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Scientists uncover exciting lead into premature ageing and heart disease

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Scientists have discovered that they can dramatically increase the life span of mice with progeria (premature ageing disease) and heart disease (caused by Emery-Dreifuss muscular dystrophy) by reducing levels of a protein called SUN1. This research was done by A*STAR's Institute of Medical Biology (IMB) in collaboration with their partners at the National Institute of Allergy and Infectious Diseases in the United States and the Institute of Cellular and System Medicine in Taiwan. Their findings were published in the prestigious scientific journal, Cell, on 27th April 2012 and provide an exciting lead into developing new methods to treat premature aging and heart disease.

Children with progeria suffer symptoms of premature ageing and mostly die in their early teens from either heart attack or stroke. Individuals with Emery-Dreifuss muscular dystrophy (AD-EDMD) suffer from muscle wasting and cardiomyopathy, a type of heart disease that weakens and enlarges the heart muscle making it harder for the heart to pump blood and deliver it to the rest of the body leading to heart failure. Both diseases are caused by mutations in Lamin A, a protein in the membrane surrounding a cell's nucleus which provides mechanical support to the nucleus. SUN1 is a protein also found in the inner nuclear membrane, but there have been no previous studies to show how SUN1 interacts with the Lamin proteins.

The scientists wanted to investigate if SUN1 had any involvement in diseases caused by mutations in Lamin A, so they inactivated SUN1 in mouse models developed for progeria and AD-EDMD. These mouse

models for progeria and AD-EDMD usually thrive poorly and have markedly short life spans as they die from premature ageing and heart failure respectively. However, by inactivating SUN1 and reducing SUN1 levels in these mouse models, the scientists observed that the life spans of the mouse models for progeria and AD-EDMD doubled and tripled respectively.

“We actually expected that knocking out Sun1 in these mouse models would worsen their conditions and cause them to die faster but surprisingly we observed the opposite. This is the first time that Sun1 protein has been implicated in diseases linked to Lamin A and it is exciting how basic research has led to a discovery that can potentially have significant impact on us,” said Rafidah Abdul Mutalif, who is pursuing her PhD at IMB and one of the main authors of this paper.

Prof. Colin Stewart, Principle Investigator at IMB, said, “Notably, the heart muscle of the mice was restored to near normal function and cardiac function improved when the levels of SUN1 were reduced. Mutations in Lamin A are frequently reported as a cause of heart disease and especially within a group of hereditary cardiomyopathies. This opens up a possibility that from these observations, reduction in SUN1 maybe of therapeutic use for other forms of heart disease. We are very excited about this discovery and look forward to further pursuing this lead which could potentially lead to development of new treatments for heart diseases.”

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