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MicroRNA controls malignancy and resistance of breast cancer cells

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Many breast cancer patients are treated with a drug called tamoxifen. The substance blocks the effect of estrogen and thus suppresses the growth signals of this hormone in cancer cells. When resistance to the drug develops, tumor cells change their growth program: They change their behavior and shape, become more mobile and also adopt the ability to invade surrounding tissue. Scientists working with PD (Associate Professor) Dr. Stefan Wiemann of the German Cancer Research Center (DKFZ) have now also observed these changes in tamoxifen resistant breast cancer cells.

"Resistances to drugs are the main reason why therapies fail and disease progresses in many cancers," Wiemann explains. "We want to understand what goes on in the cells when this happens so we can develop better therapies in the future." Wiemann's co-worker, Dr. Özgür Sahin, suspects that tiny pieces of RNA known as microRNAs play a role in resistance development. "These minuscule RNA snippets control many cellular processes by attaching themselves to target gene transcripts and thus repressing protein production."

By treating breast cancer cells in vitro with regular doses of tamoxifen, Sahin's team induced resistance of these cells to the drug. As resistance developed, the cancer cells switched to the development program that makes them grow even more invasively and more malignantly. Checking the complete spectrum of microRNAs in the resistant tumor cells, the investigators noticed that production of microRNA 375 was more strongly reduced than others. When they boosted the production of

microRNA 375, the cells started responding again to tamoxifen and switched back to their normal growth program. "This strongly suggests that a lack of microRNA 375 both increases malignancy and contributes to resistance development," says Özgür Sahin.

If microRNA 375 levels are low, breast cancer cells increase the production of metadherin. Apparently, microRNA 375 suppresses the production of this cancer-promoting protein in healthy cells. In patients receiving tamoxifen therapy the team found that high metadherin levels in the cancer cells go along with a high risk of recurrence. This suggests that microRNA 375 and metadherin are involved in the development of resistance to tamoxifen.

"The analysis of microRNAs in breast cancer has put us on the track of metadherin. We will possibly be able to specifically influence the cancer-promoting properties of this protein in the future," says Wiemann describing the goal of further research.

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