Too much of a good thing: Important mechanism in hormone-sensitive breast cancer uncovered

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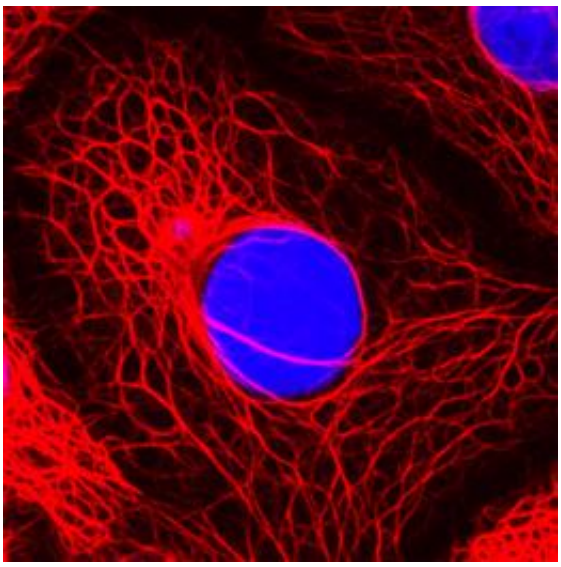

Fluorescence micrograph of breast cancer cells. Credit: Lutz Langbein, Deutsches Krebsforschungszentrum

In two out of three breast tumors, extraordinarily high levels of the estrogen receptor ERalpha are found. Scientists of the German Cancer Research Center have now uncovered a mechanism which causes this overproduction. This result might contribute to developing new strategies for fighting the most frequent type of cancer affecting women.

Two thirds of breast cancers are ERalpha-positive, i.e., many estrogen

receptors of the ERalpha- type are found in their cells. "These molecules can interact with the estrogen hormone and, thus, even lead to cancer," explains Dr. Joerg Hoheisel; molecular biologist at DKFZ. "The connection between the levels of the estrogen receptor alpha and the occurrence of breast cancer has been known for some time now. Early-stage breast cancer cells already produce too many of these receptors. This is associated with increased cell division, which is ultimately responsible for tumor development," says Hoheisel.

Jointly with his coworkers, Dr. Yasser Riazalhosseini and Pedro de Souza Rocha Simonini, Joerg Hoheisel has now been able to show that a tiny little nucleic acid, a microRNA known as miR-375, causes the high receptor levels which, in many cases, lead to cancer. MicroRNAs are important intracellular signal mediators, which have a substantial influence on the effectiveness of genes. The DKFZ group discovered that miR-375 blocks the production of an enzyme which influences the production of ERalpha-receptors. Thus, high levels of miR-375 lead to production of many estrogen receptors. At the same time, elevated ERalpha-levels lead to production of more miR-375. This feedback loop further boosts the multiplication of cancer cells.

The research group headed by Joerg Hoheisel has now published the results of their experiments in the journal *Cancer Research*. They also present a first indication of a possible medical application of the newly gained knowledge: "We were able to block the miR-375 microRNA in ERalha-positive breast cancer cells. This effectively slowed down cancer cell growth." Whether and how miR-375 will play a role in breast cancer treatment in the future is a question which Hoheisel cannot answer yet. "But we hope to be able to use our results in the future for developing new strategies against tumors with too many estrogen receptors."

More information: de Souza Rocha Simonini P, Breiling A, Gupta N, Malekpour M, Youns M, Omranipour R, Malekpour F, Volinia S, Croce

CM, Najmabadi H, Diederichs S, Sahin O, Mayer D, Lyko F, Hoheisel JD, Riazalhosseini Y.:Epigenetically Deregulated microRNA-375 Is Involved in a Positive Feedback Loop with Estrogen Receptor alpha in Breast Cancer Cells. *Cancer Research* 2010; DOI:10.1158/0008-5472.CAN-10-1318