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Press Release

Cell competition in the thymus is crucial in a healthy organism

July 30th, 2020 – Researchers identified a group of cells that regulates the development of a particular type of cells of the immune system – the T lymphocytes. The study published in Cell Reports demonstrates that the development of T lymphocytes lays on the coordination of signals followed by cells in order to ensure the maintenance of a healthy organism. The cells identified in the study integrate information regarding the needs of more mature cells and define their own development accordingly: adjusting the speed of the production of T lymphocytes and purging the system of other less efficient cells, that tend to cause leukaemia.

The thymus is one of the organs of the immune system where T lymphocytes develop, a type of cells that is essential to fight infections and prevent cancer. Without them, it's impossible to live. The thymus is located just above the heart, being large in children and gradually reduces size as age progresses. In this organ, T lymphocytes develop from progenitor cells, which are born in the bone marrow and travel to the thymus through the blood stream. This is a continuous process, where cells enter the thymus, proliferate and develop into T lymphocytes. In the end, these cells leave the thymus to scout and defend the body.

The development of T lymphocytes is a tightly regulated process that aims at producing cells that protect the organism. However, these cells can also accumulate errors and cause cancer. Blood cell cancers, which include T lymphocytes, are called leukaemia. In the case of this study, the focus was on T cell acute lymphoblastic leukaemia and how it is normally prevented. This type of leukaemia is quite aggressive and, despite rare, it severely impacts mostly children, albeit affecting some adults.

The research team led by Vera Martins, principal investigator at Instituto Gulbenkian de Ciência, proposed to identify the cells that prevent this type of leukaemia and show that they are involved in a process of cell competition in the thymus. In this process, younger (and healthier) cells replace older (and less healthy) ones. Thus, younger cells always "win" and purge the older ones, which have the potential of causing leukaemia. But the researchers managed to go even further in their findings. Besides the leukaemia preventive role of these cells, they were also shown to receive signals that provide information on how fast (or slow) they are supposed to develop. The speed at which the development of T lymphocytes occurs is adjusted according to the intrinsic needs of the pool of precursor cells.

The team of researchers used mice as model organism, since the development of T lymphocytes is similar to what happens in humans, and made use of thymus transplants combined with different genetic models to explore the cellular interactions and the genes involved in this complex process. According to Vera Martins "the competitive cell interactions occur early in development and are regulated by a cytokine (interleukin 7) which is important throughout several developmental processes of the T lymphocytes". "We discovered that it is the availability of this cytokine that defines the size of the competing cell population"

explains the researcher, reinforcing that "it is through the adjustment of the duration of the cell cycle during proliferation that interleukin 7 regulates the speed at which these cells differentiate and promote competition".

This study reveals that the development of T lymphocytes in a healthy thymus is not merely achieved because cells follow a pre-determined path of extrinsic signals. Rather, it is achieved through the integration of external signals and intrinsic properties of the cells that contribute to the normal functioning of the thymus.

In the future, it will be important to determine the importance of space constraints and resource availability for T lymphocyte precursor cells in shaping the observed competition. The team is also interested in understanding how deficiencies in cell competition in the thymus may promote the initiation of leukaemia. With this work, the researchers hope to contribute to a better prevention, or earlier diagnostics, of diseases about which very little is still known. "I am convinced that this approach, which integrates the healthy organism and the disease condition, is the best way to understand what causes leukaemia and I hope that the generated knowledge will pave the way to the development of more adequate responses for whomever has to face such a severe disease".

This study is a clear example of the contributions of fundamental science to the understanding of what maintains individuals healthy and what changes to cause disease.

Scientific article: https://doi.org/10.1016/j.celrep.2020.107910

For more information:

Ana Morais | Head of Institutional Communication

@: anamorais@igc.gulbenkian.pt

Tlm: +351 965249488