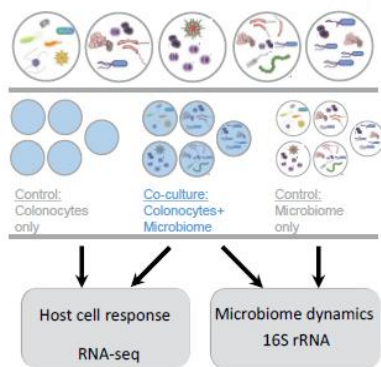


HIGHLIGHT PAPER: Gut microbiota has a widespread and modifiable effect on host gene regulation - Richards, A.L. et al. October 2018



The composition of the gut microbiota is related to several diseases and in mice was shown to impact gene expression and regulation. To investigate the effects of inter-individual variation in the gut microbiome on human gene regulation, the scientists used an *in vitro* system in which colonic epithelial cells (colonocytes) were treated

with live gut microbiota extracted from 5 healthy individuals. Changes in gene expression were assessed at different time points after exposure to the microbiota, through RNA-seq (Figure). Results showed that inter-individual variation in the microbiome can lead to different gene expression responses in host cells. To test whether the observed gene expression changes may be attributed to the abundance of specific taxa, bioinformatics tools (DESeq2) was used to associate host transcripts to the abundance of specific microbial taxa. Genes were clustered into 2 groups according to their functions and to the microbial genera they positively correlate with. One of the genera associated with changes in the expression of a large number of genes, *Collinsella*, was used to test whether a specific microbe can impact host gene expression. Colonocytes were treated with a microbiota in which *Collinsella* was added in titrated doses, and RNA-seq validated that gene expression changes depended on *Collinsella* abundance. To investigate the regulatory mechanisms behind the observed phenomenon, changes in chromatin accessibility were assessed by ATAC-seq in microbiota-inoculated colonocytes. Although few differentially accessible regions were identified, they were found enriched near genes that change their expression following treatment and also transcription factors were found enriched in these regions. This work showed that it is possible to influence host cell regulatory response by manipulating the microbiome composition and provided information valuable to determine which microbes may be most beneficial for future microbiota-based health therapies.