GULBENKIAN CIÊNCIA

Press Release

On the origins of leukaemia
Revealing the causes of a rare and aggressive disease

13 April 2021 – Researchers identify the cells that can sustain immune cell differentiation in the thymus and lead to leukaemia initiation, long before the disease manifests. The study published in **Cell Reports** reveals that these precursor cells ensure that the thymus keeps generating T cells, even in conditions that should compromise this function. But this entails serious consequences: the appearance of abnormal cells, which accumulate errors and trigger leukaemia initiation.

The thymus (an organ located above the heart) is responsible for the production of T cells, a type of immune cell that protects us from infections and cancer. In normal conditions, T cells develop from precursor cells generated in the bone marrow, which travel to the thymus to mature. "Studying the mouse thymus, we found that, if bone marrow precursors are compromised, some precursor T cells can self-renew over prolonged periods of time. This enables T cell differentiation to carry on autonomously in the thymus", reveals **Vera Martins**, principal investigator at IGC and leader of the project.

Previous work developed by the team showed that T cell development depends on cell competition: younger precursor cells, which have been in the thymus for a short time, outcompete older precursors and replace them. If cell competition is compromised, leukaemia emerges. "We sought to determine which cells maintain T cell development if cell competition is impaired. And not only we identified those cells, which are rare, but also, we demonstrated that these conditions enable the emergence of abnormal cells, which originate leukaemia. This is important for us to understand how cells otherwise healthy change their cellular programs and decide to become leukemic in the first place", explains Vera Martins.

According to **Rafael Paiva**, first author of the study, "the leukaemia that develops in mice is very similar to the disease that develops in humans, making the mice an essential model to study the causes of this disease. This is impossible to achieve by directly studying humans or by using simpler systems like cell cultures." This study results from several years of research conducted by the team and relies on cutting edge technology, that can access the information of individual cells among thousands. "This technology is what allowed us to identify this very reduced and aberrant group of cells, which would never be visible otherwise among the millions of other cells that remain normal in the thymus."

This study was developed at Instituto Gulbenkian de Ciência. Funding was granted by Instituto Gulbenkian de Ciência, Calouste Gulbenkian Foundation and Fundação para a Ciência e Tecnologia (FCT).

GULBENKIAN CIÊNCIA

Press Release

Original Paper: Rafael A. Paiva, António G. G. Sousa, Camila V. Ramos, Mariana Ávila, Jingtao Lilue, Tiago Paixão, Vera C. Martins, 2021. Self-renewal capacity of double negative 3 (DN3) early thymocytes preserves thymus autonomous function but compromises the β-selection checkpoint. **Cell Reports**.

DOI: https://doi.org/10.1016/j.celrep.2021.108967

For more information
Ana Morais
Head of Institutional Communication
@: anamorais@igc.gulbenkian.pt
Phone: +351 965 249 488