Researchers identify key player in the genesis of human intestinal immunity

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The trillions of harmful bacteria that populate the human gut represent a continuous threat to our health. Proper intestinal immune function creates a protective barrier between us and the extensive microbial ecosystem in our intestines. Now, researchers at the University of North Carolina School of Medicine have identified the structures that serve as the foundation for the development of the human intestinal immune system.

Specialized immune structures in the intestines, referred to as gut-associated lymphoid tissues, or GALT, are critical components of intestinal immune function. When viruses such as HIV or autoimmune disorders such as inflammatory bowel diseases damage the GALT, intestinal immune function is compromised. The millions of people suffering from such diseases would benefit from therapies that repair damaged GALT. Developing such strategies requires a fundamental understanding of human GALT development.

In mice, specialized aggregates of cells called cryptopatches are the site of GALT development. The presence of similar cell aggregates in human intestines has been controversial. The researchers used humanized mice to demonstrate that cryptopatches serve as the foundation for human GALT formation.

To make this discovery, the researchers bioengineered human immune systems into two very closely related mouse strains that differed only in their ability to develop cryptopatches. Human GALT structures only

developed when cryptopatches were present. In mice where human GALT developed, additional studies revealed that the human GALT facilitated intestinal immune function, including the production of antibodies specifically found in the human gut.

"Our model defines a novel aspect of human GALT development and demonstrates the stepwise process of the intestinal immune system response," said Paul Denton, PhD, research instructor at UNC and an author of the study. "We found evidence that cryptopatches likely work the same way in people and mice."

The study confirms the faithful nature by which the human immune system in these human-mouse chimeric animals recapitulates a normal human immune system.

"This represents a significant advance that will facilitate the study of numerous conditions that affect the gastrointestinal tract," said J. Victor Garcia, PhD, professor of medicine and senior author of the study. "The next step," Garcia said, "is to utilize this model to test regenerative therapies to repair damaged human GALT."

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