Dartmouth researchers find new protein function

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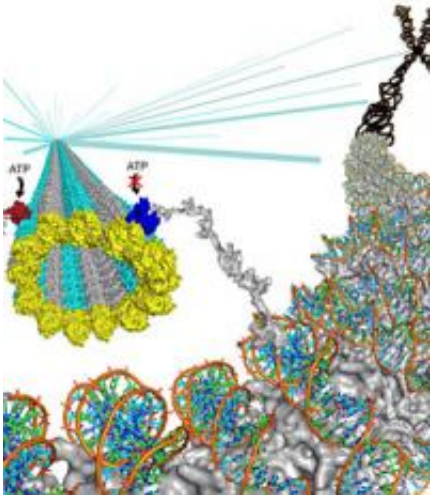

Protein NOD at the end of a microtubule (illustration by Jared Cochran)

A group of Dartmouth researchers has found a new function for one of the proteins involved with chromosome segregation during cell division. Their finding adds to the growing knowledge about the fundamental workings of cells, and contributes to understanding how cell function can go wrong, as it does with cancerous cells.

The researchers studied a protein called NOD, distantly related to the motor proteins that power diverse cellular activities, including intracellular transport, signaling, and cell division. They used X-ray crystallography to determine its structure, and then they used enzyme

kinetics to find out how it performed. While this protein is found in fruit flies, the results are helpful in determining how related proteins work in humans.

"This study on NOD provided evidence for a new way a kinesin motor could function," said Jared Cochran, a postdoctoral fellow at Dartmouth and the lead author on the study. "Rather than moving on its own, it hitches a ride on the ends of microtubules which results in a dynamic cross-linking between the arms of chromosomes and the cell's growing spindle of microtubules. If NOD doesn't function properly, then the two cells end up with either both or none of that particular chromosome, which is lethal [to the cell and the organism] in most cases."

With colleagues from Lawrence Berkeley National Laboratory, Stowers Institute for Medical Research in Kansas City, Missouri, and Kansas University Medical Center in Kansas City, Kansas, the Dartmouth group published their study in the Jan. 9, 2009, issue of the journal *Cell*. Their paper is titled, "ATPase Cycle of the Nonmotile Kinesin NOD Allows Microtubule End Tracking and Drives Chromosome Movement."

"Before this study, it had been shown that kinesin motors either walked along their microtubule tracks or functioned to break microtubules apart," says Jon Kull, the senior author on the paper, associate professor of chemistry at Dartmouth, and a 1988 Dartmouth graduate. "This work describes a novel mode for kinesin function, in which NOD does not walk, but rather alternates between grabbing on to and letting go of the end of the growing filament, thereby tracking the end as it grows. The diversity of function of these proteins is remarkable."

One of the authors on the paper, Natasha Mulko, is a 2007 Dartmouth graduate, and worked on this project as her senior honors thesis in chemistry. Mulko is currently a graduate student in dentistry at Creighton University. "Natasha's work was integral to this study as she

worked on obtaining and improving the protein crystals necessary to solve the structure," says Kull, her thesis advisor.

Source: Dartmouth College