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The Role of Microbiome in Pain Modulation

Dr. Savidge is Associate Professor in the Department of Pathology & Immunology at Baylor College of Medicine and is the Associate Director of the Texas Children's Microbiome Center. His research interests include studying microbial-neuroimmune interactions in the gastrointestinal tract and nervous systems. This work has established new disease susceptibility biomarkers of abdominal pain in functional gastrointestinal disorders, as well as identifying new host-microbiome signaling mechanisms that modulate chronic pain which are being pioneered as "precision microbial therapeutics".

Abstract: The gut microbiome is receiving increasing attention as a modulator of neurological disease, including chronic pain. Well accepted as a regulator of visceral pain by altering dorsal root ganglia neuronal excitability, the gut microbiota also plays an important role in modulating inflammatory and neuropathic pain, migraine, and opioid tolerance. These findings offer unique therapeutic scope because the gut is more externally modifiable compared to central or peripheral nervous systems, and treatments addressing pain through modulation of the gut microbiota (e.g., targeted microbial therapy) may have long-term benefits for chronic pain management. Although gut microbiota composition and function is known to be heavily influenced by diet and other malleable factors, a major deficiency in the field is understanding which microbes are involved and how they are beneficial to patients with chronic pain. Targeted metagenomic sequencing is an emerging strategy to survey pain-specific microbes for clinical diagnosis and prognosis. However, this approach often yields inconsistent or conflicting results due to inadequate study power and experimental bias. A comprehensive re-analysis of individual patient microbiome datasets using a bioinformatics pipeline that compensates for technical and demographic bias offers tremendous potential in identifying microbiome features that can reliably alleviate or induce chronic pain at a population scale-level. We designed Taxa4Meta for accurate taxonomic binning and metagenome function prediction of microbiome amplicon data acquired from different sequencing strategies. We used this workflow to facilitate combined meta-analysis of individual microbiome surveys to define the healthy human

microbiome, in order to reliably identify pain related signatures. Taxa4Meta was then used to profile 5,691 matched controls and patients with functional gastrointestinal disorders (irritable bowel syndrome), neuropathic and inflammatory pain across North America, Europe, Asia and Australasia. Combined “pan-microbiome” profiles generated from individual microbiome surveys identified distinct enterotype clusters that were significantly associated with different types of gastrointestinal pain, anxiety and depression. By linking functional omics to disease-specific enterotypes, we identified new regulatory neurotransmitter circuits associated with chronic gastrointestinal pain, which were confirmed in humanized animal models.