Why metastasic cells migrate

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Migration ability of metastatic cells is not due to an altered mechanism of tumor cells but to a natural capacity of healthy cells. The results could help to identify potential strategies for metastasis inhibition.

One of the most intriguing questions in cancer research is what causes metastatic tumour migration, why some tumour cells manage to migrate to other parts of the body but others cells don't. International investigation conducted by Enrique Martín Blanco, CSIC researcher at the Institute of Biology of Barcelona, located in the Barcelona Science Park, reveals that cells make use of a natural mechanism for this. It happens to be a family of proteins that trigger cell migration in normal processes such as growth or healing. Nevertheless, this mechanism had never been identified before in healthy cells.

The work, published in the latest issue of the *Current Biology* journal, is also signed by researchers at the Biozentrum from Basel University (Switzerland), and by the Universities of Coimbra (Portugal) and Freiburg (Germany).

As the authors explain, the ability of metastatic cells to migrate is not a proper mechanism of tumour cells - and therefore something that one might think is altered, but a natural ability of cells which, unfortunately, benefits metastasis.

Until now it was known that the metastasis of tumour cells can be induced by proteins such as BMPs (from 'bone morphogenetic proteins') or TGFβ (from 'transforming growth factor-β'). These proteins,

identified in tumour cells of vertebrates, trigger cell migration and promote metastasis: they tell the cells that they must move and migrate, although not to where. And if these proteins are not activated in tumour cells, there is neither mobility nor invasion. But the unexplored question was if this mechanism is something exclusive of tumour cells or not.

Now the work of this international team has identified the same mechanism in the healthy cells of Drosophila melanogaster, the fruit fly.

Researchers have found that the Decapentaplegic protein (Dpp), an homologous protein of BMP and TGFβ, acts as signal of cell mobility. "The cells with Dpp activated are migratory and invasive", says Martin-Blanco. "If we block the signal of Dpp in the cells, they stop moving. However, if the Dpp protein is over expressed, cells have even more and enhanced migratory and invasive capacities.

The authors have worked with embryos of the fly Drosophila melanogaster, during the formation of its abdominal epithelium, in metamorphosis. This is a process where histoblasts (embryonic cells) that will form the fly abdomen replace larval epidermal cells. The histoblasts remain at the beginning in small nests or groups of cells, and they progressively multiply, spreading and invading the space to substitute all larval epithelial cells.

This is the most clear example that scientists have seen this gene family (Dpp, BMP and TGFβ) playing the role of controlling mobility and invasiveness in normal cells. Martin-Blanco adds that "now we can study this mechanism in healthy cells, and we hope to discover more about the conditions that can inhibit or accelerate it." They expect not only to understand better this mechanism but also to find alternative strategies to inhibit metastasis.

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