Only a minority of cancer cells affect the growth and metastasis of tumors

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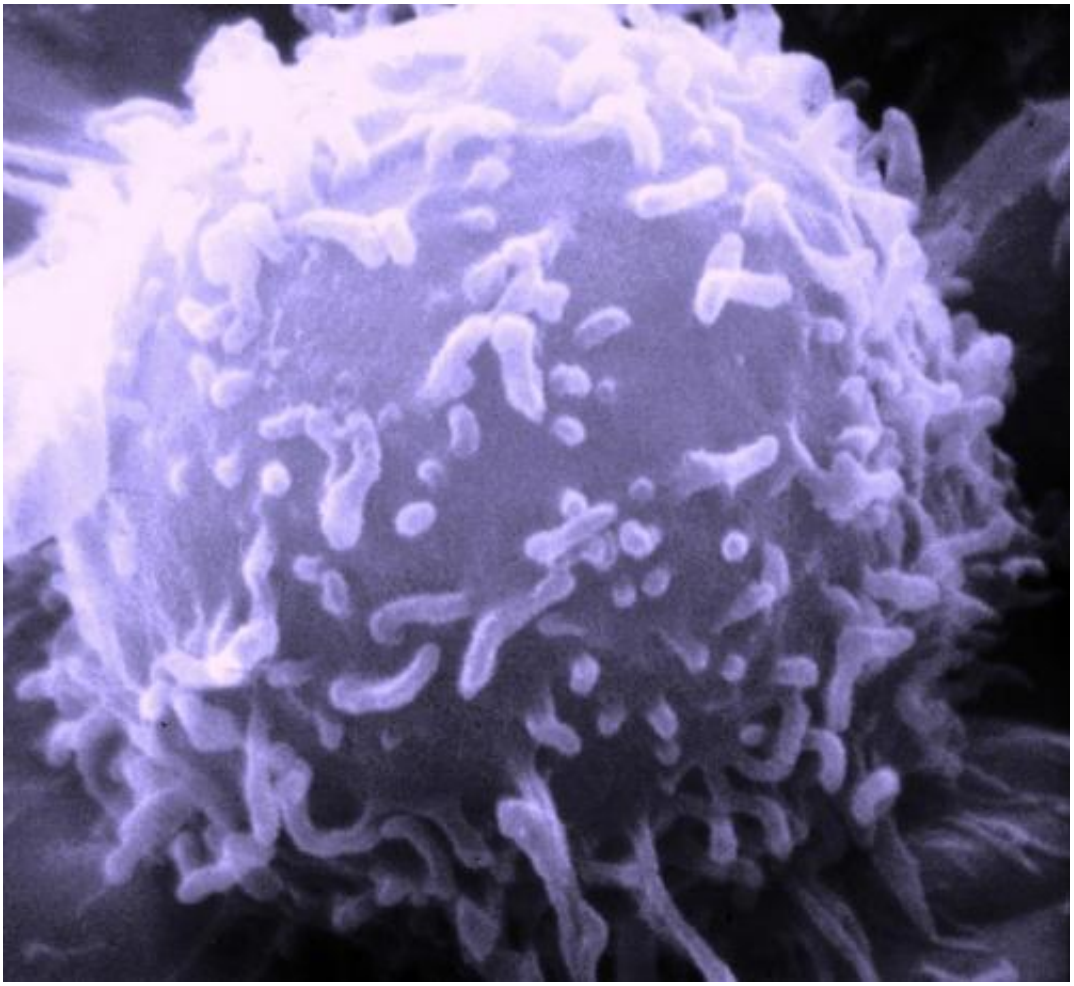

Electron microscopic image of a single human lymphocyte. Credit: Dr. Triche National Cancer Institute

New research shows that a small minority of cancer cells in neuroendocrine tumours of the pancreas contribute to the overall growth and metastasis of the tumour. This discovery was made by a research group at Lund University, in collaboration with researchers at Karolinska Institutet, in Sweden.

The findings are of fundamental biological importance for the understanding of the different functions of cancer cells, and are now published in the scientific journal *PNAS*.

Cancer emerges when mutations and other genetic alterations shut down the control system for growth that can normally be found in our cells. All cancer cells in a tumour were previously believed to have the same potential to grow and metastasise, but recent studies show that tumours are comprised of several types of cancer cells with different genetic alterations.

"The fact that there are so many different types of cells within a single tumour could explain why only some cancer cells are able to metastasise, and why some patients experience recurrence of their tumorous disease, despite having undergone extensive treatment", explains Professor Kristian Pietras at the Department of Laboratory Medicine at Lund University.

Neuroendocrine tumours, NET, is a generic name for a type of hormone-producing tumour. In their study, the research group showed that in neuroendocrine tumours of the pancreas, a small minority of tumour cells significantly contributed to the overall growth of the tumour.

"These tumour cells represent less than one per cent of all the cells in the tumour, yet they essentially control the tumour's ability to grow and metastasise", says Eliane Cortez, doctoral student at the Department of Laboratory Medicine, Lund University, and lead author of the study.

A type of protein (PDGFD) is secreted from the blood vessels of the tumour, and sends signals to a receptor (PDGFRβ) located on the surface of a small percentage of cancer cells. In turn, this minority of cancer cells secrete growth factors to other cells in the tumour, resulting in the growth of the entire tumour. Through animal testing using mice, the researchers disabled the PDGFD, which made the overall growth of the tumour dramatically decline, even though the measure only had a direct impact on a very small percentage of the tumour cells. PDGFD signalling through PDGFRβ has been previously described in other tissues and tumours, but never in this type of cancer.

"It was also very interesting for us to find that early metastases almost exclusively contained cancer cells with PDGFRβ on the surface, suggesting that this cell has an important function when it comes to preparing and promoting the metastasis of cancer cells to other organs", explains Eliane Cortez.

The discovery is of fundamental biological importance because it increases the understanding of how a tumour consists of different types of cancer cells with different functions. To understand the level of aggression of a tumour, it is important to accurately describe its structure, as also smaller populations of cancer cells may have a major impact on the tumour's overall growth.

"We have studied the occurrence of these growth-controlling cancer cells in humans as well, but the next step is to more systematically and in larger studies examine the cells and see how they respond to treatment", says Kristian Pietras.

More information: Eliane Cortez et al. Functional malignant cell heterogeneity in pancreatic neuroendocrine tumors revealed by targeting of PDGF-DD, *Proceedings of the National Academy of Sciences* (2016). DOI: 10.1073/pnas.1509384113

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