Gene analysis generates spatial map of intestinal cells and traces their trajectories during gut inflammation

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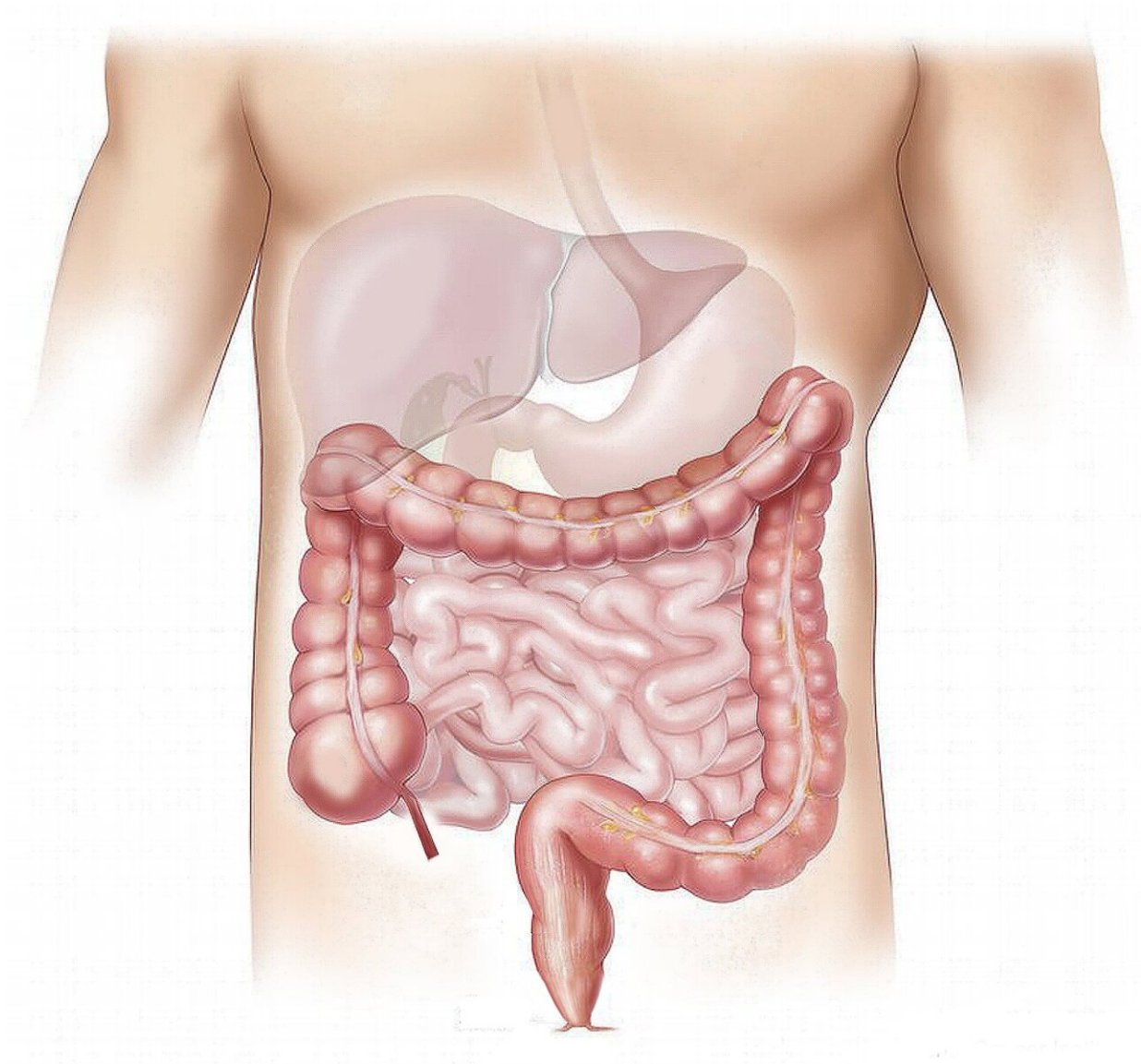

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Cells within the intestines perform various roles including nutrient absorption, sensing, and maintaining homeostasis. Certain chronic disorders are distinctly characterized by gut inflammation, which disrupts intestinal cells and can lead to a remodeling of the gut and the introduction of new immune cells.

To better understand the types of cells and their positioning within the intestines, researchers at Brigham and Women's Hospital in collaboration with investigators at Boston Children's Hospital, used a new technique known as MERFISH (multiplexed-error robust-fluorescence in situ hybridization) to analyze 940 genes in 1.35 million intestinal cells in a mouse model of colitis. Their work has been published in Cell.

They identified cell populations associated with healthy and inflamed states, mapped their spatial neighborhoods, and traced the evolution of these populations during the inflammation process. One significant cell type to note was fibroblasts, that, when in a distressed state, can induce inflammation associated fibroblasts (IAFs), which may help remodel extracellular matrices, recruit immune cells, and produce inflammatory cytokines.

However, some key questions still remain, including the specific diversity of IAF populations, their precise tissue locations, and how they emerge during inflammation.

Nevertheless, the researchers were able to generate a unique spatial atlas of a mouse colon both in a healthy state, and during intestinal inflammation, which has the potential to assist with therapeutic treatments for chronic inflammatory diseases.

In previous studies, IAFs have been observed in a variety of diseases, including cancers and autoimmune diseases, so understanding the role and mechanisms of IAFs may help with the development of treatments for these other diseases.

"Our team wanted to better understand how cells are organized within the gut, and how inflammation can impact cellular interactions and communication at the tissue scale," said senior author Roni Nowarski, Ph.D., of the Brigham's Department of Neurology and Harvard Medical School's Department of Immunology.

"This work is particularly exciting and has given us a better understanding of the tissue context of cellular responses during inflammation, which we hope will help us design better therapeutics to fight serious chronic inflammatory diseases."

More information: Cadinu, P et al. Charting the cellular biogeography in colitis reveals fibroblast trajectories and coordinated spatial remodeling, *Cell* (2024). DOI: 10.1016/j.cell.2024.03.013. www.cell.com/cell/fulltext/S0092-8674(24)00254-X

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