

Autophagy-addicted breast cancers killed by anti-malaria drug, chloroquine

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The process of autophagy cleans cells – they wrap up the bad stuff and then dispose of it. And so it stands to reason that inhibiting autophagy would make cancer cells less able to cleanse themselves of chemotherapy and so more susceptible to the drugs. That's what the traditional anti-malaria drug, chloroquine, does – it inhibits autophagy. Existing clinical trials are testing chloroquine/chemotherapy combinations against breast cancer.

Research presented at the AACR Annual Meeting 2013 shows that some [breast cancer](#) subtypes depend on autophagy more than others – and that inhibiting autophagy in breast cancers that depend on it may be enough alone to kill the disease.

"When you inhibit autophagy either with [chloroquine](#) or with [genetic switches](#), you see that some [breast cancer cells](#) don't care. Some are only moderately distressed. And still others just die straight away," says Andrew Thorburn, PhD, deputy director of the University of Colorado Cancer Center and senior author on the study with first author Paola Maycotte, PhD.

"Ultimately what we'd like to do is use this as the basis for a test to identify tumors in which autophagy inhibition is most effective. You find out what a cancer needs and you take it away – this is the model of modern, targeted therapies," Thorburn says.

With or without additional [chemotherapy](#), identifying breast cancer and

other cancer subtypes that are especially addicted to autophagy and so especially sensitive to its inhibition could allow an old drug to be used in a new, powerful way. For example, this study identified two likely sensitive breast cancer subtypes – basal-like and claudin-low – both of which are highly represented in aggressive, triple-negative breast cancers. The survival of triple-negative cells depends in part on the activation of the STAT3 gene, which is regulated by autophagy. It's likely that inhibiting autophagy in these cells blocks STAT3 activation, which in turn results in the death of triple-negative breast cancer cells.

"There's more lab work to be done," Thorburn says. "For example, we're just finishing up work with autophagy [inhibition](#) in primary xenografts – taking the work from cells to mouse models. And other work presented at the conference by graduate student Rebecca Barnard is exploring when in the cell cycle is the best time to inhibit autophagy. But this is an especially exciting line of reasoning. What Paola's data suggest is that for some breast cancers, just inhibiting autophagy may be enough to successfully treat the disease."

Provided by University of Colorado Denver

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