PRESS RELEASE

Master switch for brain development

18 November 2015, Mainz, Germany. *Scientists at the Institute of Molecular Biology (IMB) in Mainz have unravelled a complex regulatory mechanism that explains how a single gene can drive the formation of brain cells. The research, published in* The EMBO Journal*, is an important step towards a better understanding of how the brain develops. It also harbours potential for regenerative medicine.*

Neurodegenerative disorders, such as Parkinson's disease, are often characterised by an irreversible loss of brain cells (neurons). Unlike many other cell types in the body, neurons are generally not able to regenerate by themselves, so if the brain is damaged, it stays damaged. One hope of developing treatments for this kind of damage is to understand how the brain develops in the first place, and then try to imitate the process. However, the brain is also one of the most complex organs in the body, and very little is understood about the molecular pathways that guide its development.

Scientists in Dr Vijay Tiwari's group at the Institute of Molecular Biology (IMB) at Johannes Gutenberg University Mainz have been investigating a central gene in brain development, *NeuroD1*. This gene is expressed in the developing brain and marks the onset of neurogenesis.

In their research article, Tiwari and his colleagues have shown that during brain development, *NeuroD1* is not only expressed in brain stem cells but acts as a master regulator of a large number of genes that cause these cells to develop into neurons. They used a combination of neurobiology, epigenetics and computational biology approaches to show that these genes are normally turned off in development, but *NeuroD1* activity changes their epigenetic state in order to turn them on. Strikingly, the researchers show that these genes remain switched on even after *NeuroD1* is later switched off. They further show that this is because *NeuroD1* activity leaves permanent epigenetic marks on these genes that keep them turned on, in other words it creates an epigenetic memory of neuronal differentiation in the cell.

Abhijeet Pataskar and Johannes Jung (joint first authors on the paper) explain the significance of this discovery: "Our research has shown how a single factor, *NeuroD1*, has the capacity to change the epigenetic landscape of the cell, resulting in a gene expression programme that directs the generation of neurons."

Dr Tiwari is excited about the implications of these findings, "This is a significant step towards understanding the relationship between DNA sequence, epigenetic changes and cell fate. It not only sheds new light on the formation of the brain during embryonic development but also opens up novel avenues for regenerative therapy."

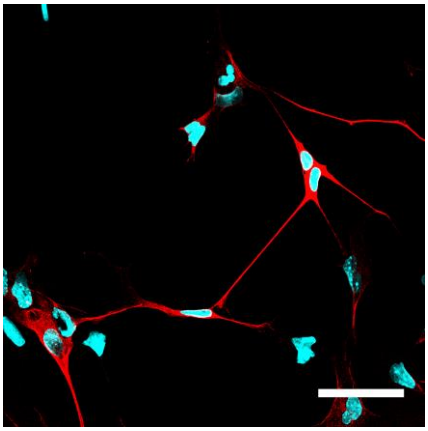

Figure 1: Cells in which* NeuroD1 *is turned on are reprogrammed to become neurons. *Cell nuclei are shown in blue (Höchst stain) and neurons, with their characteristic long processes, are shown in red (stained with neuronal marker TUJ1). Image credit: A. Pataskar/J. Jung & V. Tiwari*

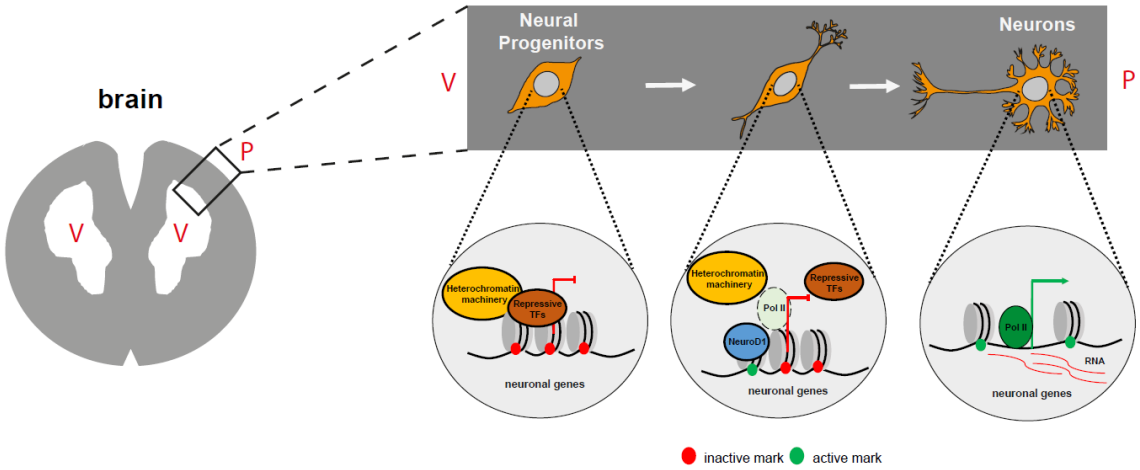

Figure 2: Diagram showing how* NeuroD1 *influences the development of neurons. During brain development, expression of NeuroD1 marks the onset of neurogenesis. NeuroD1 accomplishes this via epigenetic reprogramming: neuronal genes are switched on, and the cells develop into neurons. TF: transcription factor; V: ventricle; P: pial surface. *Image credit: A. Pataskar/J. Jung & V. Tiwari*

Further details

Pataskar A*, Jung J*, Smialowski P, Noack F, Calegari F, Straub T and Tiwari VK (2015). NeuroD1 reprograms chromatin and transcription factor landscapes to induce the neuronal program. EMBO J, pii: e201591206. [Epub ahead of print]. (*indicates equal contribution)

News & Views by Glahs A, Zinzen RP (2015). Putting chromatin in its place: the pioneer factor NeuroD1 modulates chromatin state to drive cell fate decisions. *EMBO J*, Nov 13, DOI: 10.15252/embj.201593324

Further information about Dr Vijay Tiwari's research can be found at www.imb.de/tiwari.

About the Institute of Molecular Biology gGmbH

The Institute of Molecular Biology gGmbH (IMB) is a centre of excellence in the life sciences that was established in 2011 on the campus of Johannes Gutenberg University Mainz (JGU). Research at IMB concentrates on three cutting-edge areas: epigenetics, developmental biology, and genome stability. The institute is a prime example of a successful collaboration between public authorities and a private foundation. The Boehringer Ingelheim Foundation has dedicated 100 million euros for a period of 10 years to cover the operating costs for research at IMB, while the state of Rhineland-Palatinate provided approximately 50 million euros for the construction of a state-of-the-art building. For more information about IMB, please visit: www.imb.de.

About the Boehringer Ingelheim Foundation

The Boehringer Ingelheim Foundation is an independent, non-profit organisation committed to the promotion of the medical, biological, chemical and pharmaceutical sciences. It was established in 1977 by Hubertus Liebrecht (1931-1991), a member of the shareholder family of the company Boehringer Ingelheim. With the PLUS 3 Perspectives Programme and the Exploration Grants, the foundation supports independent group leaders. It also endows the internationally renowned Heinrich Wieland Prize as well as awards for up-and-coming scientists. In addition, the foundation pledged to donate 100 million euros to finance the scientific running of the IMB at Johannes Gutenberg University Mainz for ten years. In 2013, the Boehringer Ingelheim Foundation donated a further 50 million euros to Johannes Gutenberg University Mainz. www.boehringer-ingelheim-stiftung.de.

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