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Cell cycle length of neuroepithelial cells in the zebrafish embryo

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Two sets of factors determine the fate of a cell. Intrinsic factors operate in a cell-autonomous manner, whereas extrinsic factors are provided by the environment of the cell. The aim of my thesis was to determine whether the cell cycle length of a neural progenitor cell is controlled primarily intrinsically or extrinsically. To answer this question we had chosen the method of single cell transplantation, using the zebrafish embryo as a model organism. Transplantation *per se* did not alter cell cycle length. A labeled cell was transplanted from one area of the neuroectoderm into a different area. Transplanted NE cells integrated into the receiving tissue. Following the transplantation, the cell cycle length of the transplanted donor cell and its descendants could be directly measured in a long-term time-lapse recording.

Within one area of the neuroectoderm (eyefield or hindbrain area, respectively), the cells did not behave uniformly with regard to the cell cycle length. The high variability within the same domain reflects an intrinsic heterogeneity of the population of NE cells.

Nevertheless, homotopic transplantation experiments revealed that there were differences in the average cell cycle lengths between different areas of the neuroepithelium (eyefield vs. hindbrain area). These differences could be observed already at the shield stage (6 hpf), when the neuroectoderm was morphologically still homogeneous. NE cells transplanted within the eyefield divided on average earlier than cells transplanted within the hindbrain area. The resulting daughter cells showed a shorter average cell cycle length in the eyefield than in the hindbrain area.

If transplanted heterotopically from the eyefield to the hindbrain area at the shield stage, cells divided later compared to cells transplanted within the eyefield. The resulting daughter cells had a longer average cell cycle. If transplanted heterotopically from the

hindbrain area to the eyefield at the shield stage, cells divided earlier compared to cells transplanted within the hindbrain area. The cell cycle of a transplanted NE cell could therefore not only be slowed down, but also accelerated. Likewise, the resulting daughter cells had a shorter average cell cycle.

The cell cycle length increases during development. A neuropeithelial cell transplanted homochronically at the 5-somite stage needed on average about three times longer until it divided than a NE cell transplanted homochronically at the shield stage. The resulting daughter cells needed on average at least two times as long to complete their cell cycles. Homochronically transplanted neuroepithelial cells at the 5-somite stage integrated into the host tissue and formed part of the host embryo.

In contrast to this observation, heterochronically transplanted NE cells, taken from a donor embryo at the shield stage and placed into a host embryo at the 5-somite stage, did not integrate into the receiving neuroepithelium. If placed into the developing eye, they did not elongate, but could morphologically be distinguished from the surrounding cells. Nevertheless, the transplanted cells survived and continued to divide with their original cell cycle length. Their descendants formed a ball-like structure within the host tissue.

Upon heterotopic, homochronic transplantation, the cell cycle length of a NE cell appeared to be controlled extrinsically. Upon homotopic, heterochronic transplantation, the cell cycle length of a NE cell appeared to be controlled intrinsically. This apparent contradiction could be explained by the lack of integration of heterochronically transplanted NE cells.