A. Homeostatic balance of microbiota-nociceptor-immune system B. Disruption of nociceptor function results in dysbiosis and exacerbated drive intestinal damage and inflammation b. Gram+ Clostridium spp. are sufficient to promote intestinal tissue protection in intestinal damage and inflammation in nociceptor-disrupted mice nociceptor-sufficient mice Gut lumen Clostridium Clostridium Dysbiosis (Expansion of Gram+) Microbial homeostasis Mucus Mucus Immune cells Immune cells TRPV1+ TRPV1 TRPV1+ nociceptor TRPV1 Crypt

0

nociceptor

Nociceptor function	Normal	Disrupted	Disrupted	Normal
Microbiota status	Normal	Dysbiosis	Clostridium spp mono-colonized	Clostridium spp mono-colonized
Inflammation/tissue protection	Homeostasis	Severe inflammation	Severe inflammation	Tissue protection

nociceptor

nociceptor