Integrin cell adhesion receptors are risky cancer drug targets

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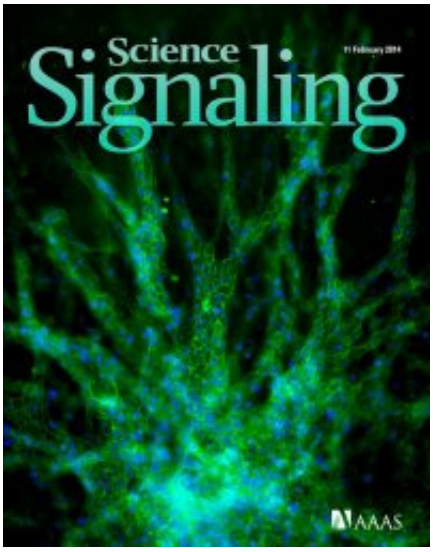

A possible cancer treatment strategy might in fact lead to increased metastasis in some cases. This finding from a team of LACDR researchers led by Erik Danen made the cover of the February 11 edition of Science Signaling.

The treatment strategy that is being considered involves blocking so-called "integrin" receptors. Cancer cells use these receptors to physically interact with their environment and when this is prevented the cancer cells become much weaker causing tumors to shrink. Integrin inhibitors

are tested in very early clinical studies at the moment.

Some recent genetic studies had suggested that there might also be adverse effects causing some cancers to become even more aggressive. This phenomenon was not understood. The LACDR researchers discovered that so-called triple-negative breast cancer cells respond to integrin inhibition with marked changes in cell migration.

It is known that integrin receptors send important signals into the cells and when these are missing cancer cells no longer effectively form tumors. However, it turns out that this can also stimulate cancer cells to "reprogram". The researchers found that triple-negative breast cancers, which originate from epithelial cells, lost their epithelial shape and became much more motile. For this switch, the cancer cells rewired an intracellular signaling network very much like normal epithelial cells do when they have to migrate to other locations during embryonic development. As a result, the cancer cells were no longer glued together but started spreading throughout the body.

The work indicates that although inhibition of integrin receptors can effectively inhibit tumor growth, it can also cause unwanted reprogramming of cancer cells that leads to enhanced metastasis. Triple-negative breast cancers show this response but some others do not. Future research should unravel for which integrin antagonists in combination with which cancer types this might represent a problem when considering integrins as drug targets.

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