

underlies this network disruption, we have investigated the integrity of peri-neuronal nets (PNNs), part of the extracellular matrix of proteins that preferentially ensheathes 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.

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### Electroencephalographic suppression from anesthesia and cognitive recovery

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**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.

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

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**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.

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

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