# ID3 provides career counseling for blood progenitors, driving the creation of gamma-delta T cells

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Like an unusually forceful career counselor, the Id3 protein decides the fate of a given white blood cell precursor, according to researchers at Fox Chase Cancer Center. Their findings, published today in the journal *Immunity,* describe how Id3 directs blood cell progenitors to become gamma-delta T cells.

Gamma-delta T cells are unique in that they possess attributes of both the adaptive arm of the immune system, which is invigorated by vaccination, and the innate arm, which represents the body's first line of defense against infections.

"Unlike the other major type of T cells (alpha-beta), gamma-delta T cells seem to focus most of their efforts on protecting the body surfaces in contact with the outside world, like skin, gut, and lung and in fact are required to repel invaders at those sites," says co-author David Wiest, Ph.D., Fox Chase professor and co-leader of the center's Immune Cell Development and Host Defense Program. "Their origins have been something of a mystery and, as it turns out, their creation requires distinct molecular machinery than the other major type of T cells."

In recent years, studying the origins of blood cells has provided researchers with useful insights on how all the cells in the body form from a small group of embryonic stem cells. All blood cells originate from a type of stem cell - called hematopoietic ("blood-forming") stem

cells - located in bone marrow. A small portion of these cells move on to the thymus - a small organ near the lungs - where their ultimate fate as one of many types of white blood cells is decided through a series of molecular pathways.

Among these cells are T cells, of which there are two recognized types, based on the structure of their most defining feature, the T Cell Receptor (TCR), which enables the cell to detect bits of foreign molecules called antigens. The majority of T cells are alpha-beta T cells, meaning their TCR are comprised of alpha and beta subunits. Only five percent of T cells are gamma-delta T cells, yet researchers believe that they have a remarkable effect on human health.

Using a mouse model of human blood cell development, Wiest and his colleagues demonstrated that gamma-delta T cells require the Id3 gene for formation. Moreover, they showed that elevating the levels of Id3 alone was sufficient to push progenitor cells in the thymus into becoming delta-gamma T cells. This is not true of the development of other major T lineage, alpha-beta, for which the function of Id3 is dispensable.

One of the weapons utilized by gamma-delta cells is a substance called interferon-gamma, which has known anti-viral and anti-tumor properties. Interferon-gamma is also known to contribute inflammation at the site of infection, such as a wound, but also may be a source of autoimmune disease.

"By better understanding the process that drives gamma-delta T cell production, we may one day become capable of producing them outside of the body for use as a therapy in people when warranted," Wiest says.

"While we are only beginning to understand the functions of gamma-delta T cells, one setting where they might be useful therapeutically, is cancer," Wiest says, "since gamma-delta T cells seem to be well

equipped to combat cutaneous malignancies."

Source: Fox Chase Cancer Center (news : web)

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