Karl Friedrich Bonhoeffer Lecture

Donnerstag, den 25.3.2010 -11:00 Uhr

Manfred-Eigen-Hörsaal,
Max-Planck-Institut
für biophysikalische Chemie

Am Fassberg 11, 37077 Göttingen

Dr. Jürgen A. Knoblich

Institut für Molekulare Biotechnologie
der Österreichischen Akademie der Wissenschaften, Wien

Asymmetric cell division and proliferation control in *Drosophila* and mouse neural stem cells

Stem cells can generate self-renewing and differentiating daughter cells at the same time. We are using *Drosophila* as a model system to understand how they control the balance between these two fundamentally different types of progeny. Using a proteomics approach for proteins that segregate into one of the two daughter cells in neuroblasts (stem cell like precursors of the central nervous system) we have found the growth regulator *brat (brain tumor)*. During mitosis, Brat segregates into one of the two daughter cells, where it downregulates protein synthesis, stops proliferation and prevents cell growth. In *brat* mutant animals, all daughter cells of the stem cell undergo self-renewal and continue to proliferate. This leads to dramatic overproliferation and the formation of a stem cell derived tumor which grows indefinitely and kills the animal. Tumors will continue to proliferate indefinitely, even when transplanted into other flies, thus indicating that cells become immortalized. Very similar phenotypes are observed in flies mutant for Lethal (2) giant larvae (Lgl), where Brat is present but does not segregate asymmetrically. Thus, the asymmetric segregation of Brat into one of the two daughter cells regulates proliferation in *Drosophila* neural stem cells.

Brat is a member of a conserved protein family characterized by a similar domain composition. We have analyzed the function of Brat homologs during the development of the mouse brain and find a remarkable functional conservation that indicates an important role of this protein family in controlling stem cell proliferation.

Gastgeber: Helmut Grubmüller