IMP Press Release

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Research Institute of Molecular Pathology

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Illustration:
www.imp.ac.at/pressefoto-kinetochor/

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Of Yeast and Men: An evolutionary tale

Scientists at the Research Institute of Molecular Pathology in Vienna discover and elucidate the function of conserved cell division proteins in yeast

The adult human body consists of trillions of cells. Cell proliferation is accomplished by means of cell division in which an existing cell serves as the exact blueprint for its progeny. This process follows the same basic principles in all higher organisms. First, the genetic information is precisely copied and subsequently equally distributed between the mother and daughter. The major task for the dividing cell is to drag two complete sets of chromosomes to the opposite sides of the nucleus, respectively. A logistic challenge accomplished by the interplay of two factors: the spindle apparatus that acts as the molecular motor driving chromosome movements, and the kinetochore that constitutes the physical platform between the DNA and the mitotic spindle.

The attachment site formed by the kinetochore is an intricate protein network. While its components providing the direct contact point for the spindle are very well preserved from yeast to human, evolution of the DNA-binding proteins remained puzzling given that the underlying DNA template is highly variable.

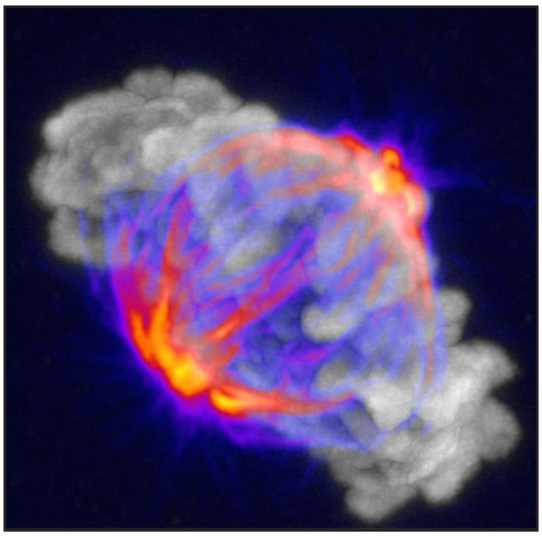
Now, a novel study published in the June edition of Nature Cell Biology sheds light onto the cryptic molecular relationship between the yeast and human kinetochore. Principal investigator Stefan Westermann and his team tracked the missing evolutionary link and opened up new insights into the architecture and function of the key division organelle.

The correct shape pieces the puzzle together

“The clue was to take a close look at the protein sequence as well as specific sequence motifs that get an amino acid chain into its particular shape.” says Stefan Westermann. “In this way, our bioinformatician Alexander Schleiffer was able to predict a number of novel DNA-binding kinetochore proteins and assigned them to the respective human homolog.” Follow-up experiments strongly supported analogous function of the proteins. “Yeast is still an informative model organism and very easy to handle. Our current findings can now direct similar studies in more complex systems. There erroneous chromosome segregation is deleterious for the cell and a common cause of cancer” explains the scientist.

Pull chromosomes together

One of the novel proteins, termed Cnn1, turns out to be of special interest. It connects to the kinetochore molecule Ndc80 that is the major contact point for the spindle apparatus. “This particular interaction is not essential for the initial attachment of the spindle. It rather plays a supporting role that timely overlaps with maximal pulling forces acting on the chromosomes” says Stefan Westermann.



Illustration

Dividing human cancer cell. The DNA (gray) is attached to the spindle apparatus (pseudocolored). This cell is in metaphase, the cell division stage where duplicated chromosomes are optimally positioned for subsequent distribution to either spindle pole. (Courtesy René Ladurner)

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The paper "CENP-T proteins are conserved centromere receptors of the Ndc80 complex" by Schleiffer et al. will be published online on Nature Cell Biology's website on 06 May, 2012 (DOI 10.1038/ncb2493).

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