

RANK protein promotes the initiation, progression and metastasis of human breast cancer

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Researchers from the Bellvitge Biomedical Research Institute (IDIBELL) have shown that overactivation of the RANK signalling pathway promotes the initiation, progression and metastasis of tumours in human breast epithelial cells by dedifferentiation of breast cells to stem cells. The results of this study have been advanced in the electronic edition of the journal *Cancer Research*.

The study was coordinated by Eva Gonzalez-Suarez, head of the IDIBELL research group on Transformation and Metastasis. A year ago, the team published a paper which showed that this pathway is also relevant in breast tumours in mouse models. "We saw that when this pathway is overactive, animals were more susceptible to developing [breast cancer](#) and that tumours decreased when we pharmacologically inhibited the pathway" (Gonzalez-Suarez et. Al. *Nature* 2010).

The starting point of this study was to observe the effect in humans of overexpression of RANK. First, the researchers used healthy mammary epithelial cell lines and found that "RANK receptor overexpression induces characteristics of stem cells and epithelial-mesenchymal transition to our cells, taking on characteristics of malignancy but without developing tumours."

The next step was to observe the effects of protein overexpression in breast tumour cells. "We saw how it generated an increasing in tumour

stem cells, and when we injected it in animal models, tumourogenesis and metastasis increased."

Finally, they used clinical samples of [breast tumours](#). [Cancer cells](#) with high levels of RANK were associated with basal type tumours, high-grade tumours, and more aggressive ones with more proliferation and metastasis. This means that "high levels of protein are associated with [poor prognosis](#) tumours."

Therefore, this study corroborates in [human cells](#) what it had already been seen in mice, "an increasing in the activation of the RANK signalling pathway may be associated with an increased initiation, progression and metastasis of breast cancer."

Clinic applications

The next step, according to researcher Eva Gonzalez-Suarez, would be "first, confirm these studies with a larger number of samples and secondly explore the therapeutic possibilities."

As explained Gonzalez-Suarez, "there is a theory which says that chemotherapy treatments kill tumour cells but do not affect cancer stem cells, which could reinitiate the tumour after treatment. If indeed this pathway has the ability to restart the tumours and metastatic capacity increase, a combination of RANK inhibitor with chemotherapy may have important therapeutic effects. "

Currently, there is a pharmacological inhibitor of RANK signalling pathway used in clinics, in the treatment of osteoporosis and bone metastases.

More information: RANK induces epithelial-mesenchymal transition and stemness in human mammary epithelial cells and promotes

tumorigenesis and metastasis. *Cancer Research*. Published OnlineFirst April 10, 2012; [doi: 10.1158/0008-5472.CAN-12-0044](https://doi.org/10.1158/0008-5472.CAN-12-0044)

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