

## **A comprehensive genome catalog of the human oral microbiome expands our understanding of its phylogenetic diversity and clinical implications**

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The human oral microbiome is essential for oral health and significantly influences overall well-being. Existing genome reference databases mainly focus on isolate genomes, which fail to capture the diversity of non-isolate genomes present in the oral cavity. To address this shortcoming, we developed the Human Reference Oral Microbiome (HROM) catalog. This resource contains 5,113 species-level genomes from a total of 145,149 genomes, with 67% being near-complete or high-quality species. HROM spans 21 phyla, including Patescibacteria from the candidate phyla radiation (CPR). It surpasses current databases by offering higher classification accuracy and a more detailed representation of the oral microbiome, particularly in detecting fast-evolving species. Through genome-wide analysis, we uncovered unique functional traits of the oral microbiome, such as the abundance of fast-evolving species and their reduced DNA repair capabilities. Additionally, notable compositional differences were observed between the oral and gut microbiomes. Our findings highlighted specific biological traits of species shared between the gut and mouth, including greater metabolic independence and sporulation abilities. We also detected the potential enrichment of certain bacterial sub-groups in the gut microbiomes of individuals with various diseases. Comparative genomic analysis revealed that Patescibacteria associated with mammalian hosts, including those cataloged in HROM, form a distinct clade from environmental Patescibacteria. This catalog will be a valuable tool for advancing research into the human oral microbiome.