

German Genetics Society Meeting 2009: Session IV

Martin Fenner, Gobbledygook

September 21, 2009

Another guest post by Alex Knoll reporting from the German Genetics Society Meeting in Cologne.

The first session on Friday started with a talk by Frauke Melchior from the ZMBP in Heidelberg on SUMO. Apart from being interesting to work with, it also is good for some rather funny paper titles

At the start, she gave a short introduction on the properties of SUMO. It is similar to Ubiquitin (it stands for Small Ubiquitin-like MOdifier) and gets covalently bound to lysines of hundreds of proteins to change their protein or DNA interactions, localization, or activity. A good example I also know from my work is the yeast DNA repair helicase Srs2, which only interacts with the SUMOylated form of the replication protein PCNA at the replication fork to suppress recombination. Many protein-protein interactions that are dependent on SUMOylation can be traced back to non-covalent recognition of a SUMO-interaction motif, SIM.

Like with ubiquitin, there is an enzymatic cascade to bind a SUMO unit to a target protein; however, there is only one E1 activating and one E2 conjugating enzyme, and a handful of E3 SUMO ligases (compared to hundreds for the ubiquitin pathway). Target recognition is not understood very well, but there is a known consensus site which is recognized by the E2 enzyme for SUMOylation. The problem is: many proteins are SUMOylated at non-consensus sites. Another mechanism turns the usual direction of the pathway on its head: The target protein interacts with SUMO via a SIM, while it is still bound to the E2 enzyme. This allows the E2 to transfer SUMO to the target protein.

Finally, Frauke Melchior told us about an interesting pair of proteins that are involved in SUMOylation: RanGAP (RanGTPase activating protein) interacts with RanBP2 at the nuclear pore complex after it gets SUMOylated. RanBP2 itself is a SUMO E3 ligase, but not for RanGAP. Without going into too much detail (unpublished data), the story unraveled by Frauke Melchior and her coworkers showed a really complex and intriguing picture of the role SUMO plays in regulating the activity of this complex and the effect on nuclear transport.

In the second talk of the session, Chris Wylie from the Developmental Biology division of the Cincinnati Children's hospital threw out the simple model of germ cell migration in mouse embryos found in the textbooks: During embryo development, the stem cells of the gametes, the germ line stem cells, have to migrate to their niche in the gonads. They start their travels in a structure called the allantois, go through the hindgut and from there to the genital ridges, where the gonads will form. Classically, it was thought that long range signals guide their migration. But this is problematic, because the target organ supposed to produce the guiding signal is not formed when the germ cells start their migration, and during the migration the surroundings and distances will change dramatically! That means there must be short range signals for guidance.

A nice example to test this is the trip from the midline above the gut to the genital ridges. Germ cells that stay at the midline will die by apoptosis. The previously known stem cell survival factor Steel is involved in preventing apoptosis in the cells. Its concentration decreases from the ridges to the midline; adding Steel everywhere experimentally saves the midline germ cells from apoptosis, while blocking Steel everywhere kills the germ cells laterally. They were able to show that Steel is not only involved in apoptosis, but also in the migration and proliferation of the germ cells. Steel is not only required at the late migration from the midline to the genital ridges; from the start in the allantois, loss of Steel leads to loss of germ cell number and migration.

Essentially, this means that not only is Steel one (of probably many) short range signals, but it also travels with the germ cells along their migration route, giving them a mobile stem cell niche!