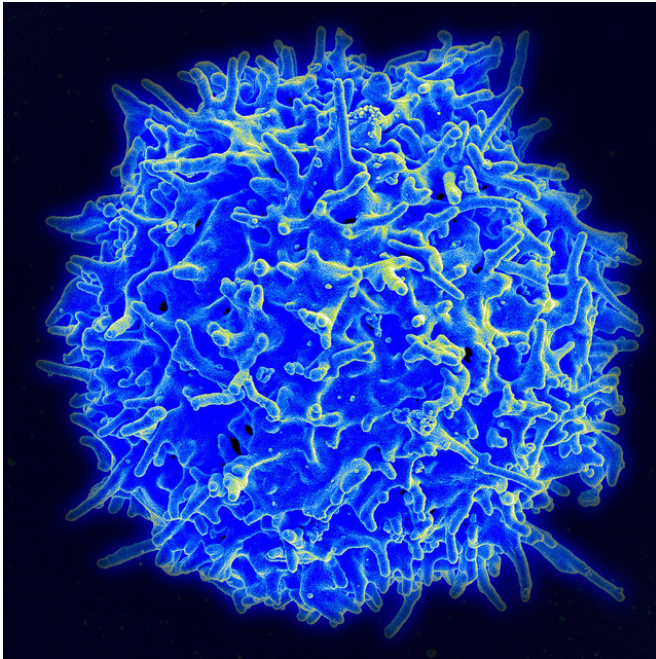


# How organs form helps stem cell researchers in their quest to develop future treatments of diabetes and cancer

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Scanning electron micrograph of a human T lymphocyte (also called a T cell) from the immune system of a healthy donor. Credit: NIAID

In a new study, researchers at the University of Copenhagen show that the development of a certain type of immature stem cells—also known as progenitor cells—depends on the quantity of a special protein and interaction with other cells in the body. The new study has just been published in the scientific journal *Developmental Cell*.

Many diseases are caused by the loss of certain types of [cells](#), such as the insulin-producing beta cells in diabetes—or dysfunction of cells, as in [cancer](#). Stem cell researchers have struggled for years to restore the normal healthy cell types. However, the question is how stem cells can be induced to behave the same way in a petri dish as

they do in the body.

## Closer to a mechanism that can control cellular development

The Semb Group at the University of Copenhagen aims to find out how the insulin-producing [beta cells](#) are formed naturally in the pancreas, so that this process can be replicated in the laboratory.

"We examined how much [progenitor cells](#) move around as the pancreas develops in the embryo, and if their journey to distinct areas (so-called niches) within the organ can explain what they eventually will become. We discovered that before the progenitors have decided their [fate](#), they move around a lot. We could also show that their movement to specific niches, where they acquire their final fate, is determined by how much of the protein P120ctn they produce. By understanding this mechanism, we can improve our methods for making the correct cell type from [stem cells](#) in a petri dish for future cell-replacement therapy of diseases, such as type 1 diabetes, and get new insight into how to prevent spreading of cancer," explains Henrik Semb, Professor and Executive Director, Novo Nordisk Foundation Center for Stem Cell Biology, DanStem, University of Copenhagen.

## Cell fate is dictated by how sticky the cell is

Restoring dysfunctional organs requires understanding of how organ shape emerges and its influence on cell fate. Previous research has generated conflicting results. Some results suggest that the future fate of progenitor cells is predetermined, meaning their fate is decided by inheritance before they end up in their final niche, while other results suggest the opposite, namely that their destiny is determined at their final destination in the environment.

"We therefore decided to take a closer look at this problem by examining in greater detail how progenitor cells move around and whether their movements correlate with their final fate. By recording three-dimensional movies of fluorescently labelled individual progenitor cells within the early pancreas, we realized that the progenitor cells, prior to their fate decision, continue to change their positions to shape the architecture of the pancreas," explains first author of the study Pia Nyeng, Assistant Professor, DanStem, University of Copenhagen.

This observation strongly indicates that the fates of cells do not appear to be predetermined, but rather determined by the particular niche at their final destination. To examine how the final positioning of cells in the organ is controlled, the researchers found that the signalling protein, P120ctn, plays an important role.

"This protein affects adhesion (stickiness) between the cells. Cells with high expression of P120ctn are more adhesive compared to cells with low expression of P120ctn. We observed that cells with high expression of P120ctn remain in the central part of the pancreas, while cells with low expression of P120ctn migrate toward the peripheral part of the pancreas. To test our theory, we reduced adhesion in a few progenitors within the central part of the pancreas by inactivating the gene encoding P120ctn. By using movies to analyse the behaviour of these cells we saw that they migrated to the peripheral part of the pancreas and developed into enzyme-producing acinar cells."

### **Might slow down metastasis**

Spreading of cancer is strongly connected to a decrease in the adhesive properties of cancer cells. Decreased adhesion enables the cancer cells in an organ to leave the niche they came from and invade the surrounding tissues, including the blood vessels, to metastasize to other organs. Therefore, cancer research has focused on trying to prevent the decrease in adhesion, or to reinstate high adhesion in cancer cells without worrying so much about whether this could lead to higher adhesion than in the healthy cells.

"Our experiments show that what drives segregation of cells is their intrinsic differences in adhesion. This suggests that it is not the cell's adhesive characteristics per se but rather its relative adhesion to the neighbouring cells that dictates whether they will segregate (invade neighbouring tissue in cancer). Therefore, to counteract metastasis, cancer therapy should try to reinstate normal levels of [adhesion](#)."

"p120ctn-Mediated Organ Patterning Precedes and Determines Pancreatic Progenitor Fate" has been published in *Developmental Cell*.

**More information:** Pia Nyeng et al, p120ctn-Mediated Organ Patterning Precedes and Determines Pancreatic Progenitor Fate, *Developmental Cell* (2019). [DOI: 10.1016/j.devcel.2019.02.005](https://doi.org/10.1016/j.devcel.2019.02.005)

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