“Investigating variability of *Fusobacterium nucleatum* virulence depending on host cells and their environments: implications for colorectal cancer”

From birth, microbes colonize our bodies. Most either directly or indirectly benefit us; some are less mutualistic. *Fusobacterium nucleatum* commonly resides within the human mouth but has been isolated from diseased extra-oral body sites, including colorectal carcinomas. Although research has focused on identifying potential *F. nucleatum* virulence determinants, the extent of its disease involvement is unclear. Multiple studies have applied murine models of *F. nucleatum*-linked colorectal cancer, yet whether human and murine cells respond comparably remains unknown. Additionally, the surrounding microbiome may influence fusobacterial virulence: other opportunists may work synergistically to elicit a cancer-promoting response, while a normal colonic community may dissuade pro-cancerous responses. This proposal aims to [1] justify the use of murine models in *F. nucleatum*-associated colorectal cancer studies, and [2] further the understanding of *F. nucleatum* in the context of the colonic microbiome. Various noncancerous immortalized primary human cell lines, and equivalent murine cell lines, will be co-incubated *in vitro* with *F. nucleatum* to characterize the transcriptional response of host and bacterium in tandem. Additional colorectal cancer-associated bacteria will be isolated from cancerous colonic biopsies and co-incubated *in vitro* with *F. nucleatum* and a noncancerous human colonic cell line to investigate potential pro-cancerous bacterial synergy. Finally, metabolites from a normal colonic bacterial community will be applied during fusobacterial and human colonic cell co-incubation to determine whether colonic microbiota influence *F. nucleatum* virulence. Altogether, the results of the experiments described will illuminate whether host cells and their environments modulate *F. nucleatum* virulence.