in ventricular fibrillation has a 90% chance of survival if defibrillated within the first minute. However, for each minute that passes a person's chance of survival decreases by 10%. Although Emergency Medical Services (EMS) or first responders are able to respond to an incident, lengthy response times may jeopardize a person's chance of resuscitation. Thus, having an AED in the general vicinity of the incident could dramatically increase an individual's chance of survival. For this to be effective, the lay public must be trained and feel confident and comfortable in use of the AED.

Project Description
In order to reduce the call-to-shock time for people suffering from SCA, the concept of Public Access Defibrillation (PAD) endorses an expansion in the traditional role of the AED in the pre-hospital setting by increasing public placement of the AED and training the public in CPR and AED operations. This project's goal is to increase public access to the AED in Vermillion, South Dakota, including schools, churches, the city golf course, and other businesses. Grants will be used to defray cost for locations at higher risk for SCA. For facilities that already have an AED, information pertaining to that AEDs location was gathered and given to the 9-1-1 dispatch system. The CPR training in the community is being improved by coordinating and providing CPR certification classes to schools, churches, and businesses throughout Vermillion. Also, the concept of "Sidewalk CPR" is being used to raise public awareness.

Outcome
Twenty-two AEDs already existing in the community were linked with the 9-1-1 dispatch system. Although this is a good start for a PAD program in Vermillion, it must be noted that 73% of the community's AEDs are located within the campus of the University of South Dakota and about one-third of those are at the Lee Medical Building. Thus, more AEDs are needed for public locations in Vermillion to provide a more equal distribution for the community. For facilities that do not have an AED, funding was cited as the main barrier. Others voiced concerns about liability, either from the misuse or the decision not to use the AED.

Conclusion
My future goals for this project are to meet with the Vermillion Ministerial Association, which is made up of a leader from each church in the community. After this assessment, I will have an idea of how many churches already have an AED and how many would like to obtain one. In addition, I will continue to work with the local foundations in applying for funding to help reduce the cost of the AED.

The role of family involvement in a nutrition and physical activity education program

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Background
Childhood obesity is associated with many future health complications such as insulin resistance, diabetes mellitus, blood lipid abnormalities, and hypertension. Nationally, 14.8% of children aged 2-19 are overweight (classified as having a BMI for age between the 85th and 94th percentile) and 16.9% are obese (classified as having a BMI for age ≥ 95 percentile). In South Dakota, 16.7% of children aged 5-19 are overweight and 16.0% are obese (32.7% combined). Childhood obesity has been shown to be a strong predictor of obesity in adulthood. It has been reported that 69%, 83%, and 77% of obese children 6-10 years of age, 10-15 years of age, and 15-18 years of age, respectively, will still be obese at age 25. Systematic reviews have highlighted the importance of family involvement in childhood obesity interventions; however, few have been community-based or used objective measures to assess physical activity.

Purpose and Hypothesis
This study examines the role of family in a nutrition and physical activity education program. We hypothesize that children in the parent and child education group will show greater improvements in health and behavioral outcomes compared to children in the child-only education group. In particular, children in the parent and child group will have greater reductions in BMI and body fat, greater increases in the number of daily steps they take, and their families will report greater reductions in obesity generating factors compared to children in the child-only group.

Methods
Subjects were enrolled in the Let's Get Moving program, a nutrition and physical activity education program at Brookings Health System in Brookings, South Dakota. Subjects were randomized into either a parent and child group or a child-only group. Groups were taught separately, but received the same education. Height and weight were measured and total body dual x-ray absorptiometry was used to measure body composition. To assess ambulatory activity, subjects wore a New Lifestyles NL-1000 pedometer for one week. Subjects were given a log sheet to record when they put the pedometer on and when they took it off each day. These times were then used to calculate an average number of steps taken per hour of wear. Subject-specific questions from the Youth Risk Behavior Survey were used to measure self-reported fruit and vegetable intake, physical activity, and screen time. The Family Eating and Activity Habits Questionnaire was used to assess four factors that affect obesity in children: activity level, stimulus exposure, eating related to hunger, and eating style. All measurements and questionnaires were completed before and after the ten week program. Analysis of baseline characteristics showed no significant differences between groups. Groups will be compared using Student's t-test and general linear models.

Next Steps
This study may be underpowered to determine significance. However, if a trend is identified, we will use the estimates to determine the sample size needed for a future study. In addition, we will be investigating the relationship between parental and child activity levels in a larger cross-sectional study of children aged 2-5 years of age.

Perceptions of spirituality and religion in medical care

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Background
Spirituality and religion are important factors in many aspects of patient health. These factors include patient understanding of disease, decision making processes, and coping mechanisms. Despite this relationship, however, a gap exists between medicine and spirituality. A majority of patients and physicians consider spirituality and religion relevant to clinical practice, yet few individuals report having discussed spiritual matters in a medical setting. The purpose of this study is to expound upon previous research by surveying South Dakota physicians of differing specialties, personal religious backgrounds, and practice locations (urban or rural) in order to determine which factors have the greatest impact on incorporating spiritual issues into clinical care.

Project Description
A questionnaire was developed using the templates of previous research on spirituality in medicine. It surveyed physician demographics (gender, age, specialty, and practice location) and individual spirituality (personal denomination and perceived level of spirituality/religiousness) as well as the physician's incorporation of spirituality into clinical practice. Integration of religion in medicine was investigated through questions about frequency of performing a spiritual history, praying with patients, and discussing religious issues with patients. In addition, physicians were asked about their personal perception of importance, pertinence, and comfort regarding religious aspects of interactions with patients.

Outcome
Data analysis is pending.

Next Steps
Upon receipt of the completed surveys, analysis will be conducted to investigate whether there is a specific demographic of physician who is more likely to incorporate spirituality and religion into his/her practice and whether that demographic coincides with that of previous research in the field of spirituality in medicine. Other areas of inquiry may involve the main barriers to incorporation of spirituality and religion in medicine, perceptions of residents and medical students regarding the incorporation of spirituality and religion into medical care, and whether there are things that can be improved in medical education in order to better prepare physicians to address issues of spirituality with their patients.

Comparison of the CNS signs used in early and late diagnosis of fetal alcohol spectrum disorders

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Background

In the US, an estimated 13% of infants are exposed to alcohol at some point during pregnancy, although often only at small levels and prior to the mother's knowledge of the pregnancy. Still, 2-4% of children will suffer from a fetal alcohol spectrum disorder (FASD). This has a tremendous financial and social burden for the families as well as the nation's social services, primarily due to the functional deficits in learning, language, memory, adaptive behaviors, and attention. There is evidence that early diagnosis and subsequent treatment can provide a significant improvement in quality of life for individuals with prenatal alcohol exposure. Unfortunately many people with FASDs either go unidentified altogether or are referred for testing later in childhood, and miss the potential window to remediate neuronal damage. Fetal alcohol syndrome has long been identified by the characteristic facial dysmorphology, while a neurobehavioral phenotype has been difficult to identify. The aim of this study is to examine the FASD diagnosis with regards to central nervous system signs and symptoms, and then to determine how this process differs between patient age groups.

Methods

A search of the electronic medical records in the Sanford Health System for the ICD-9 code (760.71) for fetal alcohol spectrum disorders provided a patient base for a chart review. These charts were abstracted for data related to the diagnosis within the spectrum. This data will later be analyzed to identify differences between patient age groups.

Results

The data has not been analyzed at this time; however certain trends can be drawn from the chart abstraction process. Making a confirmed diagnosis within the fetal alcohol spectrum disorders remains difficult, even with reported prenatal alcohol exposure and a history of cognitive, behavioral, or developmental delays. Patients with a history of prenatal alcohol exposure often deal with multiple factors of growing up in an unstable environment such as neglect, abuse, and moving between legal guardians, which can manifest as behavioral issues or developmental delays. Without the characteristic physical findings, a confirmed FASD diagnosis is rare.

Next Steps

The first goal is to run statistical analysis of the abstracted data and draw conclusions. Subsequent work will develop educational materials regarding the effects of prenatal alcohol exposure on the developing brain.

IHI Open School: An educational model for patient safety and quality improvement

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Background
Since the release of the 1999 report from the Institute of Medicine, "To Err is Human", which demonstrated that approximately 98,000 die each year in the US from preventable medical errors, safety and quality have been given a central focus in health systems. Despite this emphasis however, national improvement has been slow. More than ever, a change in culture is needed within the entire healthcare community. To this aim, the IHI Open School has become a driving force, serving to accelerate the incorporation of safety, quality and performance improvement disciplines into medical education and therefore "…fill the current gap in the professional preparation of improvement leaders while the educational institutions catch up with the need" (Berwick S60). Since its establishment in 2008, over 300 health professions schools around the world have established IHI Open School chapters and over 50,000 students have registered on IHI.org. The purpose of the chapter is to bring together multiple disciplines for collaboration on patient safety and quality improvement by building teamwork, breaking down communication barriers, fostering a patient-centered environment, building awareness of issues affecting patients, and equipping students with the necessary tools to be leaders in patient safety and quality improvement.

Project Description
An IHI Open School chapter was established on the campus of the University of South Dakota to bring students, faculty, and healthcare providers together. The chapter was designed to approach 21st century healthcare as an interdisciplinary team of experts. Initially, a core leadership team consisting of students from medicine, physician assistant, physical therapy, occupational therapy, nursing and health science disciplines was constructed. Nearly 120 students across these health disciplines joined the founding group. A chapter structure was developed to provide maximum opportunities for students, including in-person chapter events, online collaboration through IHI Open School resources and social media, as well as student-initiated projects, interaction with health systems, and curricula implementation.

Outcome
The chapter will hold numerous events during the academic year in conjunction with demonstrated student interest. Ongoing collaboration with health systems aims to provide students with opportunities for hands-on improvement work. Additionally, a student-developed pilot project for safety and quality will be implemented in the first year curriculum, using IHI Open School courses, case studies, reflection papers, and small group discussion.

Conclusion/Next Steps
Given the vast initial student interest across disciplines, students appear inherently motivated to learn patient safety and quality improvement concepts. This certainly coincides with the growth of IHI Open School around the world. In the coming year, membership will be expanded and the chapter structure will be assessed to determine future directions. Results of the pilot project will be analyzed and shared with school leaders, with the hope that in the near future this type of educational and professional improvement opportunity will be permanently embedded into emerging curricula, and so address the rapidly escalating challenges of 21st century healthcare delivery. Our model for using IHI Open School to address safety and quality in health professions education will be developed further as the chapter grows and expands its reach.

Analysis of blood donor motivations

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Background
Medicine depends on a sufficient, clean, blood supply. For most, this need is not threatened on a daily basis, and we can lose sight of the dangerous implications of blood supply shortages. Blood donations are an essential part of providing needed life-saving products. In fact, every 3 seconds someone needs blood, and eight out of ten people will require blood or blood products in their lifetime. Fortunately, blood banks and other systems have been established to meet these needs. Since only 5% of the eligible population donates, blood banks fight a constant battle to ensure an adequate supply. Finding new and improving current blood donor recruiting strategies is essential so that blood products will continue to be available when they are most needed.

Project Description
This project aims to assess the attitudes of blood donors in age 18-36 demographic. Blood donors in this demographic were recruited to participate in this study when they checked-in for a blood donation appointment. Participation in the study required the one-time completion of a thirteen question survey during their appointment.

Outcome
Data analysis is pending.

Next Steps
The goal of this study is to determine what factors most strongly influence the decision to donate blood. Once the factors are identified, it will be possible to create educational material or other marketing that specifically targets these individuals. Through more focused targeting of this age demographic, it is our hope that donation rates within this demographic will increase.

Medical School Boot Camp: Promoting early interest in medicine

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Background
It has become increasingly difficult to predict what the future of medicine holds. As debates about health care reform and the growing physician shortage stir in the political and medical arenas, the medical profession is seemingly at a crossroads. Although many bright young men and women and will continue to be attracted to attend medical school, some potential students may be turned off by the long road through medical school and residency training and also by the possibility of decreased physician income and stature in the future. Other students may see admission to medical school as an unattainable goal. Even as students begin their undergraduate career, many believe that a person has to major in a science discipline in order to become a physician. There is a need to better educate young persons, particularly high school students, about the path to becoming a physician. Medical School Boot Camp provided a day when high school students were able to ask questions of and hear stories from physicians, residents and medical students about their paths to and careers in medicine.

Boot Camp Design
Two Sessions of the Medical School Boot Camp were held at the Wegner Health Science Center in June 2011. Ten high school students, sophomores through seniors, attended one of the sessions. Each session began by asking the students what they wished to take away from the camp. This was followed by a talk given by Sioux Falls family physician Dr. Tricia Knutson about her career path and practice of medicine. The day continued with a PowerPoint presentation which focused on how students can become mentally engaged in considering a career in medicine, considerations for selecting the right college for them personally, and how students can major in a number of disciplines and still pursue a career in medicine. The day also included a tour of Sanford USD Medical Center and concluded with an open discussion with medical students and residents from the Sanford School of Medicine of The University of South Dakota and the Sioux Falls Family Medicine Residency Program. The students were asked to complete a survey inquiring about their interests in health care at the end of the camp. A follow-up survey is planned for these students as they continue through their high school and college careers.

Results
All ten students completed the survey. When asked about particular specialty interests, only two of the ten students ranked family medicine as their top choice. Five of the ten students ranked some form of primary care in their top three fields of interest. All of the students strongly agreed that the Medical School Boot Camp was helpful in providing information about a medical career. All students either agreed or strongly agreed that they would be interested in having a medical student as a mentor during high school.

Next Steps
Many of the students commented that they would be interested in having medical students speak to their classes, and they would welcome medical students as mentors. In response to this, a fall Boot Camp is planned. This session will take place on a weekend, in order to engage more students and to have a larger cohort of students to survey. Future summer session are also planned. An informal mentorship program, primarily focused on email communication, has also been considered. The ultimate goal of the project is to identify as many high school students as possible who may have interest in medicine and nurture this interest by providing them with facts about a medical career, with opportunities to hear from physicians about their personal professional experiences and the rewards they have enjoyed from the practice of medicine.

Globalizing Global Health: Educating tomorrow's health care leaders on the state of the world

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Background
The medical community has undoubtedly made considerable advancements in the field of global health. Unfortunately, this field presents problems that are numerous and will become increasingly more complicated given our rapidly changing society. Medical students are fortunate to be in a position to effect major change in the future of global health, but this opportunity is being thwarted by a lack of education. At the Sanford School of Medicine (SSOM), first year students are currently given little training in global health. The school's Introduction to Clinical Medicine class is a platform to introduce its students to areas of medicine not covered by basic science classes. Using this class to educate students and promote global health is a very real possibility. It would expose individuals who already have a profound interest in medicine to a world they may have never encountered with the current curriculum. Thus, this class has the capability of having a significant impact on the field of global health.

Project Description
During the 2011-2012 school year, a four to eight hour session based on global health will be synthesized. The session will eventually be presented to first year medical students at SSOM through the Introduction to Clinical Medicine class. To develop the framework for the class, research will be done on the current issues in global health. By combining the results of this research with global health committee recommendations on core competencies, the class will aim to be both educational and interesting for the students of SSOM. Collaborations with key faculty will be vital in producing an outstanding final project. If time permits, a pilot class can be debuted to first year students in the spring of 2012. Feedback from these students as well as the faculty will help the session evolve into a mainstay of the SSOM curriculum.

Outcomes
This project aims to introduce new and engaging information from the field of global health to the first year students of SSOM. More importantly, however, it will be a learning tool on how to construct a global health curriculum for other medical schools currently lacking one. In addition, this project presents a large number of research opportunities to investigate the educational effects of this style of class on medical students and their future career choices.

Conclusions
Creating a healthy global community is a very real possibility. Of course, knowledge is essential in accomplishing this task. It is particularly important to inform those with the capability and desire to effect change about the health of other parts of the world. By making students aware of these issues, the potential effect on the field of global health can be substantial.

Correlation between saccadic eye movements and symptom scores in patients with MTBI

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Background
Over the past few years the topic of sports-related concussion has garnered significant media attention. It is estimated that 1.6 to 3.8 million concussions occur annually in the United States as a direct result of participation in sports. Concussed patients experience a variety of symptoms that are unique in severity and type to each patient. Due to the variable nature of the concussion, patients must be treated individually, and a unique plan of action must be carried out by their health care provider based on the symptoms experienced. Concussion assessment and return to play guidelines are commonly based on self-reported symptom scores, balance testing, and neuropsychological testing. The physician makes his or her recommendation regarding the treatment of the patient based on the outcomes of these tests. Recently, the King-Devick test has been marketed as a revolutionary test for sideline diagnosis of concussion. This test was initially developed in the 1980s as a tool to assess saccadic eye movement in children to evaluate reading problems and dyslexia. It is known that eye movements are impaired in patients who have experienced a concussion or traumatic brain injury, but further research is needed to determine the efficacy of this test as a diagnostic tool.

Project Description
Approximately 200 concussed individuals between the ages of 14-22 will perform the King-Devick test as a part of their initial clinical evaluation post-concussion. This study will look at how performance on the King-Devick test correlates to performance on other aspects of the physical exam, including neurocognitive and balance testing as well as self-reported symptom scores. Results on this test will then be compared with the results of all other aspects of the clinical exam. By identifying correlations between results on the King-Devick test and other symptoms, practitioners will be better able to establish unique return-to-play guidelines for each patient they see.

Outcomes
Participant recruitment is ongoing with data analysis pending.

Next Steps
After the data has been collected and analyzed, we will be able to evaluate the validity of the King-Devick test and potentially recommend return-to-play guidelines using this test. This study will open the door for future studies including the establishment of normative data for the King-Devick test and its use as a diagnostic tool for concussion assessment.

Influence of cosmetic dermatology on dermatology residency programs

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Background
The field of cosmetic dermatology has grown tremendously in the past decade, creating a lucrative market for cosmetic products and procedures. However, it is unknown whether residency programs have increased cosmetics training in order to meet this growing demand. Dermatology residents have consistently reported inadequate exposure to cosmetic dermatology, and recent studies have raised the concern that residents may have less interest and expertise in academic dermatology due to growing emphasis on cosmetic dermatology. There clearly exists a widening gap between academic and cosmetic dermatology, yet it will be important to offer resident education that is comprehensive for all areas of dermatology. The aim of this study is to survey dermatology residency directors in order to ascertain how programs currently incorporate cosmetics training, as well as interest in and attitudes toward cosmetics training during residency.

Methods
A survey with 19 questions and an additional program information section was developed to be distributed to residency program directors at institutions nationwide. Questions inquire into current prevalence of cosmetics training in residency, how cosmetics training is conducted, perceived resident interest in cosmetics, attitudes toward cosmetic dermatology, and the future of cosmetic training in residency programs. The additional program information section was designed to shape a profile for the residency program while still maintaining anonymity, and includes questions about size, faculty number, and university versus non-university affiliation. The survey will be distributed by email and administered via an online survey program.

Results
The survey is currently in distribution with data analysis planned for Fall 2011.

Conclusion/Next Steps
While the results of the survey have not yet been analyzed, it is expected that the data will be able to provide a baseline estimate for the current level of cosmetics training provided in the dermatology residency. The data may also suggest a need for greater cosmetics training in the future, whether in residency or in subsequent fellowship. At present, the American Board of Dermatology offers formal fellowship training in Dermatopathology, Pediatric Dermatology, and Procedural Dermatology. While cosmetic procedures are included in the surgical-focused Procedural Dermatology fellowship, it might be worth exploring the creation of a purely cosmetics-based fellowship. Future considerations beyond this study include the development of a survey intended for dermatology residents and recent residency graduates in order to more fully gauge interest in and intent to perform cosmetic procedures while in practice, as well as satisfaction with the dermatology residency. It is the author's belief that further study may show an incongruity between the how the residency currently operates and what residents desire in order to best serve their future practice. This could segue into future research projects about tangible reforms that could be introduced into the dermatology residency that fully encompass the skills necessary to practice dermatology in today's society.

Sanford Program for Medical Student Research

Poster Session, 12:00-1:00 pm, Lee Med Atrium

Laura Luick
Is Clean Really Clean?: An Evidence Based Approach to Monitoring Environmental Contamination

Joel Tjarks
Evaluation of balance, neurocognitive, and symptom scores of adolescent athletes who have suffered a head injury.

Sanford Program for Medical Student Research Abstracts

Is Clean Really Clean?: An Evidence Based Approach to Monitoring Environmental Contamination

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Background: Hospital acquired infections (HAIs) are increasingly a problem within healthcare. In 2007, an estimated $28.4-45 billion was spent treating these preventable infections. Poor hand hygiene has been associated with the spread of HAIs in the healthcare setting, however environmental contamination also plays a role. The Centers for Disease Control has now recommended level I and II montoring of environmental disinfection in healthcare facilities. The recommended program includes a structured education of environmental services staff, including baseline evaluation of thoroughness of cleaning and evaluation of competency as well as a need for regular, on-going, structured monitoring of the program to be performed and documented by health care facilities. However, it is not clear what strategies are optimal for monitoring of cleaning and neither guideline specifies how such monitoring should be performed. We aimed to evaluate different methods of measuring cleanliness as compared to standard aerobic bacterial colony counts. We utilized a transparent marking solution that fluoresces when exposed to ultraviolet light and an adenosine triphosphate (ATP) bioluminescence assay which utilizes the firefly enzyme luciferase to tag ATP causing luminescence which is then measured by a luminometer as surrogates for efficacy of terminal cleaning.

Methods: A total of 250 frequently-touched surfaces from 50 rooms were evaluated for cleanliness based on visual evaluation, obtaining aerobic bacterial cultures using premoistened swabs and simulated hand contamination as well as measurement of ATP reading (Accupoint2®, Neogen, Lansing, Michigan) before and after terminal cleaning. The fluorescent marker dye (Dazo®, Ecolab, Eagan, Minnesota) was also placed before and removal was assessed after cleaning. Student's *t* test were used to compare colony counts before and after cleaning in relation to removal of the fluorescent dye while measures of correlation with linear regression were done for the ATP bioluminescence assay.

Results: The visual assessment showed a significant difference in the number of surfaces deemed clean before and after cleaning (218, 87% versus 237, 95%, $p<0.01$). The results of the ATP assay showed no significant correlation between the change in colony forming units (CFU) from swab and the level of ATP readings ($r_{swab}=0.0303$, $p=0.63$), but hand culture and the level of ATP readings had significant correlation ($r_{hand}= 0.1345$, $p=0.03$). The mean log CFU for surfaces on both swab culture (1.27+/- 0.8, $p<0.0001$ versus 0.59+/-0.72, $p<0.0001$) and hand acquisition (1.61+/-0.61, $p<0.0001$ versus 0.87+/-0.64, $p<0.0001$) were significantly decreased from baseline on all surfaces with incomplete or complete removal of Dazo.

Conclusions: The methods to measure ATP bioluminescence and fluorescent dye removal as surrogate markers provide quick results which may be used in feedback and monitoring of housekeeping environmental disinfection. Higher levels of ATP may predict risk of hand contamination from the environment. However, both methods have limitations that may affect the correlation in surface bacterial load or hand contamination. More studies should be done to investigate these technologies.

Evaluation of balance, neurocognitive, and symptom scores of adolescent athletes who have suffered a head injury.

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Background

Concussion assessment and return to play guidelines are usually based on self-reported symptom scores, balance testing, and increasingly, neuropsychological testing. Return-to-play guidelines suggest the patient be completely asymptomatic not only while at rest, but also while participating in non-contact physical activity (running, cycling, etc.). It is important to recognize that the reporting of concussion symptoms may not always be reliable or accurate from an athlete. This is primarily due to the fact their desire to play outweighs the value of an honest response. This problem is addressed by using dual-task methodology. In 2005, Broglio stated: "*Dual-task methodology is a testing model that requires a person to simultaneously perform a cognitive and motor task. Currently, this is the closest paradigm to replicate sport performance to evaluate multiple systems concurrently."* The dual-task methodology that we utilized in this project involved adding a cognitive component to a basic balance test. The purpose of this study is to obtain balance-testing data on healthy, adolescent athletes to develop reference data and to analyze the longitudinal symptom scores and balance and neurocognitive testing used to evaluate concussion patients.

Methods

Approximately 300 young (14-22 yrs old), athletic individuals will take part in this study. Of that group, about 250 individuals will have suffered a concussion, while approximately 50 will have been free from a head injury for the past year. Four balance tests will be performed on a strain gauge force plate that will measure the center of pressure positional changes of the subjects. Their changes in cognitive and noncognitive COP will be measured.

Results

This study is ongoing, but basic preliminary data analysis shows the addition of a cognitive task impairs balance in both concussed and healthy individuals. However, there was a notable change in magnitude across the two groups. The area of the 95% ellipse increased by 47% in concussed individuals compared to 37% in healthy individuals. Likewise, the average velocity of concussed individuals increased 12% with the addition of the cognitive task and in healthy individuals it only increased 4%. A more in-depth statistical analysis will be applied once all the data has been collected.

Discussion

This data will provide a baseline upon which physicians can base their return-to-play guidelines. It will also evaluate the utility of the dual-task paradigm and it's use in the physician's physical exam. We will also be able to look at how dual-task performance correlates with other symptom checklists and neurocognitive scores.

Keynote Address

1:00-2:00 pm, Lee Med Room 111

Addressing Cancer Disparities Among American Indians Through Innovative Technologies and Patient Navigation: The Walking Forward Experience

Daniel G. Petereit, MD

ABSTRACT

Purpose/Objective(s): American Indians (AIs) present with more advanced stages of cancer and, therefore, suffer from higher cancer mortality rates compared to non-AIs. Under the National Cancer Institute Cancer Disparities Research Partnership Program (CDRP), we have been researching methods of improving cancer treatment and outcomes since 2002, for AIs in Western South Dakota, through the Walking Forward (WF) Program.

Materials/Methods: This program consists of a) a culturally-tailored patient navigation program that facilitated access to innovative clinical trials in conjunction with a comprehensive educational program encouraging screening and early detection, b), surveys to evaluate barriers to access c) clinical trials focusing on reducing treatment length to facilitate enhanced participation using brachytherapy and intensity modulated radiotherapy (IMRT) for breast and prostate cancer, as AIs live a median of 140 miles from the cancer center , and d) a molecular study (ATM - Ataxia telangectasia mutation) to address whether there is a specific profile that increases toxicity risks.

Results:

We describe the design and implementation of this program, summary of previously published results, and ongoing research to influence stage at presentation. Some of the critical outcomes include the successful implementation of a community based research program, development of trust within tribal communities, identification of barriers, analysis of nearly 400 navigated cancer patients, clinical trial accrual rate of 10%, and total enrollment of nearly 2,500 AIs on WF research studies.

Conclusions:

This NCI funded pilot program has achieved some initial measures of success. A research infrastructure has been created in a community setting to address new research questions and interventions. Efforts underway to promote cancer education and screening are presented, as well as applications of the lessons learned to other health disparity populations - both nationally and internationally.

Acknowledgments

The Medical Student Research Committee wishes to thank the following:

- The Office of the Dean of Sanford School of Medicine for funding the Summer Medical Student Research Fellowships and support of the Medical Student Research Forum;
- The participating medical students for their research efforts;
- The mentoring laboratories for providing guidance and support to the students;
- Dean Paul Bunger of Medical Student Affairs and the MSI and MSII course directors and faculty for facilitating the Research Forum.
- Darla Tassler, Wendy Pederson, Nicole Bennett, and Mike Olson of BBS for assisting with the abstract booklet, lunch, rooms, poster boards, and fliers.

Extracurricular Opportunities for Medical Students At Sanford School of Medicine

Medical Student Research Program

The School of Medicine provides funding in the form of a student stipend and funds for the mentoring laboratory to help cover the cost of supplies. Awards are available to both MD and MD/PhD students on the basis of competitive student research applications. Furthermore, awards are available to students in the summer prior to their first year of medical school and to students between their first and second years. Opportunities are available in basic or clinical research and at many of the SSOM campuses.

Scholarship Pathways Program

The Scholarship Pathways Program is an elective opportunity that was developed to enrich the student experience by promoting rigorous independent scholarship and scholarly excellence at Sanford School of Medicine and to produce leaders in medical education, research, and service.