Researchers map the immunology of the gut in children with IBD

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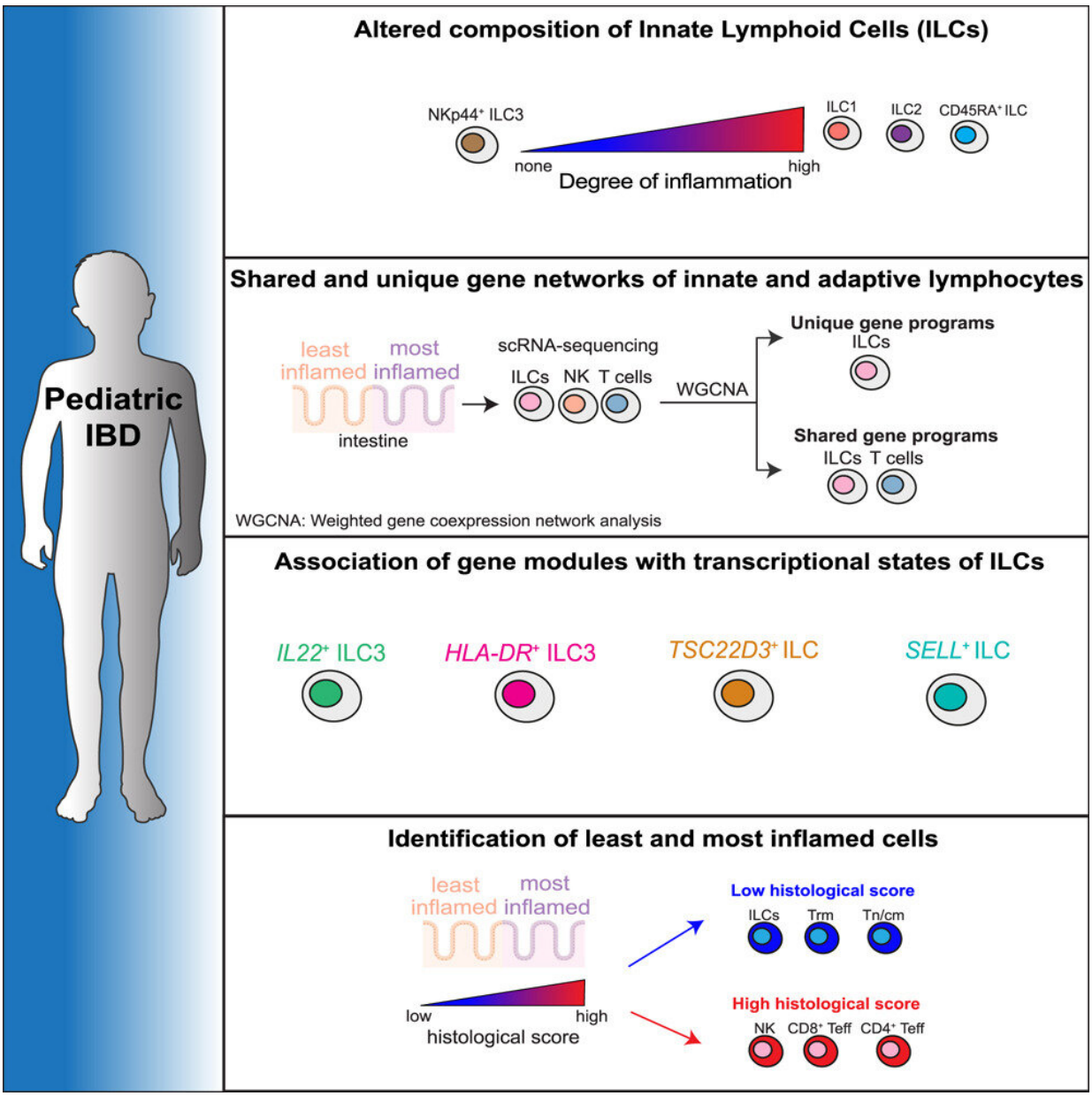

Graphical Abstract. Credit: *Cell Reports Medicine* (2023). DOI: 10.1016/j.xcrm.2023.101038

Researchers from Karolinska Institutet and Sachs' Children and Youth Hospital have mapped the immune system in the gut of children with inflammatory bowel disease (IBD). The results, which were published in *Cell Reports Medicine*, can be used to design more targeted therapies.

Today, we know relatively little about how the immune system functions in children with IBD and how this differs from adults. About 40 percent of patients, including both children and adults, do not respond to the treatments that are currently available. It is therefore very important to identify biomarkers that can both predict treatment response and help identify new treatment methods.

Understanding what happens in the gut

"There is still no cure for inflammatory bowel disease such as Crohn's disease or ulcerative colitis, only symptomatic treatment," says Jenny Mjösberg, professor of tissue immunology at the Department of Medicine (Huddinge) at Karolinska Institutet. "IBD often first appears in early adulthood, sometimes in childhood. This study is a response to a clinical need to understand why the disease occurs and what happens in the gut in children with IBD."

Jenny Mjösberg has worked in close collaboration with colleagues at Sachs' Children and Youth Hospital and Karolinska University Hospital in Sweden to study the intestines of 25 children and eight adults with IBD, as well as ten children and eight adults without IBD. Researchers used flow cytometry and sophisticated single-cell technology, two relatively new techniques that enable the analysis of immune cells from

the colon even on small biopsy samples.

Fewer tissue-protective immune cells

The researchers found that pro-inflammatory cell types, such as innate lymphoid cells type 1 (ILC1) and cytotoxic cells, such as T cells and NK cells, were found to a greater extent in children with intestinal inflammation. But they also found that a particular subtype of protective cells—type 3 innate lymphoid cells (ILC3)—and tissue-resident T cells were present to a lesser degree in the intestinal mucosa of children with IBD.

"Inflammation seems to be linked not only to aggressive cells that drive inflammation, but also to the loss of function in the cells that help maintain a healthy gut," says Mjösberg. "The treatments that are currently available only aim to suppress inflammation, but it can be just as important to strengthen the tissue-protecting component."

Children and young people with IBD are also a valuable group to study. These cases are easier to catch as they just presented with symptoms and thus have not undergone any form of treatment. In addition, they are usually otherwise healthy, are non-smokers and rarely have other confounding health factors. The hope is that the results from this study can be a piece of the puzzle in the development of new treatments.

"Collaborating on this type of basic clinical research is tremendously important," says Helena Rolandsdotter, senior consultant at Sachs' Children and Youth Hospital and researcher at the Department of Clinical Science and Education, Södersjukhuset, at Karolinska Institutet. "Our knowledge of biologic drugs and why they work or don't work is still rather poor. Biomarkers are therefore very important. In the long run, we hope to see more individually tailored treatments. This study is a step in that direction."

More information: Efthymia Kokkinou et al, The single-cell transcriptional landscape of innate and adaptive lymphocytes in pediatric-onset colitis, *Cell Reports Medicine* (2023). DOI: 10.1016/j.xcrm.2023.101038