

# Researchers uncover Achilles' heel in aggressive breast tumors

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In an unexpected twist, Fox Chase Cancer Center researchers find that the loss of a single protein, Nedd9, initially slows cancer formation but then makes the tumors that do arise more aggressive. The good news, though, is that the lack of Nedd9 also makes the aggressive tumors more sensitive to a class of drugs that are already used in the clinic.

"If a tumor is able to overcome the loss of this protein, this clearly makes it undergo complicated changes that ultimately select for a more aggressive tumor," says Erica A. Golemis, Ph.D., professor and co-leader of developmental therapeutics at Fox Chase, and senior author on the new study, published online October 12 in [Cancer Research](#). "It is reminiscent of the situation you get when you treat cancer patients with a drug and get an initial response. However, eventually their tumor overrides the drug, and then you have a really tough tumor."

A number of studies have shown that increased Nedd9 expression is associated with metastasis in a variety of human cancers, including breast cancer. Last year, Golemis's group reported that deleting Nedd9 from a [mouse model](#) of breast cancer delayed [tumor growth](#), compared with control animals. Now, they report that the cells isolated from the Nedd9-deficient tumors more rapidly form new tumors in mice, and more readily give rise to lung metastases, in contrast to tumors with normal levels of Nedd9.

Because Nedd9 interacts directly with Src, a protein that has been a major drug development target, lead author on the study, Mahendra K.

Singh, Ph.D., tested whether the Src inhibitor dasatinib, already approved for [cancer treatment](#), would control the aggressive Nedd9-deficient tumors. He found that dasatinib rapidly killed the Nedd9-deficient [tumor cells](#), even at low doses.

Golemis, Singh, and colleagues now hope to partner with clinician colleagues in trials to compare action of the drug in [breast cancer](#) patients whose tumors have low Nedd9 expression. "My hunch is that this is going to be very important for understanding how best to treat patients in the future," Singh said.

Provided by Fox Chase Cancer Center

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