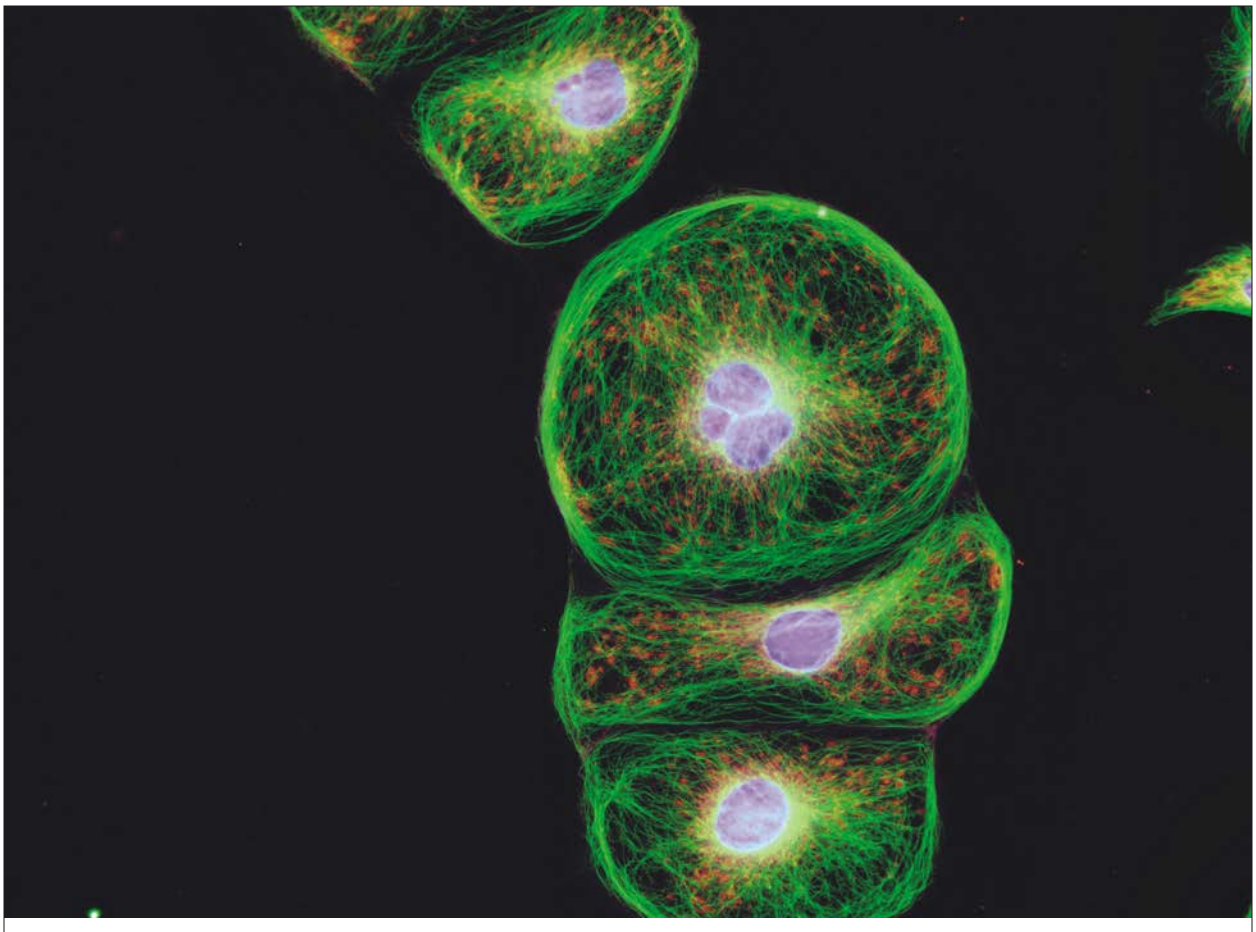

Asian Journal of Cell Biology

ISSN 1814-0068

Academic Journals Inc.

www.academicjournals.com

Key Role for a Protein in Cell Division Described

Just before a cell divides into two -- the basic act of reproducing life -- the cellular environment must be exquisitely prepared. The exact timing and localization of the vast array of molecules and processes involved in duplicating chromosomes and separating the offspring from the parent is one of the basic wonders of biology and is at the core of both healthy living and diseases such as cancer, which arise when the process goes away.

Now scientists at Rockefeller University have detailed the role of one protein, PRC1, that acts in the penultimate stage of cell division, helping to form the architectural structures, called central spindles, needed before the cell splits in two.

The findings expand the understanding of how these microtubules are fashioned into place. "In the absence of PRC1, the central spindle does not form, and that's a major problem, because then the cell doesn't divide," says Radhika Subramanian, lead author on the paper published by Cell in August. "So we wanted to know how PRC1 works, and now we've got a much better idea."

Scientists have known that PRC1, for "Protein Regular of Cytokines 1," is required in yeast, plants and humans for linking together the polymers that make up spindles, called *microtubules*, in a specific orientation. However, how PRC1 mediates microtubule binding and crosslinking was poorly understood? Subramanian, a postdoctoral fellow in Tarun Kapoor's Laboratory of Chemistry and Cell Biology, worked with Seth Darst's Laboratory of Molecular Biophysics to solve the atomic structure of the portion of PRC1 that interacts with microtubules using X-ray crystallography. The researchers determined that PRC1 binds microtubules through a domain which includes a structure called a *spectrin* fold. This is surprising, the scientists say, because it's a new role for the spectrin-fold, which has not been previously shown to mediate microtubule interactions.

Going further, the scientists, in collaboration with the laboratory of Ronald Milligan at the Scripps Institute, used electron microscopy to determine the structure of pairs of microtubules crosslinked by PRC1. A high resolution image revealed a defined crossbridge conformation of PRC1 which is attained only when the crosslinker is interacting with two microtubules. These structural features provide a model for how PRC1 achieves specific crosslinking of antiparallel microtubules.

PRC1 is a nonmotor protein, meaning it does not actively drive microtubules around the cell, but rather organizes their structure. (Another family of proteins, motor proteins, do the moving.) Subramanian and her colleagues set up an in vitro fluorescence microscopy based assay in which they could observe PRC1 activity as well as that of a motor protein on the same microtubule pair and found that PRC1 did not interfere with microtubule movements driven by motor proteins.

"So, it doesn't act as a brake as was previously thought," Subramanian says. "By itself, it's capable of recognizing antiparallel overlaps regions in a dynamic, moving system, which is important. We think it could act as a mark that recruits other proteins to these specialized structures in cells."

That's one hypothesis Subramanian and colleagues want to explore next.

Cell, 2010; 142 (3): 433 DOI: 10.1016/j.cell.2010.07.012