Study shows clathrin protein moonlights, playing key role in cell division

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A protein called "clathrin," which is found in every human cell and plays a critical role in transporting materials within them, also plays a key role in cell division, according to new research at the University of California, San Francisco.

The discovery, featured on the cover of the Journal of Cell Biology in August, sheds light on the process of cell division and provides a new angle for understanding cancer. Without clathrin, cells divide erratically and unevenly—a phenomenon that is one of the hallmarks of the disease.

"Clathrin is doing more than we thought it was doing," said Frances Brodsky, DPhil, who led the research. Brodsky is a professor in the UCSF Department of Bioengineering and Therapeutic Sciences, a joint department of the Schools of Pharmacy and Medicine, and she holds joint appointments in Microbiology and Immunology, as well as Pharmaceutical Chemistry.

A Protein Essential for Transportation in More Than One Route

Akin to a three-pronged building block in a child's construction set, clathrin can provide links to create larger complexes. When lots of these proteins are assembled together, they can form tough little cages into which cells packs many of their essential biological molecules —hormones, neurotransmitters, membrane proteins and other payloads

that need to be transported throughout the cell.

Once thought to be solely involved in transport inside cells, scientists have uncovered more and more of the protein's hidden functions in the last half-dozen years, including some roles it plays in cell division.

For instance, they learned several years ago about its role in the function of "spindles." Normally when a cell divides, it forms a spindle by laying down tracks of structural proteins, and uses them as scaffolding to separate the cell's DNA (in the form of chromosomes) into two equal collections—one identical set of DNA for each of the new daughter cells . Scientists found that clathrin is involved in stabilizing these spindles.

Now, however, Brodsky and her colleagues have shown that clathrin does even more. They deleted clathrin from cells using a technique called RNA interference, which involves infusing in small genetic fragments that block the cell from making the clathrin. Doing so, Brodsky and her colleagues showed that clathrin stabilizes the structures in dividing cells known as centrosomes.

Tagged with fluorescent chemicals and viewed under a microscope, the centrosomes within a cell that is about to divide look like two glowing eyes peering through the dark. But without clathrin, the team determined, the eyes increase in number.

Brodsky and her colleagues traced this effect to a protein complex formed by one particular component of clathrin called CHC17, which directly stabilizes the centrosome and helps it mature. Deleting CHC17 or chemically inactivating it, led to cells with a strange appearance. These cells contained multiple, fragmented centrosomes instead of the normal two and built abnormal spindles.

This discovery may reveal pathways towards abnormalities of

chromosome segregation associated with cancer, said Brodsky.

More information: The article, "Clathrin promotes centrosome integrity in early mitosis through stabilization of centrosomal ch-TOG" by Amy B. Foraker, Stéphane M. Camus, Timothy M. Evans, Sophia R. Majeed, Chih-Ying Chen, Sabrina B. Taner, Ivan R. Corrêa Jr., Stephen J. Doxsey and Frances M. Brodsky appears in the August 20, 2012 issue of the *Journal of Cell Biology*. dx.doi.org/10.1083/jcb.201205116

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