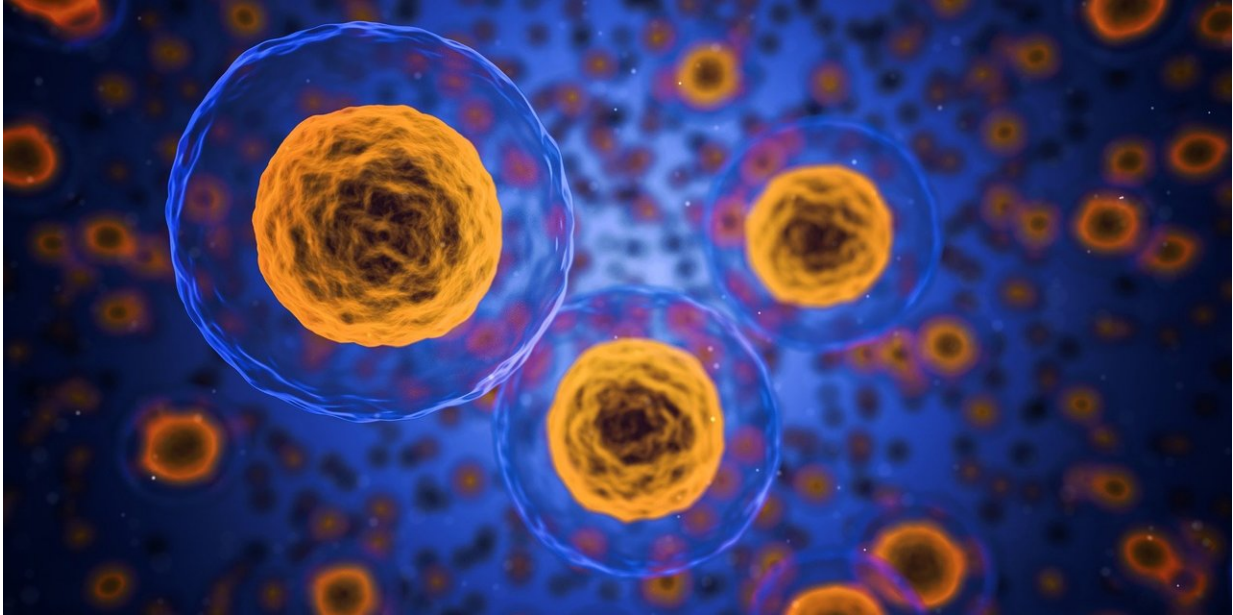


Staying young, from the cells on up

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Researchers at Université de Montréal and McGill University have discovered a new multi-enzyme complex that reprograms metabolism and overcomes "cellular senescence," when aging cells stop dividing.

In their study published today in *Molecular Cell*, the researchers show that an [enzyme complex](#) named HTC (hydride transfer complex) can inhibit cells from aging.

"HTC protects cells from hypoxia, a lack of oxygen that normally leads

to their death," said senior author Gerardo Ferbeyre, an UdeM biochemistry professor and principal scientist at the CRCHUM, the university's affiliated teaching hospital research center.

"Importantly, HTC can be hijacked by certain [cancer cells](#) to improve their metabolism, resist to a hypoxic environment and proliferate," said Ferbeyre, who made the discovery with Sebastian Igelmann, a Ph.D. student in his lab and first author of the study.

HTC is made up of three enzymes: pyruvate carboxylase, malate dehydrogenase 1 and malic enzyme 1. They were all highly expressed in samples from a prostate cancer mouse model generated at the University of Veterinary Medicine Vienna, in Austria, and in [tissue samples](#) from [prostate cancer patients](#).

"Most interestingly, inhibition of these enzymes stopped the growth of prostate cancer cells, suggesting that HTC could be a key target to develop new therapeutics for a variety of cancers, including [prostate cancer](#)," said Ferbeyre.

Most key metabolic cycles were identified more than 50 years ago, but HTC remained hidden to researchers. "We found it by performing state-of-the-art metabolomic analysis, the study of chemical processes of cell metabolism," said co-author Ivan Topisirovic, a McGill researcher and medical professor.

The scientists were able to assemble the enzyme complex from purified proteins and obtain biophysical data about its composition. Their next step will be to generate a detailed high-resolution structure of the enzyme complex in order to design drugs able to modulate its functions.

"A hydride transfer complex reprograms NAD metabolism and bypasses senescence," by Sebastian Igelmann et al., was published September 16,

2021 in *Molecular Cell*.

More information: A hydride transfer complex reprograms NAD metabolism and bypasses senescence, *Molecular Cell* (2021). [DOI: 10.1016/j.molcel.2021.08.028](https://doi.org/10.1016/j.molcel.2021.08.028) , [www.cell.com/molecular-cell/fulltext/S1097-2765\(21\)00695-X](https://www.cell.com/molecular-cell/fulltext/S1097-2765(21)00695-X)

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