Commensal microbe gene selection platform for efficient gut colonization

Technology #cu14197

Commensal gut microbes play an important role in maintaining gut homeostasis. Despite their prominent use in probiotics, little is known regarding their colonization of the mammalian gut, limiting the efficiency of these products. This technology, called Functional Metagenomic Selection and Sequencing (FUMES-seq), provides a strategy to quantitatively measure increases in microbial fitness, thus identifying genes enriched during host gut colonization. By determining which genetic factors lead to successful gut colonization, this technology may both improve our understanding of disease states caused by perturbations in the gut microbiome and lead to optimal probiotic therapies. Therefore, this technology represents an efficient method of identifying and selecting metabolically relevant genes capable of improving digestive medicine.

Versatile genomic strategy for identifying clinically beneficial genes in the gut microbiome

This technology achieves the difficult task of identifying which genes within probiotic microbes are responsible for efficient gut colonization. FUMES-seq begins by cloning small DNA fragments that span the entire genome of a metabolically relevant, Gram-negative commensal microbe into E.coli, which acts as a carrier for the gene 'library'. These E. coli are introduced by gavage into healthy, germ-free mice over the period of a month. The selected library is extracted from fecal pellets and subjected to Illumina deep sequencing analysis, which identifies and quantifies genes that are enriched in the mouse gut. The physiological relevance of the enriched genes is assessed by investigating the metabolic pathways stored in the readily available KEGG and COG databases. Genes that feature prominently in the listed metabolic pathways are likely to improve gut colonization, and can be selected for and enriched in vivo or can be synthetically engineered; thus, they can be used in future probiotic formulations to yield highly efficient gut colonizers that can out-compete pathogenic bacteria. While E. coli is used as a Gram-negative recipient for Gram-negative DNA sources, B. subtilis or C. butyricum can be used as Gram-positive DNA carriers, allowing this technology to screen both kinds of bacteria and cover a wide spectrum of potentially beneficial microbes. Additional versatility can be incorporated by introducing treated mice to different diets, which can lead to diverse sets of beneficial colonization genes.
Preliminary FUMES-seq results have shown a statistically significant enrichment for three metabolic genes from a gram-negative, commensal microbe that conferred improved fitness in both culture conditions and within the mouse gut.

**Lead Inventor:**

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**Applications:**

- Facilitate basic research into mechanisms of gut microbe colonization
- Systematic method of identifying genes that enhance bacterial fitness in the mammalian gastrointestinal (GI) tract
- Can yield new probiotic compositions comprising microbes enriched for beneficial gut colonization genes to improve gut health
- Treated mice can be used to test drug compounds against pathogenic gut colonization

**Advantages:**

- Utilizes public databases for analyses
- Uses numerous commercially available reagents/equipment
- Can act as both a clinical and basic research tool
- Highly versatile - can be used with both Gram-negative and -positive bacterial carriers

**Patent Information:**


Tech Ventures Reference: IR CU14197

**Related Publications:**


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