

The cell biology of neurogenesis

Wieland B. Huttner

Max Planck Institute of Molecular Cell Biology and Genetics, Dresden, Germany

Our group studies the cell biological mechanisms underlying the switch of neuroepithelial (NE) cells from proliferation to neurogenesis in the mouse embryo (1-3). Prior to, during, and as a consequence of, neurogenesis, NE cells down-regulate a number of epithelial features (4,5). Expression of the anti-proliferative gene TIS21 can be used as a tool to distinguish between proliferating and neuron-generating NE cells (6). Time-lapse microscopy of neuron-generating divisions of NE cells using transgenic mouse embryos expressing GFP under the control of the TIS21 promoter reveals the existence of a novel neuronal progenitor dividing at the basal side of the neuroepithelium (7). We also investigate the role of cell cycle length in determining the onset of neurogenesis (8,9). To study the distribution, during mitosis, of cellular components in the context of the apico-basal axis of NE cells, we focus on prominin-1, a pentaspan membrane protein sorted to the apical surface of NE cells and specifically retained in plasma membrane protrusions (10-12). Prominin-1 is associated with a novel, cholesterol-based lipid raft which is involved in prominin's retention in microvilli (11). Using prominin-1 to define the apical surface of NE cells, we investigate the symmetric vs. asymmetric distribution of the apical plasma membrane during proliferating vs. neuron-generating divisions of NE cells (13). Remarkably, during neurogenesis, the prominin-1-containing apical plasma membrane microdomain is released into the neural tube lumen as novel extracellular vesicles (14). Finally, we have developed a method to knock-down gene expression in NE cells using RNA interference in the developing mouse embryo (15).

1. Huttner and Brand (1997) *Curr. Opin. Neurobiol.* 7, 29-39.
2. Wodarz and Huttner (2003) *Mech. Dev.* 120, 1297-1309.
3. Götz and Huttner (2005) *Nature Reviews Mol. Cell Biol.*, in press.
4. Aaku-Saraste et al (1996) *Dev. Biol.* 180, 664-679.
5. Aaku-Saraste et al (1997) *Mech. Dev.* 69, 71-81.
6. Iacopetti et al (1999) *Proc. Natl. Acad. Sci. USA* 96, 4639-4644.
7. Haubensak et al (2004) *Proc Natl. Acad. Sci. USA* 101, 3196-3201.
8. Calegari and Huttner (2003) *J. Cell Sci.* 116, 4947-4955.
9. Calegari et al (2005) *J. Neurosci.* 25, 6533-6538.
10. Weigmann et al (1997) *Proc. Natl. Acad. Sci. USA* 94, 12425-12430.
11. Röper et al (2000) *Nature Cell Biol.* 2, 582-592.
12. Corbeil et al (2001) *Traffic* 2, 82-91.
13. Kosodo et al (2004) *EMBO J.* 23, 2314-2324.
14. Marzesco et al (2005) *J. Cell Sci.* 118, 2849-2858.
15. Calegari et al (2002) *Proc. Natl. Acad. Sci. USA* 99, 14236-14240.