

Molecular glue with new effect

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Ten years ago, researchers at the IMP - a basic research institute in Vienna - discovered a fundamental and amazingly plausible mechanism of cell division. They identified a protein complex, which, as a ring-shaped molecule, slides over the doubled chromosomes and holds precisely these together until the time they again separate. Because of its function as molecular glue, the protein complex was given the name cohesin.

In the working group of Jan-Michael Peters, Senior Scientist at the IMP, the molecule was continually monitored over the last ten years. Now Peters and his colleague, Kerstin Wendt, in cooperation with Katsuhiko Shirahige from the Tokyo Institute of Technology, were able to find evidence of another, also essential function of cohesin.

As the researchers report in the online issue of the journal *Nature*, the molecule acts as a regulator of gene expression, and therefore plays an important role in the reading of genes. The molecule fulfills this function entirely independently of its thus far known activity.

Various inhibiting and promoting elements within the genome affect whether genes can be read in a particular situation and how intensively this process proceeds. Promoters initiate the reading process, whereas enhancers strengthen it, and silencers suppress it. The combination of these factors must be very finely tuned. The areas that are each influenced by the regulators are separated from each other by so-called insulators. It has now been ascertained at the IMP for the first time ever that cohesin is necessary for the function of such insulators.

This discovery not only enriches basic research by contributing to further fundamental knowledge. It should also be of medical interest: a number of rare but serious disorders can be traced back to mutations in cohesin. If the regulation of gene expression proceeds abnormally, developmental disorders are the result. The range of symptoms extends from subtle and hard-to-diagnose changes to massive, physical and cognitive impairments. One of the more well-known disorders of this kind is called Cornelia de Lange Syndrome. Affected persons suffer from numerous anomalies and malformations. A causative treatment is not available.

“We cannot cure the disease, but we now know the molecular mechanisms that cause it. This helps us to better understand the disorder and its symptoms. Moreover, we expect that our findings will stimulate new exciting research”, stated Jan-Michael Peters.

A valuable resource for this has already been created by the researchers in the course of their work: they have systematically searched the entire human genome for cohesin binding sites – that is, the areas where cohesin is effective. Thus, the first genome-wide cohesin map in a mammalian species was developed. The database is open to the entire scientific community.

Source: Research Institute of Molecular Pathology

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