New drug candidate starves dormant cancer cells

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In a study published in *Nature Communications*, researchers at Karolinska Institutet and Uppsala University in Sweden present a new drug candidate, which selectively kills dormant cells within a cancer tumour through starvation. These tumour cells, which are found in less oxygenated parts of solid tumours, are resistant to conventional treatments.

In solid tumours larger than a few millimetres, there is usually a lack of both oxygen and nutrients due to insufficient blood vessel growth. This in turn results in cancer cells falling into a state of dormancy. After treatment, such dormant cells will start to divide and tumours will grow. This phenomenon therefore contributes to resistance of solid tumour to radio- and chemotherapy.

In their newly published study, the researchers show that cancer cells located in tumour regions that are poorly oxygenated and lack nutrition are unable to compensate for deficient mitochondrial energy production.

"We have identified a small molecule that we call VLX600, which in various in vitro and in vivo models has proven effective against dormant colon cancer cells that are otherwise very difficult to treat. VLX600 is a mild inhibitor of mitochondrial respiration, and we have found that dormant cancer cells have a limited possibility to compensate decreased mitochondrial function by increased glycolysis. The dormant cancer cells therefore die by starvation" says Stig Linder, the professor of experimental oncology leading the study.

More information: "Induction of mitochondrial dysfunction as a strategy for targeting tumour cells in metabolically compromised microenvironments", Xiaonan Zhang, Mårten Fryknäs, Emma Hernlund,Walid Fayad, Angelo De Milito, Maria Hägg Olofsson,Vladimir Gogvadze, Long Dang, Sven Påhlman, Leoni A. Kunz Schughart, Linda Rickardson, Padraig D'Arcy, Joachim Gullbo, Peter Nygren, Rolf Larsson2 & Stig Linder, *Nature Communications*, online 18 February 2014, DOI: 10.1038/ncomms4295

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