New function for glucose metabolism enzyme
23 March 2022, by Will Doss

Fluorescent staining of hexokinase, mitochondria, nuclei and a merged image. Top row shows mitochondrial hexokinase 1, bottom row shows cytosolic hexokinase 1. Note that mitochondrial hexokinase is only near mitochondria, while cytosolic hexokinase one is distributed throughout the cell. Credit: Northwestern University

The function of the glycolytic enzyme hexokinase 1 differs depending on its location within the cell, according to a Northwestern Medicine study published in *Molecular Cell*.

Most hexokinase is bound to the mitochondria, preparing glucose for glycolysis, but hexokinases are also present in in the cytosol, the liquid-filled interstitial space between organelles within a cell. The specific function of cytosolic hexokinase was poorly understood, so Ardehali, De Jesus and their collaborators studied the effects of removing mitochondrial binding domains from hexokinase in mice macrophage cells—forcing hexokinase into the cytosol of these cells.

"After glucose is processed by hexokinase, it's committed to being utilized by the cell in a variety of different ways," said Adam De Jesus, a student in the Driskill Graduate Program in Life Sciences (DGP) and lead author of the study.

"We found the exclusive activation of this pathway creates a bottleneck, so you have this accumulation of metabolites upstream," De Jesus said. "Instead, these metabolites are shunted to other pathways such as the pentose phosphate pathway, which is very important in regulating inflammation."

The discovery of an entirely new function of a well-known enzyme based on its location raises questions about its effects in other cell types, such as..."
as T-cells and neurons, according to Ardehali.

"Just displacing it from the mitochondria to the cytoplasm gives you an entirely different function," Ardehali said. "How it affects cellular function in cells besides macrophages is the focus of the current studies in our lab."


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