Doctors will tell you that the very drugs that often save lives also can cause collateral damage. Such is the case with typical treatments for heart attacks. Upon the clearing of blocked arteries, mitochondria – the energy-creating organelles inside cells – are frequently damaged, resulting in cell and tissue death.

Researchers at The Ohio State University are investigating ways to prevent damage to the mitochondria during these cardiovascular events. Findings from the research first appeared in the *Free Radical Biology and Medicine* journal, and more recently in the *Annals of Biomedical Engineering* (the official journal of the Biomedical Engineering Society) titled “Mitochondrial Dynamics and Motility Inside Living Vascular Endothelial Cells: Role of Bioenergetics,” by Randy J. Giedt, Douglas R. Pfeiffer, Anastasios Matzavinos, Chiu-Yen Kao and B. Rita Alevriadou. Giedt was awarded his PhD in biomedical engineering in June; Pfeiffer is a professor of molecular and cellular biochemistry; Kao is an associate professor of mathematics and Alevriadou is an associate professor of biomedical engineering and internal
medicine (cardiovascular medicine) at OSU. Matzavinos
is an assistant professor of mathematics at Iowa State
University. Alevriadou and Pfeiffer also are investigators
at the OSU Davis Heart & Lung Research Institute.

“The goal of our research is to elucidate the role that
hemodynamic forces – in particular fluid shear stress – play
in cardiovascular disease development in human arteries,”
Alevriadou explains.

“To evaluate the role of hemodynamics in
cardiovascular disease, we utilized isolated cells that line our
arteries, called endothelial cells, as these cells are known to
be both responsive to mechanical forces and key players in
all stages of cardiovascular disease. To subject these cells to
shear stress, we cultured them on glass slides, and placed
them in a chamber with a fluid flow entrance and exit.
Shear stress was generated by pumping media to an upper
reservoir, from which a gravity-driven flow through the
chamber was established.”

To simulate a heart attack, Alevriadou says the cells
were subjected to a low flow of oxygen-deprived media
followed by normal oxygenated media flow at a shear stress
similar to that found in human arteries. Following exposure
to these conditions, Alevriadou and her students studied the
morphology and behavior of the mitochondria.

“We study the contribution of mechanical forces on
mitochondrial damage inside endothelial cells exposed to
a simulated heart attack,” Giedt says. “By varying the heart
attack conditions, we regulate the extent of mitochondrial
changes. Extensive mitochondrial fragmentation and loss of
motility can lead to cell death.”

By designing defined hemodynamic environments and
exposing cultured cells to them, Alevriadou says, “We can
study the molecular and cellular pathways and test chemical/
biological agents that may provide protection from a heart
attack-related injury. Specifically, for endothelial cells in hu-
man coronary arteries, their dysfunction/death is considered
an early and catastrophic event during a heart attack … so
finding ways to keep them alive and healthy, by preserving
their mitochondrial function, is an important goal.”

Alevriadou received a grant from the National Institutes
of Health to further study the fusion and fission processes
that take place continuously in the mitochondria of vascular
endothelial cells. As part of the grant, Christopher Scheitlin,
a biomedical engineering PhD student, and Colton Lloyd,
a biomedical engineering undergraduate student, working
in her lab, are investigating the role of cytosolic and
intramitochondrial calcium in altered mitochondrial
shape and motility, and a postdoctoral fellow, Devi Nair,
is looking into the fate of these small mitochondrial
fragments, specifically their removal by the cell’s
autophagic mechanisms.

- Nancy Richison