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New drug targets for preventing cell death

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A new compound that blocks an early step in cell death could lead to a novel class of drugs for treating heart attacks and stroke.

When cells are deprived of oxygen -- during a heart attack, for example -- they start to die through a tidy process called apoptosis or programmed cell death. Early in apoptosis, the mitochondria -- complex structures that supply energy to the cell -- divide into pieces, holes appear in their membranes and proteins such as cytochrome c leak out. These events trigger other processes, ending in cell death.

"Mitochondria divide like crazy during apoptosis," said Jodi Nunnari, professor of molecular and cellular biology at UC Davis and senior author on the paper. Nunnari's lab has been studying the fundamental processes of mitochondrial division for several years.

The researchers screened 23,000 compounds to find those that blocked mitochondrial division in yeast cells. From three "hits" they picked the most effective, named mdivi-1.

They found that mdivi-1 blocks mitochondrial division dynamin, one of a class of proteins found in both yeast and mammals that can assemble itself into a spiral garrotte around the mitochondrion and cut it in two. Mdivi-1 interfered with the self-assembly of dynamin in both yeast and mammalian cells.

Mdivi-1 also blocked the process that punches holes in the mitochondrial membrane, preventing leakage of cytochrome c. The researchers found

that this process could also be traced back to the effect of mdivi-1 on dynamin.

Dynamins could be a target for drugs that prevent cells from dying -- during strokes, for example, or during heart attacks or in diseases where nerve cells progressively deteriorate and die, Nunnari said. She also noted that the work would not have been possible without having first gained a fundamental understanding of how mitochondrial division works.

Source: University of California - Davis