The Brain-Gut Axis: Differential Expression of DNA Repair Pathways in Brain and Mucosal Gut Tissue

Meryl S. Lillenes¹, Mari Støen¹, Tahira Riaz², Trond Espen Detlie³, Alfredo Rabano⁴ and Tone Tønjum¹,²*

¹ Department of Microbiology, Oslo University Hospital, Norway
² Department of Microbiology, University of Oslo, Norway
³ Department of Gastroenterology, Akershus University Hospital, Lørenskog and Campus Ahus, Institute of Clinical Medicine, University of Oslo
⁴Fundación Centro Investigación Enfermedades Neurológicas (CIEN), Spain

*Email of Presenting Author: tone.tonjum@medisin.uio.no

The neurological and gastrointestinal systems and their biology are tightly interconnected, interacting with and influencing each other through multiple bidirectional signaling pathways. The abundant human gut microbiome influences the physiology of all organs including the central nervous system (CNS), and the CNS in turn modulates gut function, beyond the effects of the vagus nerve. Therefore, imbalance in the brain-gut axis could correlate with incipient pathology in the CNS and/or the gastrointestinal tract. We asked if and how the gut microbiome modulates susceptibility to progressive neurodegenerative Alzheimer’s disease (AD). The primary hypothesis we are testing is if imbalance in the brain-gut axis promotes neurodegeneration or gastrointestinal dysfunction or both.

The proteomic and transcriptomic expression profiles were monitored in post-mortem human brain tissue and gut mucosal biopsies from AD patients, patients with inflammatory bowel disease (IBD) and healthy controls. In terms of DNA repair, predominant base excision repair (BER) was expressed in brain tissue, while nucleotide excision repair (NER) was more highly expressed in the gut mucosa. This differential expression pattern reflects local stress and organ environments, including the nature of non-replicating versus replicating cells as well as the state of a sterile organ versus that of an organ with a rich microbiome. Different DNA repair responses were evident in the prodromal versus late stages of AD, in the various brain parts and in IBD. We have previously shown that signature reactions in BER patterns in mice brains appear before AD pathology is evident and may represent a response to increased oxidative stress. These studies extend our findings on DNA repair and bioenergetics in AD and IBD, and will encompass the potential contribution of the gut microbiome in influencing the brain-gut interactions.