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Yolk sac-derived cells are required for brain development

The maternal environment experienced by the embryo in utero has long-lasting impacts on brain development. Understanding how the embryonic brain is influenced by environmental insult is important to prevent birth defects and neurodevelopmental disorders. Neural tube closure, the first step of brain development in which the bilateral halves of the neuroepithelium converge and form the closed neural tube, occurs early in embryonic life, before the placenta is established for maternal-fetal nutrient exchange. Instead, the yolk sac supports this period of rapid morphogenesis by transporting nutrients from the maternal to the embryonic environment and generating cells that migrate into the early brain to promote neuronal differentiation during neural tube closure. How yolk sac-derived cells regulate neuroepithelial development is poorly understood. Further it is unknown whether defects in yolk sac-derived cells contribute to neurodevelopmental disorders. Here we demonstrate that miR-290 is expressed in the yolk sac where it is required for proper processing of metabolites from the maternal environment. Additionally, we find cells expressing miR-290 present within the embryo adjacent to the cranial neuroepithelium. RNA sequencing of miR-290+ cells within the embryonic cranial region revealed expression of genes involved in cell migration and neurogenesis and identified *Cd200* as a unique cell surface marker. Upon miR-290 deletion we find a significant reduction in the number of CD200+ cells in the cranial region of *mir-290*$^{-/-}$ embryos and a significant reduction in the ability of *mir-290*$^{-/-}$ cranial CD200+ cells to induce neurogenesis. Similarly, *mir-290*$^{-/-}$ embryos have a significant reduction in neurogenesis and expansion of neuroepithelial progenitors that persists until late gestation. This reduction of *mir-290*$^{-/-}$ neurogenesis results in a reduction of embryonic-born dopaminergic interneurons and is accompanied by an increase in activated microglia that is reminiscent of neurodegeneration. These findings suggest that defects in yolk sac-derived cells can have long-lasting impacts on brain development and may serve to prevent both neurodevelopmental disorders and neurodegeneration. Understanding how yolk sac-derived cells contribute to early brain development will present a new therapeutic approach to prevent neurodevelopmental disorders.