THERAPY

New diet-regulated, live bacterial drug-delivery system for bowel disorders

The human commensal colonic bacterium *Bacteroides ovatus* has been successfully engineered to secrete human keratinocyte growth factor 2 (KGF2) in the inflamed colon in response to the dietary plant polysaccharide xylan. This drug-delivery system could have "…wide applications for the delivery of … therapeutic agents to the gastrointestinal tract for the treatment of various [bowel] diseases" says Simon Carding, corresponding author.

Benefits over existing live bacterial drug-delivery systems are regulated drug secretion and the fact that *B. ovatus* dies quickly when exposed to oxygen, avoiding possible environmental contamination.

Carding and colleagues used a mouse model of acute colitis to show that human KGF2—a potential IBD therapy—could be produced by genetically engineered *B. ovatus* in the inflamed colon when dietary xylan was given. KGF2 produced by *B. ovatus* in response to xylan was biologically active and had prophylactic and therapeutic effects on the experimental colitis. Weight loss, rectal bleeding, neutrophil infiltration and proinflammatory cytokine expression were reduced, stool consistency improved, healing of colonic epithelial damage accelerated and production of mucin-rich goblet cells promoted. The development of intestinal inflammation was also limited. In the mouse model, KGF2 was found to have equal therapeutic efficacy to steroids and delivery by *B. ovatus* was more effective than systemically administering KGF2.

"The next step," concludes Carding, "is to bring this technology to phase I clinical trials."

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Original article Hamady, Z. Z. R. *et al.* Xylan-regulated delivery of the human keratinocyte growth factor-2 to the inflamed colon by the human anaerobic commensal bacterium *Bacteroides ovatus*. *Gut* **59**, 461–469 (2010)

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