Abstract for ÖAW Workshop 2019 Andi H. Hansen

Title:

Cell-Autonomous and Non-Autonomous Mechanisms Controlling Projection Neuron Migration

Abstract:

Concerted radial migration of newly born cortical projection neurons, from their birthplace to their final target lamina, is a key step in the assembly of the cerebral cortex. The cellular and molecular mechanisms regulating the specific sequential steps of radial neuronal migration *in vivo* are however still unclear. Recent evidence suggests that distinct signaling cues act cell-autonomously but differentially at particular steps during the overall migration process. Functional MADM (Mosaic Analysis with Double Markers) analyses in comparison to global knockout also indicate a significant degree of cell-non-autonomous and/or community effects in the control of cortical neuron migration. Cell-non-autonomous effects may differentially affect cortical neuron migration in distinct compartments and thus regulate critical steps in the migration process. It is therefore not only essential to determine the nature of the interplay of cell-autonomous and cell-non-autonomous mechanisms but also how they control cortical neuronal migration. Here we established a MADM-based experimental strategy for the analysis of cell-autonomous versus non-autonomous gene function and/or community effects. We pursued subtractive phenotypic analysis of genetic mosaics (wild-type/heterozygote background) with conditional and/or global knockout (mutant background), both coupled with sparse fluorescent MADM-labeling of homozygous mutant neurons, to trace the sequential steps of migration in 4D. Using these experimental paradigms we define so far unknown cell-autonomous functions of candidate signaling pathways intersecting with cell-non-autonomous effects to coordinate radial neuron migration.