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(54) Title: REG3ALPHA FOR USE IN THE PROTECTION OF OXYGEN SENSITIVE GRAM-POSITIVE BACTERIA

(57) Abstract: The invention concerns a Reg3 α polypeptide (also known as Hepatocarcinoma-Intestine- Pancreas/Pancreatitis Associated Protein (HIP/PAP)) for use in the protection of oxygen sensitive gram-positive bacteria, compositions comprising the polypeptide and their use. The inventors have shown that an increase in the concentration of the h Reg3 α lectin into the gastrointestinal tract (GIT) lumen of hReg3 α -transgenic mice induced significant changes in the composition of the gut microbiota, and dramatically improved host resistance to intestinal inflammation. hReg3 α exerted a potent antioxidant activity on intestinal epithelial cells during colitis, and in particular the ROS scavenging activity, in particular, by promoting the survival of highly oxygen sensitive bacteria. Inventors also showed that h Reg3 α -transgenic mice resist better to DSS-induced colitis after antibiotherapy. Thus, the invention concerns a Reg3 α polypeptide for use in the protection of oxygen sensitive gram-positive bacteria, notably the Ruminococcaceae, such as *Faecalibacterium prausnitzii*, and/or the Lachnospiraceae, such as *Roseburia intestinalis*; pharmaceutical compositions comprising the polypeptide and their use; and the use of this polypeptide for promoting ex vivo growth of oxygen sensitive gram-positive bacteria. The Reg3 α polypeptide may be used for preventing or treating microbiota-related disease and/or disorder, particularly selected from inflammatory bowel disease (IBD), colitis, gastrointestinal infections, irritable bowel syndrome and other gastrointestinal functional diseases, gastrointestinal tract cancer, metabolic syndrome and obesity, diabetes, liver diseases, allergic diseases, neurodegenerative diseases and psychological disorders.

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