Professor Andrea Brand

University of Cambridge

Nutritional control of neural stem cells

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Abstract

The systemic regulation of stem cells ensures that they meet the needs of the organism during growth and in response to injury. A key control point is the decision between quiescence and proliferation. In Drosophila, quiescent neural stem cells are easily identifiable and amenable to genetic manipulation, making them a powerful model with which to study the transition between quiescence and proliferation. These stem cells exit quiescence in response to a nutrition-dependent signal from the fat body. The fat body performs many of the storage and endocrine functions of the vertebrate liver and acts as a sensor, coupling nutritional state to organismal growth. We showed that the nutritional stimulus transduced by the fat body induces the expression of insulin/IGF-like peptides (dILPs) in the blood brain barrier glia, which overlie the quiescent stem cells. Activation of the Insulin/IGF receptor pathway is essential for the neural stem cells to exit quiescence. Indeed the forced expression of insulin/IGF-like peptides in glia, or activation of the insulin signalling pathway in neural stem cells, can drive proliferation in the absence of dietary protein, and thus uncouple the stem cells from systemic control. IGF-1 and the insulin signalling pathway can also promote cell cycle progression in vertebrate neural stem cells, suggesting that the pathways that regulate stem cell reactivation in Drosophila may also control reactivation in vertebrate stem cells. We are investigating the systemic and local signals that regulate neural stem cell quiescence and reactivation and the transcriptional and epigenetic changes that are induced in stem cells upon reactivation.