Different than previously assumed: The dynamics of pluripotency transcription factors

Neuherberg, 22 September 2015**. Scientists at the Helmholtz Zentrum Munich working in collaboration with colleagues at ETH Zurich have discovered that variations in the Nanog expression of embryonic stem cells are not necessarily linked to differences in the expression of other pluripotency factors. The results of the study, which has now been published in the scientific journal *Nature Cell Biology,* refute previously held assumptions.**

Nanog (a gene named after 'Tír na nÓg', the mythological Celtic land of the ever-young) is a transcription factor that is involved in regulating stem cell self-renewal. Earlier models assigned a central role to Nanog in the regulation of pluripotent*, embryonic stem cells. The group headed by Prof. Fabian Theis, Director of the Institute of Computational Biology (ICB) at the Helmholtz Zentrum München and Professor for Biomathematics at TU München, which took part in the joint research project with a group of former colleagues of the Stem Cell Dynamics research unit led by Prof. Timm Schroeder (currently at the Department of Biosystems Science and Engineering at ETH Zurich in Basle) conducted an accurate quantification and analysis of Nanog protein expression over several generations. Their study was based on embryonic mice stem cells in which the Nanog protein is marked with a fluorescent protein.

"In our experiment we were able to identify two different types of colonies," Prof. Theis reports. "While one type re-expressed Nanog in a mosaic pattern, the other did not express Nanog over many generations." Surprisingly, both colonies expressed pluripotency markers. "That was not as expected, as up to now Nanog has been assigned a key role in the regulation of embryonic stem cells pluripotency," Prof. Schroeder adds.

"The methods we developed can also be applied to other factors and cells," notes Carsten Marr, ICB. "We will use the data resource that has now been created for further model-based analyses of the regulation of Nanog protein expression."

The research findings are important for understanding protein dynamics and for regulating cell states, for example during the targeted re-programming of cells. The previous image of a strong, self-regulating core pluripotency network of the factors Nanog, Oct4 and Sox2 has thus been refuted. In future, the scientists plan to conduct further research on this topic.

Further Information

Background

* Pluripotency describes the ability of stem cells to develop into virtually any other type of cell.

Original Publication

Filipczyk et al. (2015) Network plasticity of pluripotency transcription factors in embryonic stem cells, Nature Cell Biology, DOI: 10.1038/ncb3237

Link to the Original Publication
http://www.nature.com/ncb/journal/vaop/ncurrent/full/ncb3237.html

As German Research Center for Environmental Health, **Helmholtz Zentrum München** pursues the goal of developing personalized medical approaches for the prevention and therapy of major common diseases such as diabetes mellitus and lung diseases. To achieve this, it investigates the interaction of genetics, environmental factors and lifestyle. The Helmholtz Zentrum München has about 2,300 staff members and is headquartered in Neuherberg in the north of Munich. Helmholtz Zentrum München is a member of the Helmholtz Association, a community of 18 scientific-technical and medical-biological research centers with a total of about 37,000 staff members. www.helmholtz-muenchen.de

The **Institute of Computational Biology** (ICB) develops and applies methods for the model-based description of biological systems, using a data-driven approach by integrating information on multiple scales ranging from single-cell time series to large-scale omics. Given the fast technological advances in molecular biology, the aim is to provide and collaboratively apply innovative tools with experimental groups in order to jointly advance the understanding and treatment of common human diseases.

Technische Universität München (TUM) is one of Europe's leading research universities, with around 500 professors, 10,000 academic and non-academic staff, and 36,000 students. Its focus areas are the engineering sciences, natural sciences, life sciences and medicine, reinforced by schools of management and education. TUM acts as an entrepreneurial university that promotes talents and creates value for society. In that it profits from having strong partners in science and industry. It is represented worldwide with a campus in Singapore as well as offices in Beijing, Brussels, Cairo, Mumbai, and São Paulo. Nobel Prize winners and inventors such as Rudolf Diesel and Carl von Linde have done research at TUM. In 2006 and 2012 it won recognition as a German "Excellence University." In international rankings, it regularly places among the best universities in Germany.

ETH Zurich is one of the world's leading universities for technology and the natural sciences. It is renowned for the excellence of its teaching, its pioneering basic research and its direct translation of research findings into practice. Founded in 1855, ETH now has about 18,500 students from more than 110 countries, including 4,000 doctoral students. The university provides researchers with an inspiring environment and offers students a well-rounded education.

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