MedicalXpress

Promising peptide for TBI, heart attack and stroke

February 8 2015

Strokes, heart attacks and traumatic brain injuries are separate diseases with certain shared pathologies that achieve a common end - cell death and human injury due to hypoxia, or lack of oxygen. In these diseases, a lack of blood supply to affected tissues begins a signaling pathway that ultimately halts the production of energy-releasing ATP molecules - a death sentence for most cells.

By employing derivatives of humanin, a naturally occurring peptide encoded in the genome of cellular mitochondria, researchers at Ben Gurion University of the Negev are working to interrupt this process, buying precious time for tissues whose cellular mechanisms have called it quits.

"The present findings could provide a new lead compound for the development of drug therapies for necrosis-related diseases such as traumatic brain injury, stroke and myocardial infarction - conditions for which no effective drug-based treatments are currently available [that work by blocking necrosis]," said Abraham Parola, a professor of biophysical chemistry at Ben Gurion University of the Negev in Beer-Sheva, Israel. Parola is presently a visiting professor of Biophysical Chemistry & Director of Natural Sciences at New York University Shanghai, and will speak about his lab's finding's this week at the Biophysical Society's 59th annual meeting in Baltimore, Md.

The humanin derivatives work by counteracting the decrease in ATP levels caused by necrosis. The researchers tested the effectiveness of the

humanin analogues AGA(C8R)-HNG17 and AGA-HNG by treating neuronal cells with these peptides prior to exposure to a necrotic agent. The experiments were a success.

Parola's previous work has dealt with membrane dynamics and the mechanism of action of anti-angiogenesis drugs, which cause starvation of malignant tumor growths by preventing the supply of nutrients and oxygen to the fast growing tissue, in addition to various other biophysical and molecular medicine and diagnostic topics.

"A recent paper published by our group suggested the involvement of cardiolipin [a phospholipid in inner mitochondrial membranes] in the necrotic process," Parola said. "During this work we stumbled along humanin and were intrigued by its anti-apoptotic effect, and extended it to anti-necrotic effect."

Parola and his colleagues also performed in vivo studies by treating mice that had had traumatic brain injuries with an HNG17 analogue, which successfully reduced cranial fluid buildup and lowered the mice's neuronal severity scores, a metric in which a higher number corresponds with greater degrees of neurological motor impairment.

As the peptides Parola and his colleagues used are derivatives of naturally occurring humanin, an ideal treatment might involve a drug delivery system with the HNG17 as the lead compound, a process aided by the ability of the peptides to penetrate the cell membrane without the use of additional reagents.

Future work for Parola and his colleagues includes further exploration of ischemic activity in liver cirrhosis, as induced by acetaminophen activity, in addition to searching for a synergistic effect between humanin and other anti-necrotic agents, such as protease inhibitors, to increase its clinical potential.

More information: bit.ly/1y47YVX