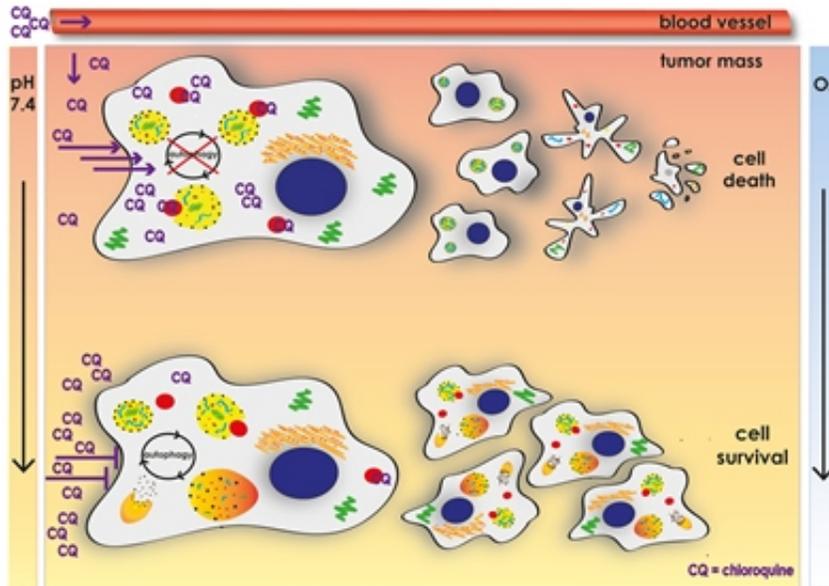


Acidic tumour pH inhibits drug effect

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Low pH in tumours counteracts the desired effect of the drug chloroquine, according to a new study from Karolinska Institutet in Sweden. The results, which are published in the journal *Autophagy*, might explain possible lack of efficacy of chloroquine in clinical studies.

Chloroquine, a widely used antimalaria drug, is currently under investigation in clinical trials on [cancer patients](#). It is the ability of [chloroquine](#) to inhibit autophagy in [tumour cells](#) that has piqued researchers' interest. Autophagy is a homeostatic process by which cells eat parts of themselves, so that damaged or unnecessary organelles and

toxic proteins are broken down and recycled. In the absence of nutrients, cells resort to autophagy to survive. This way, autophagy helps [cancer cells](#) survive in tumour regions that are poor in nutrients and characterised by low oxygen and acidic pH.

Also, tumour cells use autophagy to protect themselves from many forms of anticancer therapies, including chemotherapy. Several studies have shown that inhibition of autophagy often increases chemosensitivity and radiosensitivity in tumour cells. Chloroquine combined with existing cancer treatment is thus considered to be a promising strategy. However, in some cancer models chloroquine seems to be unable to block [autophagy](#), but the underlying mechanisms have not yet been identified.

In the present study, the scientists studied the effect of chloroquine in different cancer cells that were either cultured in acidic pH for a short time or adapted to chronic acidosis. The researchers also studied the effect in tumours grown in mice.

"We discovered that a major consequence of the altered metabolism of tumour cells, the tissue acidification, is responsible for the lack of chloroquine anti-autophagic activity", says Angelo De Milito at the Department of Oncology-Pathology at Karolinska Institutet, principal investigator of the study. "The results suggest that chloroquine might lack efficacy in patients whose tumours are characterised by acidic regions."

In the context of cancer therapy, the finding may be of importance for the translation of preclinical findings to the clinical setting in patients. The research was funded by Association for International Cancer Research, the Swedish Cancer Society, and the Sigurd and Elsa Goljes Foundation.

More information: Paola Pellegrini, Angela Strambi, Chiara Zipoli,

Maria Hägg-Olofsson, Maria Buoncervello, Stig Linder, Angelo De Milito. "Acidic extracellular pH neutralizes the autophagy-inhibiting activity of chloroquine; Implications for cancer therapies." *Autophagy*, online 31 January 2014, 10:4, 1-10, April 2014.

[www.ncbi.nlm.nih.gov/pubmed/24 ... 72?dopt=AbstractPlus](http://www.ncbi.nlm.nih.gov/pubmed/24...72?dopt=AbstractPlus)

Provided by Karolinska Institutet

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