What makes cells migrate – and what can stop them

Konstanz researchers identify an enzyme that plays a role in the migration of cells in our body - not only during normal tissue formation and wound healing, but also when tumor cells metastasize. This makes the enzyme an interesting candidate for potential future therapeutic approaches.

How do cells move from A to B through our body to build functional tissues? And how is this process regulated? The answers to these questions are essential – for example, for our understanding of how an animal or a human develops from a fertilized egg. Cells often have to travel long distances within the organism, especially during brain development, when blood vessels form, or when blood stem cells populate the bone marrow. However, the misguided migration of cells can also contribute to serious diseases – for example when malignant tumor cells spread.

In their current study published in the scientific journal BMC Biology, researchers from the University of Konstanz, led by biologist Christof Hauck, have now succeeded in identifying an enzyme present in all mammals that is necessary for the efficient migration of cells: the protein phosphatase PPM1F. In addition to its regular biological function, this enzyme also contributes to the efficient migration and invasion of malignant tumor cells into tissues. Therefore, PPM1F could serve as a promising target for suppressing tumor metastasis in the future.

Indispensable for embryonic development

PPM1F has previously been associated with the regulation of the cytoskeleton and the control of integrin activity – both important components of cellular movement. In their new study, the Konstanz researchers first investigated the effects of the complete loss of this enzyme in mice. "Just like humans, mice have two copies of each gene in their genome. If one of the PPM1F copies is defective but the other is intact, the animals develop normally and are also capable of reproducing", explains Hauck.

However, if the genetic information for PPM1F is completely lost due to two defective copies of the gene, severe misorganisation of the developing brain and vascular system can be observed, and embryonic development stops. For example, newly formed nerve cells of these embryos are stuck at their place of origin – the ventricle in the central nervous system - and they do not migrate to build the various layers of the cerebral cortex.

In experiments with isolated cells, biologists Tanja Grimm, Nina Dierdorf, Marleen Herbinger and Sarah Baumgärtner from Hauck's team also discovered that the loss of PPM1F leads to increased adhesion of the cells. The cells are severely restricted in their movement and hardly spread out on the substrate. Cells without PPM1F remain smaller than normal cells in comparison. This influence of PPM1F on cell adhesion could explain why cell migration is impaired in mice without intact PPM1F gene.

Tumour cell migration

"Cell migration is not only essential during tissue formation in the embryo. In humans, for example, it also plays a role in wound healing processes as well as in the metastasis of tumors", says Herbinger. She investigated the invasion of human tumor cells using cell cultures and was able to show that the level of PPM1F in various human tumor cell lines is directly linked to the invasive potential of the cells.

"If we specifically switch off the PPM1F gene in the cells, tumor cell invasion is prevented even in more complex tissue models", says Herbinger. "However, if we manipulate the tumor cells to produce more PPM1F, then their potential for tissue invasion significantly increases". In fact, elevated levels of PPM1F are found in a number of human tumors, meaning that the findings obtained in cell culture and from mice can very likely be transferred to the human body.

"Our results show that PPM1F plays an important role in the regulation of cell migration – both in early embryonic development and in the invasiveness of tumor cells", explains Hauck. "This makes PPM1F a promising target for future

therapeutic approaches." The scientists now hope that their fundamental insights into the molecular connections between the function of PPM1F and cell migration will provide an important impetus for developing compounds, which inhibit PPM1F.

Publication:
T.M. Grimm, N.I. Dierdorf, M. Herbinger, S. Baumgärtner, E. Sontowski, C. Paone, T. Baade, C.R. Hauck. The phosphatase PPM1F, a negative regulator of integrin activity, is essential for embryonic development and controls tumor cell invasion (2025). BMC Biology; DOI: 10.1186/s12915-025-02254-3

Key facts:

- Konstanz researchers in Professor Christof Hauck's team have identified an enzyme that plays an important role in cell migration: the phosphatase PPM1F.
- According to the study, the enzyme plays a role both in tissue formation – e.g. the formation of the cerebral cortex during embryonic development – and in the invasiveness of tumor cells. In the future, it could therefore serve as a target for suppressing tumor metastasis.
- Funding: German Research Foundation, DEAL project and Konstanz Research School Chemical Biology

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Further information

- University of Konstanz