Production of antimicrobial peptide, protegrin-1 in Pichia pastoris and its protection against DSS-induced colitis

Bacterial resistance to conventional antibiotics is a growing public health concern. One of the means to cope with this issue is to use antibiotic alternatives. Protegrin-1 (PG-1) is a porcine cathelicidin Antimicrobial Peptide (AMP) that can exert its activity against a broad range of microorganisms including bacteria and enveloped viruses, allowing it to be an attractive candidate for therapeutic use. In addition, as the peptide is an integral part of the innate immune system, protegrins may have other functions such as immune stimulating or modulating effect, similar to its human cathelicidin counterpart. Little is known about the involvement of porcine cathelicidin in this regard. We have generated codon-optimized proform PG-1 and mature PG-1 for expression in Pichia pastoris yeast. In this study, we further investigated the potential inflammatory modulating and protective role of PG-1 in well-established Dextran Sulfate Sodium (DSS)-induced colitis model in mice. Body weight, clinical symptoms, histology and gene expression of colonic tissues were assessed. Relative expression of inflammatory cytokines (COX-2 and TNF-a) was significantly reduced in protegrin treatment groups (p<0.05). Protegrin treatment prevented significant body weight loss and improved Disease Activity Index (DIA) scoring (p<0.05) compared to the untreated DSS-control mice. Histological analyses indicate reduced mucosal erosion and sub-mucosa inflammation in protegrin-treated groups. Overall, oral administration of protegrin was demonstrated to be protective against colitis induction in mice. Histological and gene expression results are reflective of the phenotype observed in protegrin DSS-treated mice and the controls. Resulting data establishes the potential use of protegrins to modulate intestinal health in vivo.

Biography

Julang Li is a Professor at the Department of Animal Bio-Science, University of Guelph, Canada. Her research program balances both the fundamental and applicable aspects of animal and biomedical science. Her fundamental research focuses on studying the regulation of follicular development and oocyte maturation. The more applicable research program in her laboratory aims to enhance animal and human health via biotechnological approaches. In this regard, they have been using food grade bacteria as a bioreactor and vehicle to produce and deliver recombinant proteins such EGF and antimicrobial peptide to the intestine for enhancing early weaned pig development.

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