Medical Xpress

Researchers generate developmental map of human T-cells

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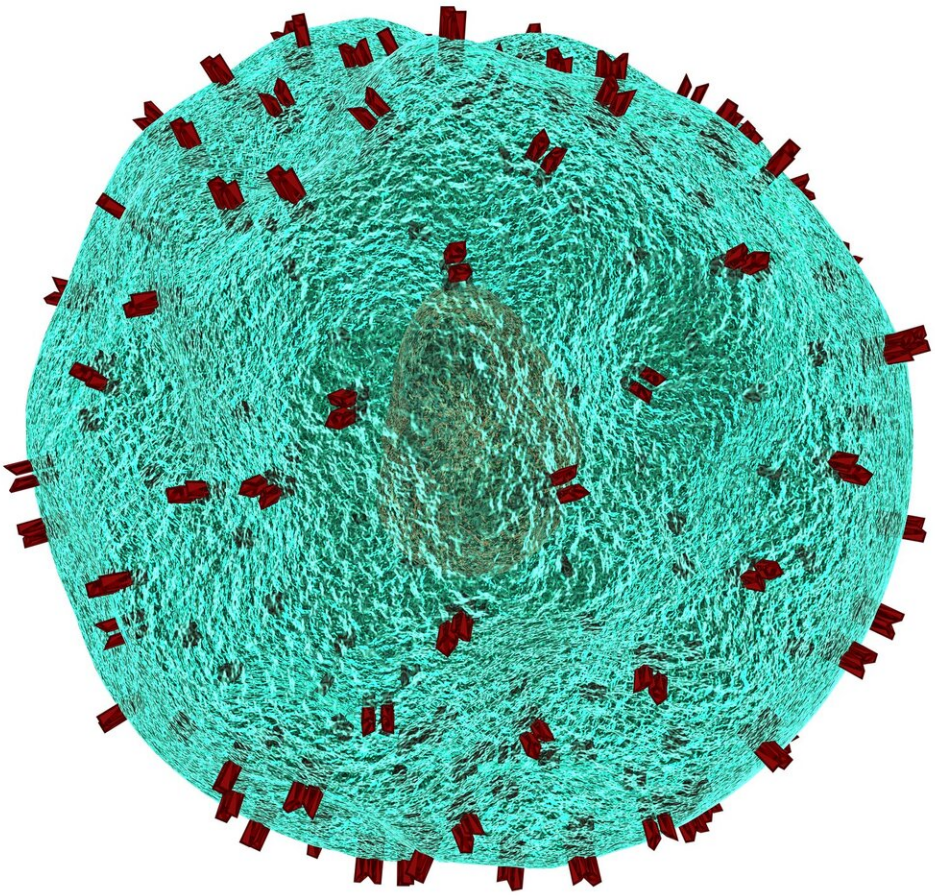

Chintan Parekh, MD, of the The Saban Research Institute of Children's Hospital Los Angeles, has led a team of investigators that generated a comprehensive roadmap for how T-cells develop in the human thymus. The study will be published in the journal *Immunity* on June 16. T-cells are a type of white blood cell involved in immune response—fighting off invaders like pathogens or cancer cells. Understanding human T-cell development is crucial for treating diseases arising from abnormal T-cell development, like leukemia and immunodeficiencies, and for developing highly effective immunotherapies, like CAR-T.

"While most previous studies have been done in mice, our study specifically reveals a high-resolution picture of human T-cell development," says Dr. Parekh. "Because of the biological differences between species, it's critical to specifically study human T-cells in order to generate the information we need to understand human disease and to design novel immunotherapies."

Using single-cell sequencing technology to study cells isolated from human thymic tissue, the investigators mapped the various stages of T-cell development in the human thymus, including the multitude of genes that switch on or off at each stage. They charted the different developmental routes that the most immature cells in the thymus may take as they progress to maturity and discovered stages of development and patterns of gene activity unique to humans.

This knowledge could lead to greater insights into diseases arising from T-cell deficiencies or abnormal T-cells such as immunodeficiency disorders (severe combined immunodeficiency disease or SCID), T-cell mediated autoimmune diseases (type 1 diabetes, rheumatoid arthritis)

and leukemia (T-cell acute lymphoblastic leukemia).

The findings could also help in the advancement of immunotherapies like CAR-T therapy, regarded as one of the most significant advance in cancer treatment. A greater understanding of T-cell development is also needed to advance treatments to expedite recovery of the immune system in patients who have undergone bone marrow transplantation for treatment of cancer and other diseases.

More information: Justin Le et al, Single-Cell RNA-Seq Mapping of Human Thymopoiesis Reveals Lineage Specification Trajectories and a Commitment Spectrum in T Cell Development, *Immunity* (2020). DOI: 10.1016/j.immuni.2020.05.010

The single cell data for developing T-cells is available on the National Center for Biotechnology Information (NCBI) Gene expression omnibus (GEO) database. This public genomics data repository ensures that other researchers have access to the data so they can learn more about which genes regulate T-cell development and use that knowledge to understand T-cell diseases and design new immunotherapies.

Provided by Children's Hospital Los Angeles