Study May Aid Efforts to Prevent Uncontrolled Cell Division in Cancer

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As a single embryonic cell of the worm C. elegans divides to form two daughter cells, and those daughter cells divide into four cells and so on, cellular rings, shown green in this image, form and contract in a precise way. The contractile rings may facilitate the coordination of the process by which the embryo is formed and develops and in other contexts.

Researchers from the Ludwig Institute for Cancer Research at the University of California, San Diego School of Medicine have uncovered a remarkable property of the contractile ring, a structure required for cell division. Understanding how the contractile ring works to divide the cell may facilitate development of therapies to prevent uncontrolled cell division in cancer.

The researchers show that - even though both cell volume and the length of the contractile ring are reduced during successive rounds of embryonic cell division - the duration or timing of cell division remains the same. Their study will be published in the May 29 issue of the journal *Cell.*

"We showed that contractile rings constrict at a constant rate that is proportional to the initial size of the cell, so that rings in larger cells constrict proportionally faster than rings in smaller cells," said Karen Oegema, PhD, associate professor at the Ludwig Institute and the Department of Cellular and Molecular Medicine at UC San Diego School of Medicine and the Moores UCSD Cancer Center. "Because of this property, the time required to complete cell division remains the same during embryogenesis, even as cells get smaller."

During their early development, embryos are progressively partitioned into smaller and smaller cells by successive rounds of cell division. The division of one cell into two is accomplished by the contractile ring, which is assembled from two protein filament types also used in muscle. During cell division, the genome is replicated and the two copies are separated to opposite sides of the cell. A contractile ring forms a belt around the cell middle; constriction or closure of this ring "tightens the belt," pinching the mother cell into two daughter cells.

In early embryogenesis, cell volume and the length of the contractile ring around the cell middle are reduced at each successive round of cell division. By contrast, the dimension of the chromosomes - which carry the genetic material that is segregated to the daughter cells - remains constant. The discovery that contractile rings constrict at a constant rate, proportionate to the initial cell size, opens the door to further studies of the mechanism.

"Further studies of the contractile ring could ultimately lead to improved therapies for cancer," said first author Ana Carvalho, PhD. "Understanding the cellular machinery required for cell division may teach us how to prevent the uncontrolled cell division that occurs in cancer."

Arshad Desai, PhD, professor at the Ludwig Institute and assistant professor of cellular and molecular medicine at UCSD also contributed to the paper. Funding was provided by the Ludwig Institute for Cancer Research, the Pew Scholars Program in the Biomedical Sciences, the Fundação para a Ciência e Tecnologia, Portugal, and The European Social Fund.

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