Scientists model a crucial component of cell division

September 9 2016

During the process of cell division, chromosomes must be distributed equally between the two emerging daughter cells. One copy of each chromosome is created and remains glued to the original until threads, called microtubules, pull the chromosome pairs apart and distribute them to the two new cells. Researchers from the Max Planck Institute of Molecular Physiology in Dortmund and the Gene Center of the University of Munich (LMU) have now analyzed and modelled the structure of the point of attachment of the chromosomes to the threads, called the kinetochore. In the process, they have discovered how the different kinetochore proteins work together to bind the chromosomes securely to the microtubules.

Cell division is vital for the continuation of life. If something goes wrong in, say, the distribution of chromosomes, abnormalities or serious diseases such as cancer may result. This is why scientists are keen to get to grips with the details of this fundamentally important process.

"What I cannot create, I do not understand." This quote from physicist Richard Feynman is a guiding principle for Andrea Musacchio, Director at the Max Planck Institute and head of the study. He uses it to make a virtue of necessity, as the interplay of the individual components of the kinetochore during cell division in real cells does easily not lend itself to examination. "Only by taking the system apart and simplifying it do we have a chance of understanding how the kinetochore works - so we modelled it in the lab", explains Musacchio.

Complex threedimensional puzzle

The nuclear complex of a kinetochore contains about 30 proteins, making synthesis in the laboratory very difficult – like a construction kit with Lego blocks that all have different shapes and functions. But it gets worse: "Unlike Lego, these protein building blocks in the kinetochore interact with each other – but we didn't know how. Besides, you can't just walk into a store and pick the blocks you need off the shelf", reports John Weir, lead author of the study.

The scientists began to synthesize the various building blocks of the kinetochore individually and eventually managed to construct an artificial kinetochore with 21 parts, which can connect chromosomes to microtubules. The whole system is far more complex in the natural world, as even more proteins have roles to play in real cells.

Using the model, the scientists were able to examine the details of kinetochore function and structure. They found that the seven subunits of the protein complex CHIKMLN interact with each other. "This increases their binding strength with certain partners", explains Alex Faesen, who participated in the study. CHIKMLN is connected to the chromosome by a protein and binds to a ten-unit assembly (the KMN network), which is responsible for microtubule contact. "The whole structure consists of 21 subunits that form a bridge between the chromosome and the microtubules", says Kerstin Klare, another member of the research team, in summary.

By modelling the kinetochore, the team has laid the foundation for further studies into the complex architecture and functionality of this vital structure. Their goal: to create an artificial model of cell division as a whole. "Because only when we can recreate these processes and cell components will we be in a position to truly understand how they work", says Musacchio.

More information: John R. Weir et al. Insights from biochemical reconstitution into the architecture of human kinetochores, *Nature* (2016). DOI: 10.1038/nature19333