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Commentary

A Comprehensive Overview of Biosynthetic Gene Clusters in the Human Microbiome

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DESCRIPTION

The human microbiome is made up of thousands of bacterial strains and hundreds of distinct bacterial species, and it varies from person to person and between various body regions in the same person. Massive efforts have been conducted over the past ten years to sequence human microbiota isolates and Meta genomic material from diverse body locations. These studies have provided a fundamental knowledge of the "healthy" human microbiome and have linked diseases including obesity, diabetes, bacterial vaginosis, and Crohn's disease to variations from the healthy condition. Recent research has started to look at the human microbiome from a functional perspective, revealing the direct molecular connections between host and bacterium.

Recent research demonstrates that the pathophysiology of obesity is significantly influenced by gut microorganisms. Children's obesity was reduced by diet-induced gut microbiota changes, and many intestinal microorganisms, such as Actinobacteria, have been strongly linked to obesity. On occasion, a microorganism linked to obesity that has been identified in one study cannot be confirmed in others. For instance, whereas some research showed no link between the aforementioned phyla and obesity, some indicate a higher *Firmicutes* to Bacteroidetes ratio in obese people. Enzymes that are encoded by biosynthetic gene clusters regulate the manufacture of Small Molecules (SMs) Biosynthetic Gene Clusters (BGCs). According to an examination of the genes surrounding these clusters, BGC61 is present in the major member of the human gut microbiome, *Eubacterium rectale*, whereas *Actinomyces* and Streptococcus are home to two and five, respectively, of the oral meta genomic thiopeptide gene clusters. The thiopeptide BGCs have an abnormally high prevalence of transposases and phage integrases (70%) and, in at least one instance, we were able to demonstrate bioinformatically and experimentally that the cluster is located on on a plasmid, indicating a possibility for mobility. At one of the body locations, four of the thirteen thiopeptide BGCs are found in > 20% of the HMP samples, and 155/406 HMP oral samples (38%) contain at least one thiopeptide BGC.

Numerous bioactive SMs with antibacterial potential have been genomic mining of gut microbiota BGCs. The majority of the genes for fundamental biosynthetic enzymes, such Polyketide Synthase (PKS) and nonribosomal peptide synthetase, have been found in microbial BGCs (NRPS). The NIH Human Microbiome Project found over 3000 small molecule BGCs, among which lactocillin shown structural similarities to various clinically used antibiotics. The *in vivo* expression was confirmed by the metatranscriptome sequencing study. These tiny chemicals modify the makeup of the gut microbiome in addition to preventing the development of rival bacteria. Microbial SMs have also been linked to human physiology, albeit it is unclear exactly how they contribute to obesity.

Discovering biosynthetic gene clusters in bacterial genome sequences has grown to be a potent approach for the discovery of natural products. Methodically analyzing 2,430 reference genomes of the human microbiota from a variety of body regions. For a variety of small-molecule classes, including saccharides, Nonribosomal Peptides (NRPs), Polyketides (PKs), ribosomally encoded and Post Translationally Modified Peptides (RiPPs), NRPs-independent siderophores, and hybrids thereof, Cluster Finder identified over 14,000 biosynthetic gene clusters (average of 6 gene clusters per genome).

The effectiveness of linking genes to activities relevant to the microbiome has been demonstrated in seminal investigations of gene clusters encoding catabolic pathways from the microbiota. The purpose of the Bactericides gene clusters that break down fructans and xyloglucans, respectively. Both discoveries provide crucial new information on the involvement of specialized catabolic modules in the gut community's struggle for food niches and show how a mechanistic knowledge of gene cluster activity can be used to anticipate how members of the gut community will react to dietary changes. Although the

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understanding of BGCs in the human microbiota is currently less established, it shows tremendous promise for providing comparable insights into the interactions between microbes and their hosts and other microbes. The BGCs' small-molecule byproducts are frequently employed in medical settings and make up a sizable portion of the chemical vocabulary used in interspecies interactions. The fact that the human microbiome contains hundreds of widely dispersed BGCs with unknown functions, and they serve as a model for future experiments aimed at identifying physiologically active small compounds. These compounds provide a potentially rich supply of medicines as well as a viable starting point for research into the molecular mechanisms underlying microbe-host interactions.