Programmed cell death contributes force to the movement of cells

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In addition to pruning cells out of the way during embryonic development, the much-studied process of programmed cell death, or apoptosis, has been newly found to exert significant mechanical force on surrounding cells.

This mechanical force may be harnessed throughout biology by tissues to aid wound formation, organ development and other processes that require cell movement, according to a Duke University team that melds biology with physics to investigate force at the cellular level.

Cells are known to move in coordinated fashion during the closure of an eye-shaped opening on the back of a developing fruit fly embryo, a model system Duke biophysicists have been working on for nearly a decade. Duke biology chair Dan Kiehart likens this dorsal closure event to drawing the strings on a sleeping bag.

The newly discovered force created by apoptotic cells imploding and withdrawing "is making a force sort of like a friend helping you tuck the edge of the sleeping bag in," Kiehart said.

Dying cells appear to occur at random times across the plane of cells comprising the shrinking opening, in a pattern that totals about 10 percent of the population of cells. When Kiehart first observed them in 2000, he thought "well if it's only 10 percent, I can ignore it."

Physics post-doctoral researcher Yusuke Toyama thought that the

apoptotic cells might be particularly significant for force production. Toyama, who's training started in particle physics but has moved toward biology, began carefully measuring the motion of cells immediately surrounding a dying cell.

What he saw through the microscope, by laser-induced fluorescence, was that as a dying cell collapsed and sunk beneath the surface, it contributed to the forces pulling the edges of the opening closer together.

"So apoptosis is not a single cell event but is amplified by the five-to-seven surrounding cells," Toyama said.

On balance, these dying cells exert perhaps a third to a half of the force that is moving the edges of the opening together, so it's a very significant part of the process, said Glenn Edwards, professor of physics and director of Duke's Free Electron Laser Lab. "The forces at work here are measured in perhaps billionths of a Newton, but that's because you're moving cells," Edwards said. At the cellular scale, these forces are quite substantial.

The group's findings appear in the Sept. 19 edition of *Science*. Funding for the research was provided by the National Institutes of Health.

Though this finding is so far limited to dorsal closure in the fruit fly embryo, Edwards and Kiehart are going to begin looking for the mechanical force of apoptosis elsewhere. Their earlier findings on the fruit fly model so far have appeared applicable to wound closure and organ development in vertebrates like humans.

It's entirely possible, Kiehart said, that evolution has harnessed the mechanical force created by dying cells in many other ways. "In evolution, biology uses what is available to it."

Source: Duke University