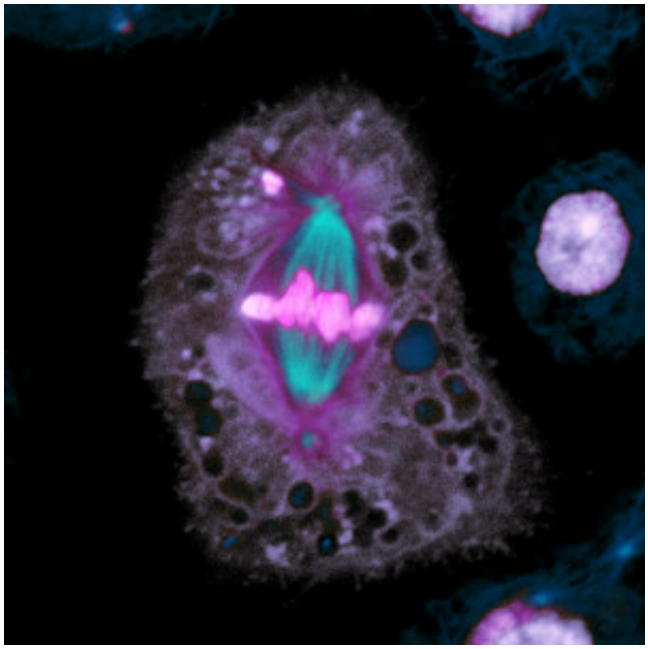
An intracellular membrane system helps cells to divide

Cell duplication is the fundamental requirement for the development of multi-cellular organisms, a process that relies on two basic events: replication of the genetic information and the consequent separation of this information into two daughter cells. The first task is achieved during a “synthesis phase” where DNA strands (which encode all the genetic information of an organism) are copied with high precision.



Drosophila S2 cell during mitosis. The mitotic spindle (cyan), chromosomes (magenta) and the membranous system surrounding the spindle (magenta) are depicted.

DNA in higher organisms is packaged and organized into chromosomes, macromolecular complexes which apart from DNA contain RNA and a multitude of proteins. A phase known as mitosis serves the second critical step in the creation of two genetically identical daughter cells: equal separation of the duplicated chromosomes into two cells. The mitotic spindle plays the key role during this process. This structure is mainly composed of microtubules, filaments that are polymerized from ?- and ?-tubulin proteins. However, many other proteins are required for the formation and functioning of the mitotic spindle which “captures” chromosomes to mediate their physical segregation to opposite sides of the cell, before the cell is cleaved into two. Interestingly, several proteins implicated in spindle assembly or other mitotic processes have been shown to accumulate in the spindle region in a microtubule-independent manner in different organisms, but a binding substrate or diffusion barrier which could account for this effect has not been identified. Our

recent findings shed light on the underlying mechanism and revealed its importance for accurate cell division. We could demonstrate that the mitotic spindle in *Drosophila* (fruit fly) and human culture cells is surrounded by a fenestrated membrane system ("spindle envelope") that acts as a molecular sieve: while large membranous organelles, such as mitochondria, are prevented from entering the "spindle compartment", small proteins can easily pass the holes and freely diffuse in all available spaces within the cell. However, these are, due to the absence of membranous organelles, more abundant in the spindle region where small proteins consequently accumulate.

Since some of these proteins have a well-established role in the formation of the mitotic spindle, such as soluble tubulin, we analyzed spindle assembly in *Drosophila* cells after artificially disrupting the spindle envelope via laser microsurgery. We observed that accumulation of soluble tubulin in the spindle region significantly decreased upon this procedure and, moreover, that spindle assembly and consequently chromosome segregation were severely impaired.

Mitosis has to be executed with high precision to prevent unequal chromosome segregation, a condition that has been linked to several developmental defects and might be the primary cause of cancer. Our study has revealed the importance of an intracellular membrane system in spindle assembly, a key process for cell division. In the future it will be important to dissect whether this conserved structure assists additional mitotic processes as its existence underlies the accumulation of several, functionally unrelated proteins in the spindle region.

Publication

An organelle-exclusion envelope assists mitosis and underlies distinct molecular crowding in the spindle region.
Schweizer N, Pawar N, Weiss M, Maiato H
J Cell Biol. 2015 Aug 31