Surprising discovery: Multicellular response is 'all for one'

Real or perceived threats can trigger the well-known “fight or flight response” in humans and other animals. Adrenaline flows, and the stressed individual’s heart pumps faster, the muscles work harder, the brain sharpens and non-essential systems shut down. The whole organism responds in concert in order to survive.

At the molecular level, it has been widely assumed that, in single-celled organisms, each cell perceives its environment -- and responds to stress conditions -- individually, each on its own to protect itself. Likewise, it had been thought that cells in multicellular organisms respond the same way, but a new study by scientists at Northwestern University reports otherwise.

The Northwestern researchers demonstrated something very unexpected in their studies of the worm C. elegans: Authority is taken away from individual cells and given to two specialized neurons to sense temperature stress and organize an integrated molecular response for the entire organism.

The study, with results that show a possible parallel with the orchestrated “fight or flight response,” will be published in the May 9 issue of the journal *Science.*

“This was surprising -- that two neurons control the response of the 957 other cells in C. elegans,” said Richard I. Morimoto, Bill and Gayle Cook Professor of Biochemistry, Molecular Biology and Cell Biology in Northwestern’s Weinberg College of Arts and Sciences. He led the research team.

“It is well established that single cells respond to physiological stress on their own, cell by cell. Now we’ve shown this is not the case when individual cells become organized to form a multicellular organism. Now it is all for one -- an integrated system where the cells and tissues only respond to stress when the neuronal signal says to respond as an organism.”

The findings have implications for new ways of thinking about diseases that affect the stress pathways, says Morimoto. Neurons that sense the environment govern such important pathways as stress response and molecular chaperones, which play a significant role in aging and neurodegenerative diseases.

In their experiments, the researchers genetically blocked the two thermosensory neurons (known as AFDs) and their ability to sense temperature and discovered there was no response to stress in any cell in the organism without them. (C. elegans is a transparent roundworm whose genome, or complete genetic sequence, is known and is a favorite organism of biologists.)

“This shows, for the first time, that the molecular response to physiological stress is organized by specific neurons and suggests similarities to the neurohormonal response to stress,” said Morimoto, who was the first to clone a human heat shock gene in 1985. “The two neurons control how all the other cells in the animal sense and respond to physiological stress.”

The team also checked the “machinery” of the 957 other cells (those that are not thermosensory neurons) in the mutant animals and determined that the individual cells could sense an increase in temperature. But, because the thermosensory neurons were not working properly and sending signals, the cells did not initiate a heat shock response. No signal, no response.

The researchers proposed a model whereby this loss of cell autonomy serves to integrate behavioral, metabolic and stress-related responses to establish an organismal response to environmental change.

The researchers would predict, considering the study's results, that other organisms including humans might have similar classes of neurons that organize and orchestrate a response to stress -- a central neuronal control switch for regulating temperature and the expression of genes that protect the health of proteins.

Source: Northwestern University