Scientists study transient degradation of an actin regulator

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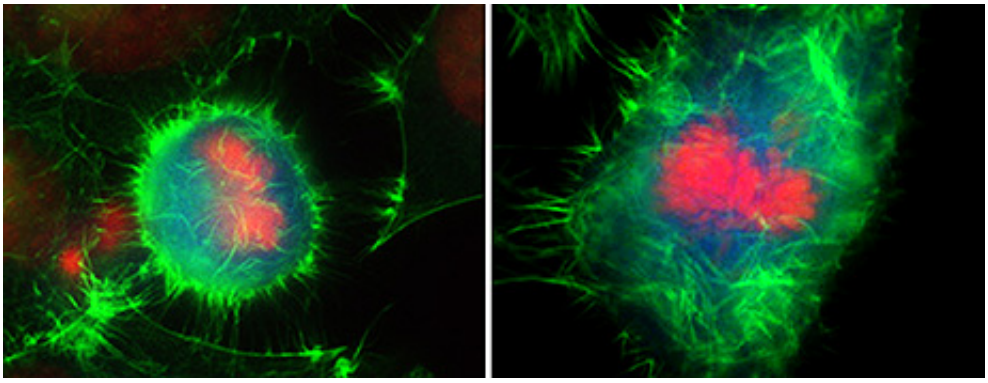

Immunofluorescence staining of a cell in early mitosis with normal (right) and with elevated (left) levels of Eps8. The actin cytoskeleton is shown in green and DNA in red. Blue colours depicts a specific marker for mitosis. Credit: Dr. Achim Werner

Scientists at the Center for Molecular Biology of Heidelberg University have gained new insight into the process of mitosis in mammalian cells. Researchers under the direction of Prof. Dr. Frauke Melchior, in collaboration with colleagues from Göttingen, Milan and Memphis, have succeeded in deciphering a heretofore unknown mechanism that plays a key role in cell shape changes during mitosis. They investigated the transient degradation of a protein that regulates specific structures of the mechanical scaffold of the cell, the actin cytoskeleton.

The results of the research on this actin regulator were published in the

journal Nature Cell Biology.

Equally dividing the chromosomes between two daughter cells during mitosis is a multi-step and precisely controlled process. After break-down of the cell nucleus and mitotic spindle formation, the chromosomes pull apart and travel towards the spindle poles. Two cell nuclei are then formed and the cell splits into two daughter cells. According to Prof. Melchior, it has long been known that the cell's actin cytoskeleton – threadlike cellular structures made up of the structural protein actin – is also a major regulating component of this process. Due to dynamic changes before, during and after the mitosis phase, the actin cytoskeleton contributes to the mechanical requirements for the symmetrical distribution of chromosomes to the two new daughter cells. "We barely understand how and why the actin network of the cell changes, especially in the early phases of mitosis. Of particular interest is how cells assume a round shape when cell division starts and then flatten out again once it ends", explains Dr. Achim Werner, a key contributing member of Prof. Melchior's research group.

The Heidelberg researchers were now able to show that the transient degradation of an actin regulator in the cell's cytoskeleton, known as Eps8, plays an important role in the mitosis phase. The degradation of Eps8, which only appears to be a "stable" protein, is mediated by a little known Ubiquitin E3 ligase. "If you turn off this degradation mechanism, cell rounding is delayed and the early phases of mitosis slow down. If, however, there is too little Eps8 during the later phase of mitosis, the shape of the cell deforms markedly", continues Dr. Werner. Thus, precise control of Eps8 levels contributes to the structural changes that eukaryotic cells must undergo to distribute the genetic information correctly to the two daughter cells. "Our work once again demonstrates that controlled protein degradation is a critical component in the regulation of cellular processes", says Prof. Melchior.

More information: *Nature Cell Biology* (published online 13 January 2013), doi:10.1038/ncb2661