underlies this network disruption, we have investigated the integrity of peri-neuronal nets (PNNs), part of the extracellular matrix of proteins that preferentially ensheathe inhibitory PV neurons and support their function. We observe a 60% decrease in intensity of PNNs ($n = 5$, $p = 0.005$), suggesting PNN integrity is impaired in amyloid-accumulating mice. Ongoing experiments into the activity and synaptic input to both inhibitory PV and excitatory pyramidal neurons seek to determine the effects of this PNN disruption on downstream micro-circuitry. DISCUSSION/SIGNIFICANCE OF IMPACT: These findings suggest that a preferential impairment to PNNs and inhibitory PV cells underlie hippocampal hyperexcitability in a mouse model of AD. As hippocampal network activity is critical for memory consolidation, these effects contribute to our understanding of memory disruption during early disease progression, which has been poorly understood to date. These findings provide a foundation for future in vivo studies employing optogenetic stimulation to this neuronal sub-type, to determine if restoring physiological network balance can ameliorate memory decline.

3147

Electroencephalographic suppression from anesthesia and cognitive recovery

Leonard Brian Hickman[1], ShiNung Ching, Mathias Basner, Wei Wang, Nan Lin, Max Kelz, George Mashour, Michael S. Avidan and Ben J. A. Palanca
[1]Washington University in St. Louis, Institute Of Clinical and Translational Sciences

OBJECTIVES/SPECIFIC AIMS: (1) Assess if the total duration of EEG suppression during a protocolized exposure to general anesthesia predicts cognitive performance in multiple cognitive domains immediately following emergence from anesthesia. (2) Assess if the total duration of EEG suppression in the same individuals predicts the rate of cognitive recovery in a three-hour period following emergence from anesthesia. METHODS/STUDY POPULATION: This was a non-specified substudy of NCT01911195, a multicenter investigation taking place at the University of Michigan, University of Pennsylvania, and Washington University in St. Louis. 30 healthy volunteers aged 20-40 years were recruited to receive general anesthesia. Participants in the anesthesia arm were anesthetized for three hours at isoflurane levels compatible with surgery (1.3 MAC). Multichannel sensor nets were used for EEG acquisition during the anesthetic exposure. EEG suppression was detected through automated voltage-thresholded classification of 2-second signal epochs, with concordance assessed across sensors. Following return of responsiveness to verbal commands, participants completed up to three hours of serial cognitive tests assessing executive function, reaction time, cognitive throughput, and working memory. Non-linear mixed effects models will be used to estimate the initial cognitive deficit and the rate of cognitive recovery following anesthetic exposure; these measures of cognitive function will be assessed in relation to total duration of suppression during anesthesia. RESULTS/ANTICIPATED RESULTS: Participants displayed wide variability in the total amount of suppression during anesthesia, with a median of 31.2 minutes and range from 0 minutes to 115.2 minutes. Initial analyses suggest that greater duration of burst suppression had a weak relationship with participants' initial cognitive deficits upon return of responsiveness from anesthesia. Model generation of rate of recovery following anesthetic exposure is pending, but we anticipate this will also have a weak relationship with burst suppression. DISCUSSION/SIGNIFICANCE OF IMPACT: In healthy adults receiving a standardized exposure to anesthesia without surgery, burst suppression appears to be a poor predictor of post-anesthesia cognitive task performance. This suggests that burst suppression may have limited utility as a predictive marker of post-operative cognitive functioning, particularly in young adults without significant illness.

3296

Endometrial cancer microbiome biomarker for disease detection and microbial role in the disease

Marina Walther-Antonio[1], Dana Walsh[1], Yuguang Liu[1], Janet Yao[1], Nicholas Chia[1], Heidi Nelson[1] and Andrea Mariani[1]
[1]Mayo Clinic

OBJECTIVES/SPECIFIC AIMS: Our primary objective is to determine whether the bacteria exerts its effect intra- or extra-cellularly. We have genomic and microscopy preliminary evidence indicating that the bacteria is capable of invading endometrial cells. Our secondary objective is to identify what type of impact the bacteria have on the host cells and whether they are capable of transforming the host cells from a benign into a malignant phenotype. We are currently testing a putative mechanism by which the bacteria may cause the overexpression of the hypoxia inducible factor (HIF), a hallmark of endometrial cancer. METHODS/STUDY POPULATION: We are utilizing our custom built optofluidics platform (microfluidics platform incorporated into an advanced microscope with optical laser tweezers) to isolate single cells from the endometrial tissues of 150 patients with and without endometrial cancer. We are utilizing single cell whole genome amplification followed by qPCR to identify if the bacteria is present intracellularly. We are coupling this procedure with standard microbiological invasion assays with endometrial cell line cultures and P.somerae. We are also utilizing our optofluidics platform to perform single cell transcriptomic amplification, followed by sequencing of cells invaded or in the presence of the bacteria to determine the impact in the transcriptome of the host cell. We are coupling this with western blots of factors hypothesized to be impacted by the bacteria in the overexpression of HIF. RESULTS/ANTICIPATED RESULTS: Based on our preliminary data we anticipate to find evidence that P.somerae is invading the host cells, in particular the cells in tumor tissues. We also expect to find that the intracellular presence of the bacteria is causing the overexpression of the HIF pathway, hence resulting in a cancerous phenotype. DISCUSSION/SIGNIFICANCE OF IMPACT: Our long-term goal is to develop primary prevention strategies that will reduce endometrial cancer incidence rates. A confirmation of our hypothesis could suggest that it is sufficient for endometrial cancer prevention efforts to eliminate P.somerae, in line with gastric and cervical cancer efforts. It could also mean that targeting P.somerae in cancer treatment is necessary to contain the disease and prevent recurrence.

3420

Estradiol levels are elevated in older men with diffuse cutaneous SSc and are associated with decreased survival

DeAnna Baker Frost[1], Bethany Wolf[1], Christine Peoples[2], Jessica Fike[2], Katherine Silver[1], Maureen Laffoon[2], Thomas A. Medsger Jr.[2] and Carol Feghali-Bostwick[1]
[1]Medical University of South Carolina and [2]University of Pittsburgh

OBJECTIVES/SPECIFIC AIMS: Our objective was to examine serum E2 levels in dcSSc males in relation to disease characteristics

https://doi.org/10.1017/cts.2019.239 Published online by Cambridge University Press

(i.e autoanitbody profile and internal organ involvement) and its impact on survival. METHODS/STUDY POPULATION: We measured serum E2 levels in 83 dcSSc men >50 years old from the University of Pittsburgh Scleroderma Center and healthy controls of similar age. Using statistical modeling, we examined the associations between circulating E2 levels, internal organ involvement, autoantibody profiles, and survival. RESULTS/ANTICIPATED RESULTS: Male dcSSc patients had significantly higher serum E2 levels compared to healthy male controls and compared to dcSSc post-menopausal women of similar age. Male dcSSc patients with high serum E2 levels had significantly more heart involvement and worse survival. Using Cox regression modeling for risk of death, increasing serum E2 levels in anti-Scl-70 antibody positive dcSSc males were associated an increased risk of death. DISCUSSION/SIGNIFICANCE OF IMPACT: DcSSc male patients have higher levels of E2 compared to healthy controls and dcSSc postmenopausal women. Elevated serum E2 levels in dcSSc males >50 are associated with heart involvement and, if anti-Scl-70 antibody positive, worse survival. Our current study expands on our previous work, not only that that E2 exerts pro-fibrotic effects on skin, but also internal organ involvement, overall survival. These data suggest an important role of estrogen imbalance in SSc.

3248

Fluorescence-Guided Neurosurgery with 5-Aminolevulinic-Acid and Second-Window-Indocyanine-Green: A murine model and investigation into suitable cell lines.

Steve Cho[1], John Y.K. Lee and Saad Sheikh
[1]University of Pennsylvania School of Medicine

OBJECTIVES/SPECIFIC AIMS: This study aims to understand the utility of 5-ALA and SWIG in detecting areas of neoplasm in a murine model of GBM. Primary outcome is the distribution of the two dyes in comparison to the true tumor extent; the sensitivity, specificity, PPV, and NPV of both dyes will be calculated. The secondary outcome is the suitability of existing cell-lines used for GBM research for studies in fluorescence-guided surgery. METHODS/STUDY POPULATION: Two cell lines are used for this research: U87, derived from human GBM; and GL261, derived from rodent stem cells. U87 are implanted intracranially into 6-week old athymic, nude, female mice, while GL261 are implanted intracranially into 10-week old female C57BL/6 mice. The mice are weighed every 3 days to monitor health and bioluminescence imaging is performed between 7-10 days after implantation to confirm tumor implantation and monitor tumor growth. The mice are sacrificed between 10-21 days after implantation. 5mg/kg of intravenous ICG is administered 24-hours prior to harvest and 250mg/kg of intraperitoneal 5-ALA is administered 3-hours prior to harvest. Once the mice are sacrificed, their brains are quickly harvested and placed in cold formalin. Using a high-resolution Odyssey CLx scanner, near-infrared fluorescence from ICG is captured in coronal cross sections of the brains through the tumor. Similarly, 5-ALA fluorescence is imaged using a 405nm LED excitation source and 610-690nm bandpass filter. Afterwards, slices of the brain are stained with H&E, which serves as the gold-standard of the extent of tumor. Images from ICG, 5-ALA, and H&E can then be compared using ImageJ to compare the extent of tumor to the distribution of the dyes. RESULTS/ANTICIPATED RESULTS: In separate, previous studies in humans, both 5-ALA and SWIG have demonstrated utility in detecting residual neoplasm in HGG resections. In general, 5-ALA is more specific for areas of neoplasm, while SWIG is more sensitive. Thus, I anticipate that in this study, SWIG will show a greater distribution than 5-ALA, with SWIG distributing to areas beyond the tumor and 5-ALA distributing within, but not completely covering, the tumor. SWIG's sensitivity and NPV for detecting tumor should be >90%, while its specificity and PPV may be closer to 50%. For 5-ALA, specificity and PPV should be close to 80-90%, but its sensitivity and NPV may be <50%. In terms of cell-line, preliminary results suggest that U87 cells are not suitable for research involving 5-ALA. We suspect that this is partly due to the limited infiltrative nature of U87 cells; in fact, the cells form a spherical mass, imitating metastases rather than true HGGs. The U87 masses do not have significant vascularity, which likely limits the amount of 5-ALA that can distribute to inside the tumor. DISCUSSION/SIGNIFICANCE OF IMPACT: 5-ALA is currently the only FDA-approved agent for fluorescence-guided neurosurgery. However, it has multiple limitations, which ultimately results in its low sensitivity and NPV. Our novel technique, which has demonstrated much higher sensitivity at the cost of specificity, offers an alternative that may help surgeons better achieve total resections in the operating room. These two agents have not been compared directly in humans or mice. Thus, this experiment sets up an important precedent, on which a human clinical trial comparing the two agents' effects on resection rates and patient outcome can be performed. Ultimately, this work will lay the foundation for future research into fluorescence-guided neurosurgery, both in the visible and NIR spectrum.

3505

Fracture Targeted Parathyroid Hormone Agonist As An Effective Pharmaceutical For Bone Repair in Mouse and Canine Models

Jeffery Jay Howard Nielsen[1], Stewart A. Low and Philip S. Low
[1]Purdue University; Purdue University

OBJECTIVES/SPECIFIC AIMS: The primary objective of this study was to evaluate the performance of a bone fracture targeted systemically administrable bone anabolic as a potential therapeutic for bone fracture repair. Currently all bone fracture repair therapeutic require local administration during surgery. However, the population that need the most assistance in repair bone fractures are not eligible for surgery. So, it was our goal to design an inject-able therapeutic to assist in bone fracture repair to reduce the invasiveness. The injectable nature of it allows for repair administration of the bone anabolic and for therapeutic effect throughout the entire bone fracture healing process. Targeting it to the bone fracture site reduces the toxicity and increases the efficacy. METHODS/STUDY POPULATION: METHODS To achieve the above objective, a bone mineral-(hydroxyapatite-) targeting oligopeptide was conjugated to the non-signaling end of an engineered parathyroid hormone related protein fragment 1-46 with substitutions at Glu22,25, Leu23,28,31, Aib29, Lys26,30 (ePTHrP). The negatively charged oligopeptide has been shown to target raw hydroxyapatite with remarkable specificity, while the attached PTHrP has been demonstrated to induce sustained and accelerated bone growth under control of endogenous morphogenic regulatory factors. The conjugate's specificity arises from the fact that raw hydroxyapatite is only exposed whenever a bone is fractured, surgically cut, grafted, or induced to undergo accelerated remodeling. The hydroxyapatite-targeted conjugate can therefore be administered systemically (i.e. without invasive surgery or localized injection) and still accumulate on the exposed hydroxyapatite at the fracture site where it accelerates the healing process

https://doi.org/10.1017/cts.2019.239 Published online by Cambridge University Press