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Protein tied to cancer drug resistance in mice

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Blocking a specific protein renders tumors more vulnerable to treatment in mice, suggesting new therapies could eventually achieve the same in humans, according to new research from Fox Chase Cancer Center to be presented at the 2012 CTRC-AACR San Antonio Breast Cancer Symposium on Friday, December 7, 2012.

"Hopefully, with further testing, this research could one day result in a new therapy that blocks the effect of this protein and, in turn, boosts the effects of cancer drugs," says study author Elizabeth Hopper-Borge, PhD, Assistant Professor at Fox Chase.

The protein in question is a type of ATP-binding cassette drug efflux pumps, known more simply as ABC proteins. These proteins sit on the membranes of cells, where they act just like pumps—removing cancer drugs from the cell, thereby making them less effective. The body contains close to 50 such proteins, explains Hopper-Borge, but only 3 appear capable of evading the effects of cancer drugs, including common types used to treat lung, ovarian, and breast cancers.

The current research, supported by the National Institutes of Health, focuses on the protein ABCC10, which has not been studied in as much detail as some other ABC proteins, says Hopper-Borge. Last year, she and her colleagues found that mice lacking ABCC10 experienced physiological changes after taking a cancer drug, suggesting the drug was having an effect.

As part of the latest project, the authors performed a similar experiment

in mice engineered to develop breast cancer. They found that, 21 days after exposure to a cancer drug, the tumors that lacked ABCC10 were much smaller than the tumors that still carried the protein. "This is probably the first time it's been shown that removing this protein helps sensitize tumors to cancer drugs," says Hopper-Borge.

Looking closely at the tumors, the researchers also found that cells that lacked ABCC10 grew faster. Strangely, this finding is encouraging, says Hopper-Borge, since chemotherapy targets proliferating cells—and so may explain why the drugs now act on the faster-growing cells that lack ABCC10.

The next step, she says, is to try removing ABCC10 in more mouse models of breast cancer, and determine how active the protein is in different types of the disease. Eventually, if blocking the protein appears to consistently boost the effects of cancer drugs, researchers can identify and begin testing inhibitors of ABCC10 as additional treatments for cancer.

"Although this research is promising, it's in its early stages," cautions Hopper-Borge. "Consequently, it's premature for patients to ask their doctors to test them for the presence of ABCC10, since knowing that can't yet affect their treatment. But these results suggest that may one day change."

Provided by Fox Chase Cancer Center