glia within the developing hippocampus expresses FGFR1 by immunocytochemistry, suggesting that FGFR1 may play a significant role in radial glial proliferation or differentiation. To investigate it, we disrupted the Fgfr1 gene in radial glia by site-dependent recombination using the Cre-loxP system. The human GFAP-cre transgenic mouse leads somatic gene recombination into radial glia of dorsolateral cortex from E13.5. By crossing this transgenic mouse with Fgfr1 floxed line, we generated conditional mutant mice lacking the transmembrane and intracellular kinase domains of the Fgfr1 gene. These Fgfr1 conditional knockout mice survive and show abnormal hippocampal development. Fgfr1 mutant have a dramatic decrease in their hippocampal volume (~50%). We also found a decline of radial glia (GLAST/nestin/BLBP) and mitotic cells by BrdU incorporation at various stages of hippocampal development. These data strongly suggest that Fgfr1 is essential for the proliferative expansion or maintenance of radial glial cells during the hippocampus development. (Supported by NSF0083104.)

139. Abstract #139 will be presented as scheduled, but the abstract cannot be published due to lack of license agreement between authors and publisher.

140. **The Role of E2F1 in Regulating Neural Stem Cells in the Mouse Brain.** Vassiliki Nikoletopoulou, K. L. Ferguson, W. C. McIntosh, J. G. MacLaurin, and R. S. Slack. Ottawa Health Research Institute, University of Ottawa, 451 Smyth Rd., Ottawa, Ontario K1H 8M5, Canada.

Recent studies have indicated the involvement of Rb family proteins in regulating the stem cell population in the brain. Our lab has previously demonstrated that loss of Rb/p107 results in increased stem cell number, as well as higher progenitor proliferation. Moreover, telencephalon-specific Rb−/− embryos exhibit enhanced neurogenesis and cellularity resulting in a 30% increase in brain size by E16.5. These embryos are further characterized by the presence of ectopic mitoses, consistent with the implication that Rb regulates neuronal commitment and terminal mitosis of neural progenitors. The E2F-1, -2, and -3 transcription factors are the key functional downstream targets of Rb. The aim of this study is to determine the molecular mechanisms of Rb-mediated neurogenesis, by investigating the role of E2F1 in neural stem cell regulation. We are currently crossing mice to generate double E2F1:telencephalon-specific Rb mutants, to determine whether loss of E2F1 can rescue the phenotype of the Rb-deficient embryonic telencephalon. Furthermore, we will be characterizing the number and self-renewal capacity of neural stem cells derived from these double knockout animals in vitro using neurosphere assays as well as in vivo by BrdU injections and immunohistochemical analysis. We hypothesize that double knockout animals will exhibit normal stem cell numbers and neurogenesis and will correct the ectopic mitoses observed in the telencephalon-specific Rb−/− brains. (Supported by CIHR.)

141. **Role of Gdf11 in Retinal Neurogenesis.** Joon Kim,* Hsiao-Huei Wu,* Sanja Ivkovic,† Karen Lyons,† and Anne Calof*. *University of California, Irvine, California 92697; and †University of California, Los Angeles, California 90095.

We have shown that growth and differentiation factor 11 (GDF11), which is produced by neuronal progenitor cells and differentiated neurons in the mammalian olfactory epithelium, mediates feedback inhibition of neurogenesis in this tissue in vitro and in vivo (Wu et al., 2003, Neuron 37, 197-207). To determine if GDF11 plays a similar role in the retina, we examined expression of genes encoding GDF11 and components of its signal transduction pathway, as well as markers for different neural progenitor cell types, in the eyes of wild-type mouse embryos and their littermates lacking functional *Gdf11*. In the developing retina, ganglion cells are among the first neuronal cells to be produced. *Gdf11* expression is evident in the retina at E12.5, and appears to be concentrated in the presumptive ganglion cell layer, where it continues to be expressed at least until birth. BrdU incorporation experiments indicate that there is ectopic overproliferation in the presumptive ganglion cell layer of *Gdf11* null embryos. Hes1, a bHLH transcription factor involved in negative regulation of retinal neural cell differentiation, is aberrantly expressed in the region of overproliferation. In contrast, expression of the proneural bHLH factors Mash1 and NeuroD appears to be delayed in the retinas of *Gdf11* knockouts. In addition, the laminar structure of the retina is disrupted in *Gdf11* mutants. These results support the hypothesis that retinal neurogenesis is regulated, at least in part, via a negative feedback mechanism mediated by GDF11. (Supported by grants DC03583 and HD38761 to A.L.C. from the NIH).

142. **Functional Interactions of the Product of the Proto-Oncogene TCL1 during Early Preimplantation Embryo Development in the Mouse.** M. T. Fiorenza,* S. Torcia,* G. Ragona,† M. G. Narducci,† A. Bevilacqua,* G. Russo,† and F. Mangia*. *Department of Psychology, Section of Neuroscience, University La Sapienza of Rome, and †Istituto Dermopatico della Immacolata, Rome, Italy.

The product of the proto-oncogene TCL1 (T-cell leukemia lymphoma 1) plays a key role in T-prolymphocytic leukemia and its overexpression under the control of a VH promoter in transgenic mouse lines results in B cell tumors resembling B-CLL, pinpointing a relevant role of this factor in both T cell and B cell leukemias. Despite its importance in leukemiogenesis, however, TCL1 normal/oncogenetic function is still unknown. We have recently found that TCL1 is also abundantly expressed in early stages of preimplantation mouse embryo development, where it shuttles between embryo cortex and nuclei according to the cell cycle, and that lack of TCL1 results in an embryo mitotic block at the 4-/8-cell stages (Narducci et al., 2002), making the early mouse embryo the system of choice to understand normal/oncogenetic TCL1 function. In light of well-established TCL1 heterodimerization with AKT and consequent enhancement of AKT transphosphorylation activity, we have investigated the intracellular distribution and movement of AKT1, AKT2, and AKT3 isoforms by confocal microscopy and FLIM using TCL1-/AKT-GFP chimeric proteins. We have also analyzed the presence of AKT isoform mRNAs during preimplantation embryo development in either normal or TCL1-KO embryos. Results obtained so far indicate AKT1/AKT2 as putative candidates for functional interaction(s) with TCL1.

143. **Regulation of Teratocarcinoma Stem Cells by the Murine Blastocyst: A Molecular Approach.** J. P. Gaillard, A. Diez, P. Vecino, and J. Arechaga. Department of Cell Biology—University of the Basque Country, 48940 Lejona, Spain.

Proliferation and differentiation of teratocarcinoma stem cells can be controlled by the blastocyst. Oddly, although documented