5 SUMMARY

Neural progenitor cells exist in the central nervous system of rodents and primates, and divide throughout life. They reside in the subventricular zone and generate neurons, which migrate to the olfactory bulb, where they integrate functionally as interneurons. Under appropriate conditions, the progenitor cells proliferate *in vitro* and form free-floating clusters, called neurospheres, that are composed of dividing progenitors and early differentiating cells. Neurospheres represent an *in vitro* model system for the analysis of adult neurogenesis.

Neural progenitors from mice were cultivated and differentiated into neurons, astrocytes, and oligodendrocytes. To shed more light on the molecular mechanisms governing the proliferation of neural progenitors and their migration and differentiation into specific cell types, dynamic gene expression changes during the first four days of neurosphere differentiation were measured with cDNA microarrays containing 13,627 clones. To identify genes with key regulatory functions, a time course study was done in which proliferating progenitors were compared to cells that had differentiated for 24, 48, or 96 hours. A cluster analysis revealed the dynamics of gene expression changes during the time course and identified groups of genes with a similar onset and course of transcriptional changes. Following literature studies and protein domain predictions, these genes were sorted into ten categories according to their function or cellular localization. This study revealed many new interesting genes that change in expression in the course of neural progenitor cell differentiation. These genes are potentially relevant for adult neurogenesis.

Differential expression of selected genes was confirmed by semi-quantitative RT-PCR. Immunofluorescence experiments on differentiating neurosphere cells demonstrated selected corresponding proteins in specific cell types. These findings correlated with the *in situ* situation in the subventricular zone, as was shown by immunohistofluorescence studies of adult mouse brain sections. Some very interesting candidate genes, their expression, and their potential functional involvement in the maintenance of progenitor cells and in the migration and differentiation of new neurons were discussed. Results from the microarray and immunofluorescence experiments support the proposed lineage relationship of embryonic radial glial cells and adult subventricular zone progenitor cells.

Among the differentially expressed genes were *Ptpns1* and *Cd47*, whose products constitute a cell-cell communication system involved in cellular recognition, aggregation, and migration. First experiments aiming at the functional characterization of PTPNS1 and CD47 in the context of neuroblast migration were described.