

Title: Quorum Quenching Decreases Metastatic Rate in a Colorectal Cancer AKPS Organoid Model

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The gut microbiome plays a key role in human health, and its composition has been linked with many diseases, including colorectal cancer (CRC). The microbiome is associated with CRC tumor growth and metastasis as well as patient outcomes. We hypothesized that disrupting communication within the gut microbiome and between the gut microbiome and host cells with quorum quenching (QQ) enzymes may affect CRC metastasis. These enzymes degrade quorum sensing (QS) chemicals used by bacteria within the gut microbiome to communicate and regulate gene expression. We administered two such QQ enzymes: GcL, an enzyme with a broad substrate specificity, and SsoPox, which is active on longer-chain QS chemicals. After being injected with an AKPS CRC tumor organoid (APC, Kras, P53, and Smad4 mutations), male mice were separated into one of two treatment groups (GcL or SsoPox) or a water control (DW), and given water with their assigned QQ enzyme at 1mg/mL ($n = 10$). Mice were housed individually for a period of eight weeks or until moribund, at which point a necropsy was performed, with blood and tissue collected. Fecal samples were collected weekly throughout the experiment. At time of necropsy, 3 of 7 DW control mice had visible metastases, while only 1 of 18 treatment mice, a GcL mouse, metastasized (McNemar's test, $p = 0.002$). When GcL and SsoPox were analyzed individually, differences in metastatic rate approached significance by Cochran-Armitage trend test ($p = 0.057$). Amplicon sequencing is ongoing, but considering how GcL has been previously shown to have reduced effects on male mice, these results are a promising first step in our investigation of QQ treatments for CRC.