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Press release

Breast cancer: identification of a molecular switch that controls cancer stem cells

Some cancer cells are resistant to treatment and persist. If they are capable of proliferating again, even a very small number of these cells may be enough to reconstitute a tumour after or despite treatment. Various approaches to eliminate these "cancer stem cells" (CSCs) have been tried in recent years: targeted therapies, vaccination and tumour starvation. In an article published in the journal *Cell Reports*, Christophe Ginestier, Inserm Research Fellow at the Cancer Research Center of Marseille (CRCM, Aix-Marseille University/CNRS/Institut Paoli-Calmettes), and his collaborators identify a specific RNA [1] molecule that plays the role of a molecular switch that can "turn off" or "turn on" CSC proliferation in breast cancers.

Scientific data accumulated in the course of recent years have shown that tumours contain a particular population of cells with different properties. Indeed, a small number of the cells constituting a tumour have the ability, when isolated and then injected into animal models, to form a tumour identical to the original one. These cells, known as cancer stem cells (CSCs), can proliferate (and thereby renew themselves), differentiate (and thereby give rise to the different populations that make up the tumour), or even become temporarily dormant, which allows them to escape most treatments, since these mainly target dividing cells.

If the tumour is to be eliminated in such a way that it cannot grow again, the CSCs must be neutralised. The development of any new therapeutic strategy requires a better understanding of the intrinsic molecular mechanisms of CSCs. MicroRNAs have been described as regulators that can direct the "cellular destiny" of stem cells, particularly during embryogenesis. They might play a major role in CSC biology. MicroRNAs are small RNA molecules that, unlike messenger RNAs, do not act as intermediates in protein production based on information encoded by genes, but regulate the activity of other RNAs or of proteins.

Christophe Ginestier, Emmanuelle Charafe-Jauffret and their co-authors screened the full complement of microRNAs present in the genome in order to identify microRNAs capable of directing the choice for a CSC between self-renewal and differentiation. They thus observed that inactivation of one particular microRNA, known as miR-600, causes an increase in CSCs, while its overexpression reduces tumourigenicity.

They then showed that miR-600 works by acting on an enzyme needed to activate a protein (WNT) known to activate a signalling cascade involved in embryogenesis. When they inactivate miR-600, the researchers observe the expansion of CSCs. Conversely, when miR-600 production is increased, differentiation of CSCs is promoted at the expense of their proliferation: tumour progression is stopped.
This mechanism, demonstrated experimentally, clearly seems to play a role in the development of breast cancers, since the researchers were also able to show, by analysing a panel of 120 human breast tumours, that a low level

[1] RNA: ribonucleic acid, a biological molecule present in nearly every living being. Often providing intermediate support to genes during protein synthesis, RNA can also be involved in many chemical reactions within the cell.

of miR-600 is found to be associated with a strong activation of the WNT protein and a poor prognosis for patients whose tumours show these characteristics.

"If miR-600 is a switch for tumour aggressiveness, it may therefore constitute an excellent therapeutic target," conclude the researchers. *"Our data also tend to prove that resistance to treatment and relapse after treatment could be due to the fact that the therapies employed are not targeting the right cancer cells."*

To find out more

Source
"miR-600 acts as a bimodal switch that regulates breast cancer stem cell fate through WNT signalling"
El Helou R, Pinn G, Cabaud O, Wicinski J, Bhajun R, Guyon L, Rioualen C, Finetti O, Gros A, Mari B, Barbry P, Bertucci F, Bidaut G, Harel-Bellan A, Birnbaum D, Charafe-Jauffret E and Ginestier C.

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