Scientists make groundbreaking discovery of cell nucleus structure crucial to understanding diseases

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Genes relocated from their correct position in the nucleus cause them to malfunction and this may lead to the heart, blood vessels and muscles breaking down. This new discovery by A*STAR scientists may be the key to finding new cures in the future.

Scientists from Singapore and Germany have identified that the proteins lamin A (Lmna) and lamin B receptor (Lbr) are essential for holding silent genes in their correct position at the edge of the nucleus, in the form of heterochromatin. A deviation from their normal position will cause the genes to malfunction, leading to heart failure, vascular disease and muscle wasting.

For hundreds of years before this discovery, scientists were puzzled by why heterochromatin clustered at the edge of the nucleus and how it was relevant to normal cell function. This recent discovery will enable scientists to gain a better understanding of the diseases of the heart and muscles, and find cures for them in the future.

The findings by Audrey Wang and Colin Stewart of A*STAR's Institute of Medical Biology and Irina Solovei, Boris Joffe and Heinrich Leonhardt of the Ludwig Maximillian University in Munich, Germany, were recently published in the prestigious journal *Cell*.

The nucleus – the brain of the cell – carries all the information, in the

form of chromatin necessary to help a cell grow, thrive, and reproduce, in the form of DNA packed into chromatin. Hence, understanding how chromatin is organised in the nucleus is important to understanding disease and normal processes such as ageing. The scientists showed that the two proteins lamin A and lamin B receptor are important to the organisation of chromatin in the nucleus. Using mouse models, they demonstrated that in the absence of the two proteins, heterochromatin collapsed into the nuclear centre. This disrupted gene expression and affected skeletal muscle development, resulting in muscle failure (Annex A).

Professor Stewart, Research and Assistant Director of IMB, said, "These findings will provide new insights into how diseases arise and may help explain how mutations in lamin proteins result in a variety of different syndromes. In particular, we are extending these findings to explore how changes in chromatin position may contribute to heart failure. Moving forward, we will collaborate with cardiologists and vascular clinicians at SGH and NUHS to translate these findings to benefit patients."

More information: The research findings described in this news release can be found in *Cell* under the title "LBR and Lamin A/C Sequentially tether Peripheral Heterochromatin and Inversely Regulate Differentiation" by Irina Solovei et al., dx.doi.org/10.1016/j.cell.2013.01.009

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