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Intraspecific diversity of Microbial Anti-inflammatory Molecule (MAM) from *Faecalibacterium prausnitzii*

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The commensal bacterium *Faecalibacterium prausnitzii* has unique anti-inflammatory properties, at least some of which have been attributed to its production of MAM, the Microbial Anti-inflammatory Molecule. Previous phylogenetic studies of *F. prausnitzii* strains have revealed the existence of various phylogroups. We address the question of whether MAMs from different phylogroups display distinct anti-inflammatory properties. We first performed wide-scale identification, classification, and phylogenetic analysis of MAM-like proteins encoded in different genomes of *F. prausnitzii*. When combined with a gene context analysis, this approach distinguished at least 10 distinct clusters of MAMs, providing evidence for functional diversity within this protein. We then selected 11 MAMs from various clusters and evaluated their anti-inflammatory capacities *in vitro*. A wide range of anti-inflammatory activity was detected. MAM from the M21/2 strain had the highest inhibitory effect (96% inhibition), while MAM from reference strain A2-165 demonstrated only 56% inhibition, and MAM from strain CNCM4541 was almost inactive. These results were confirmed *in vivo* in murine models of acute and chronic colitis. Our study provides insights into the family of MAM proteins and generates clues regarding the choice of *F. prausnitzii* strains as probiotics for use in targeting chronic inflammatory diseases.