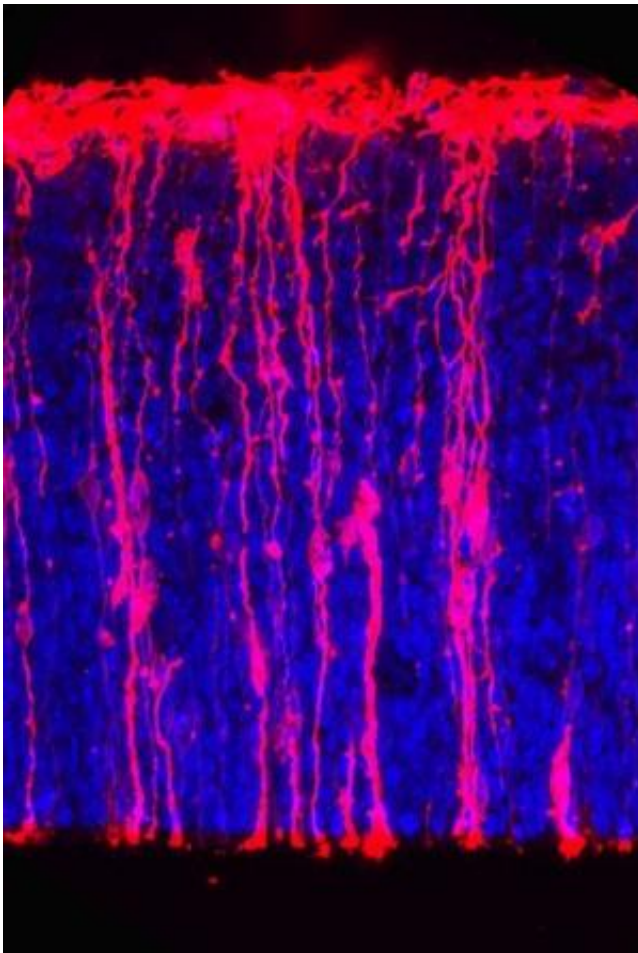


The pivotal role of the stem cell environment in brain development

February 5 2014, by Denise Stenzel



Stem cells in the cortex of a mouse embryo (cell nuclei: blue). Credit: MPI f. Molecular Cell Biology and Genetics/ D. Stenzel

(Medical Xpress)—Higher mammals, such as humans, have markedly

larger brains than other mammals. Scientists from the Max Planck Institute of Molecular Cell Biology and Genetics in Dresden recently discovered a new mechanism governing brain stem cell proliferation. It serves to boost the production of neurons during development, thus causing the enlargement of the cerebral cortex – the part of the brain that enables us humans to speak, think and dream.

The surprising discovery made by the Dresden-based researchers: two components in the stem cell environment – the [extracellular matrix](#) and [thyroid hormones](#) – work together with a protein molecule found on the stem cell surface, a so-called integrin. This likely explains why iodine deficiency in pregnant women has disastrous consequences for the unborn child, affecting its [brain development](#) adversely – without iodine, no thyroid hormones are produced. "Our study highlights this relationship and provides a potential explanation for the condition neurologists refer to as cretinism", says Wieland Huttner, Director at the Max Planck Institute in Dresden. This neurological disorder severely impairs the mental abilities of a person.

In the course of evolution, certain mammals, notably humans, have developed larger brains than others, and therefore more advanced cognitive abilities. Mice, for example, have brains that are around a thousand times smaller than the human one. In their study, which was conducted in cooperation with the Fritz Lipmann Institute in Jena, the researchers in Dresden wanted to identify factors that determine brain development, and understand how larger brains have evolved.

A cosy bed for brain stem cells

Brain neurons are generated from stem cells called basal progenitors that are able to proliferate in humans, but not in mice. In humans, basal progenitors are surrounded by a special environment, a so-called extracellular matrix (ECM), which is produced by the progenitors

themselves. Like a cosy bed, it accommodates the proliferating cells. Mice lack such ECM, which means that they generate fewer neurons and have a smaller brain.

The scientists therefore conducted tests to see whether in mice, basal progenitors start to proliferate if a comparable cell environment is simulated. The result: "We simulated an extracellular matrix for the [brain stem cells](#) using a stimulating antibody. This antibody activates an integrin on the cell surface of basal progenitors and thus stimulates their proliferation", explains Denise Stenzel, who headed the experiments.

Because a requirement of thyroid hormones for proper brain development was previously known, the researchers blocked the production of these hormones in pregnant rats to see if their absence would inhibit basal progenitor proliferation in the embryos. Indeed, fewer progenitors and, consequently, neurons were produced, likely explaining the abnormal brain development in the absence of thyroid hormones. When the action of these hormones on the integrin was blocked, the ECM-simulating antibody alone was no longer able to induce basal progenitor proliferation.

A combination of ECM and thyroid hormones thus appears necessary for basal progenitors to proliferate and produce enough neurons for brain development. Human brain stem cells produce the suitable environment naturally. "That is probably how, in the course of evolution, we humans developed larger brains", says Wieland Huttner, summing up the study. The research produced another important finding: "We were able to explain the role of iodine in embryonic brain development at the cellular level", says Denise Stenzel. Iodine is essential for the production of thyroid hormones, and an [iodine deficiency](#) in pregnant women is known to have adverse effects on the brain development of the unborn child.

More information: Stenzel, Denise; Wilsch-Bräuninger, Michaela; Wong, Fong Kuan; Heuer, Heike; Huttner, Wieland B." Integrin $\alpha v \beta 3$ and thyroid hormones promote expansion of progenitors in embryonic neocortex." *Development* (2014) [DOI: 10.1242/dev.101907](https://doi.org/10.1242/dev.101907)

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