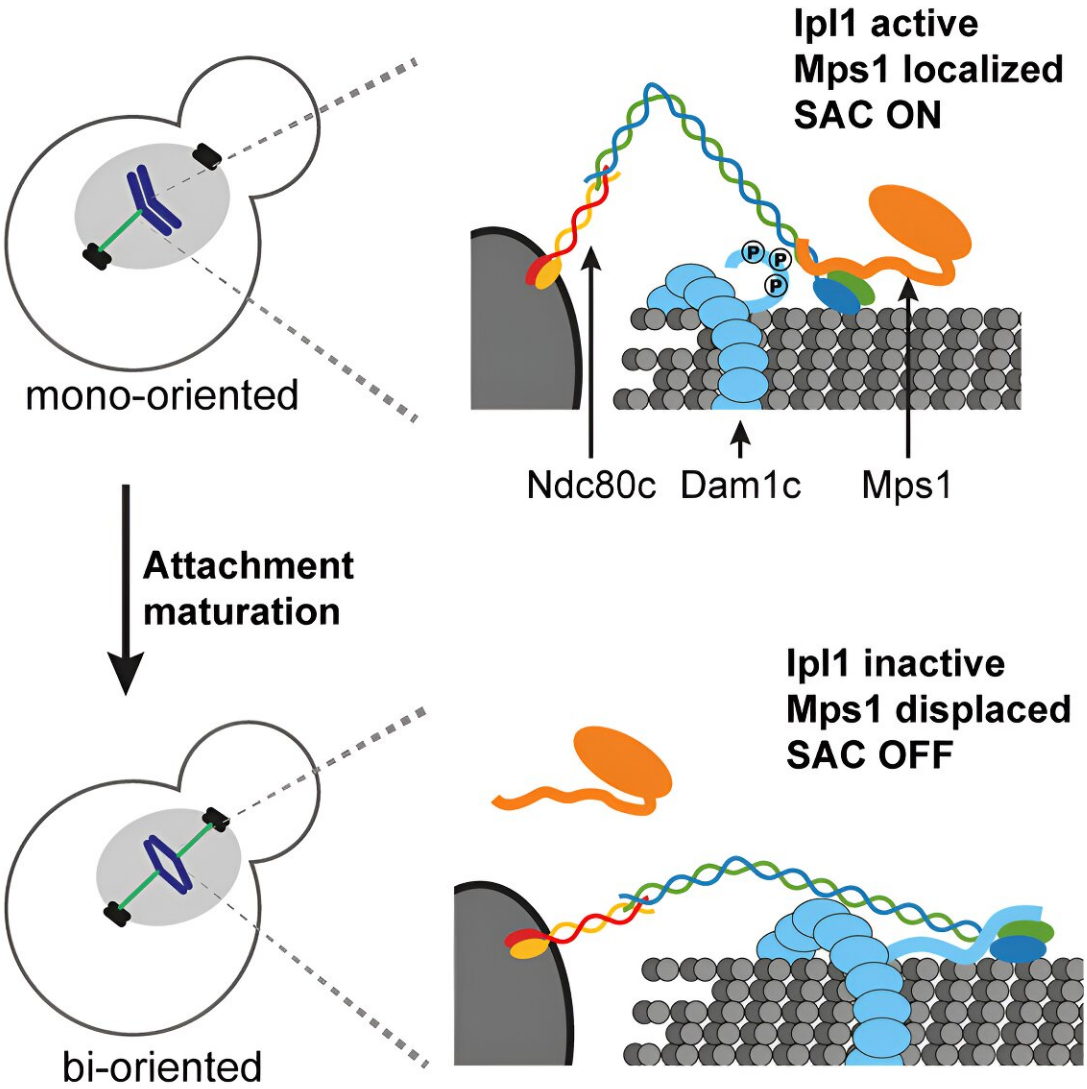
Molecular stop signal identified: The surveillance system of cell division

June 4 2024, by Birte Vierjahn



Credit: *Current Biology* (2024). DOI: 10.1016/j.cub.2024.03.062

Several million cells divide every second in our bodies. During nuclear division (mitosis), the genetic material must be distributed correctly and completely between the daughter cells—errors in this process can lead to defective developments or genetic disorders, and many cancer cells are also characterized by unequal numbers of chromosomes.

Therefore, if errors in the division process become apparent, the cell can stop it. Biologists at the University of Duisburg-Essen have been able to elucidate this process at a molecular level. Their findings are published in *Current Biology*.

During cell division, mitotic spindles are formed—tiny fibers that originate at opposite poles of the cell and bind to the chromosomes to pull one representative of each sister chromatid into one of the two resulting cells. A sophisticated monitoring system is in place to prevent errors during cell division. This system sends a "Stop! Dont divide yet!" signal to the cell as long as not all chromosomes have correctly connected to the mitotic spindle.

Researchers from the University of Duisburg-Essen (UDE) and colleagues from the Max Planck Institute of Molecular Physiology in Dortmund, have now been able to gain new insights into the molecular mechanism of this surveillance system.

They discovered how the initiator of the stop signal, a protein kinase called Mps1, is bound to the attachment site of the chromosomes and how it is only dislodged once the chromosomes are correctly bound to the mitotic spindle.

The study, carried out in the Collaborative Research Center 1430 Molecular Mechanisms of Cell State Transitions at the UDE, answers long-standing questions about the mechanism of the molecular stop signal and how it is switched off.

"We were able to establish that Mps1 is involved in other processes of chromosome division in addition to the initiation of the stop signal," explains Richard Pleuger, first author from the research group Molecular Genetics I headed by Prof. Dr. Stefan Westermann. "In the future, the mutants we have established could be used to investigate further aspects that are still poorly understood."

Predictions of atomic protein structures and binding surfaces using artificial intelligence (AI) were particularly important for the project. In the future, AI-inspired, precise experiments promise further insights into the mechanism of cell division—for example, to clarify how faulty attachments are recognized and corrected.

More information: Richard Pleuger et al, Microtubule end-on attachment maturation regulates Mps1 association with its kinetochore receptor, *Current Biology* (2024). DOI: 10.1016/j.cub.2024.03.062

Provided by University of Duisburg-Essen