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Drosophila Research For Human Health

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SEMINAR

Time to wake up: Regulation of neural stem cell quiescence

Neural stem cells (NSCs) can generate new neurons in the brain in response to a range of stimuli, including exercise, nutrition and injury. In this way, stem cells meet the needs of the organism during growth and in response to damage. A key control point is the decision between stem cell quiescence and proliferation. Drosophila NSCs enter quiescence in late embryogenesis and reactivate post-embryonically in response to nutrition. We found that feeding induces the expression of insulin-like peptides within the brain itself and that insulin signalling is essential for the stem cells to exit quiescence and resume proliferation.

Most quiescent stem cells are thought to arrest in G_0, however, we discovered that quiescent NSCs (qNSCs) in Drosophila are arrested in either G_2 or G_0. G_2/G_0 heterogeneity directs NSC behaviour: G_2 qNSCs reactivate much more rapidly than G_0 qNSCs. We showed that the pseudokinase Tribbles (Trbl) induces NSCs to enter G_2 quiescence by promoting degradation of String/Cdc25 and maintains quiescence by inhibiting Akt activation. Insulin signalling overrides Akt repression and silences trbl transcription, allowing NSCs to exit quiescence. The mechanisms controlling NSC reactivation may be conserved in vertebrates, where insulin signalling also promotes NSC proliferation.

We have developed powerful methods for whole genome profiling in specific cell- and tissue-types in vivo: Targeted DamID (TaDa), RNA-DamID and NanoDam, enabling selective profiling of transcription and chromatin binding in small numbers of cells in intact organisms. We are investigating the genome-wide transcriptional and epigenetic changes in NSCs as they progress from quiescence to proliferation. Understanding the signals that instruct stem cells to produce new neurons at will raises the prospect of future therapies for brain repair after damage or neurodegenerative disease.

Andrea H. Brand

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Professor Andrea H Brand is Frederick L. Ehrman Professor and Chair, Department of Cell Biology, and Director, Regenerative Medicine Institute at NYU Grossman School of Laboratory of Molecular Biology in New York. After a postdoctoral fellowship with Norbert Perrimon at the Department of Genetics, Harvard Medical School, she moved to the UK to become a Wellcome Trust Senior Fellow at the Gurdon Institute, University of Cambridge. She became Director of Research in Developmental Neurobiology in 2003 and Senior Group Leader in 2005. She was appointed Herchel Smith Professor of Molecular Biology in 2007 and Royal Society Darwin Trust Research Professor in 2016. She was Head of Wellcome Trust Laboratories at the Gurdon Institute from 2015-2022. Andrea was awarded the Royal Society Rosalind Franklin Award in 2006, the William Bate Hardy Prize, jointly with Professor Robin Irvine, in 2004, the Hooke Medal of the British Society of Cell Biology in 2002. She was elected a member of the European Molecular Biology Organization in 2000, a Fellow of the Academy of Medical Sciences in 2003 and a Fellow of the Royal Society in 2010.

MONDAY
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Costas Fotakis room

10:00

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