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Editorial Open Access

The Human Microbiome as a New Source for Antibiotic Discovery

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Editorial

Bacterial infection especially antibiotic-resistance "superbugs" (e.g., methicillin- and vancomycin-resistant *Staphylococcus aureus*) has caused a huge global threat of public health [1-3]. Bacterial infection currently kills more people than HIV, and will kill more people than cancer in the coming decades [4,5]. Nevertheless, new antibiotics, one of the most important treatment options for bacterial infection, unfortunately continue to be limited because the pace of antibiotic discovery and development is dramatically declining [6]. To meet the urgent need for novel drugs with combating the "superbugs", researchers are continuing to explore new natural sources such as marine resource [6], metagenome [2], and uncultured microorganisms [1] that were missed in previous screens [4].

The human microbiota (~100 trillion microbes) is the full collection of microorganisms including bacteria, fungi, and archaea that reside inside and on human tissues and biofluids such as skin, lung, and gastrointestinal tracts. The human microbiome (~8 million genes) refers to an aggregate of genes in the human microbiota [7]. Human microbiome has been considered as a counterpart to the human genome, which encodes at least 100 times as many genes as the entire human own genome [8]. Our understanding of the relationship between human and its symbiotic microbiota continues to revolutionize by the persistent studies of the human microbiome [9]. More and more studies demonstrated that the microbiota is essential for human health such as nutrition, neurobiology, immunology, and various diseases like obesity and diabetes [9,10].

With the rapid progress of human microbiome project, numerous studies showed that human microbiome has a hugely diverse and dynamic [5]. Nevertheless, contrary to the immerse diversity of human microbiome, human microbiota has only been found to produce bacteriocins with antimicrobial activities against closely related bacteria [11], not produce complex bioactive compounds. In 2014, Donia et al. used a systematic approach by combination of chemistry, genetics, metagenomics, and metatranscriptomics to identify >14,000 biosynthetic gene clusters responsible for 3,118 small-molecule from the genomes of human microbiome [12], suggesting that human microbiome as a new resource has the application potential for finding new antibiotics. More importantly, they discovered that thiopeptides, a class of ribosomally synthesized antibiotics in clinical trials, are widely distributed in the human microbiota. A new thiopeptide antibiotic, lactocillin, isolated from the vaginal microbiota, has potent antibacterial activity against a range of Gram-positive vaginal pathogens [12].

The work by Donia et al. [12] strongly inspired us that human microbiome could harbor rich and diverse bioactive compounds for human health. This opinion was further confirmed this year because of two novel complex bioactive compounds humimycins [13] and lugdunin [5] recently isolated from human microbiome. Humimycins and lugdunin, both synthesized by NRPS (non-ribosomal peptide synthetase) gene clusters, had broad antibacterial activities against human-associated commensal and antibiotic-resistance "superbugs" [5]. Despite the above works have significant effect on antibiotic discovery from human microbiome, new approaches and techniques are still required for finding more structurally unique antibiotics. I believe, with the better understanding of human microbiome in the next decade, bioprospecting of human microbiome has a great application potential for the discovery of new antibiotics.

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