Institute of Medical Biology
A*STAR

PRESS RELEASE
1 SEP 2009

SCIENTISTS UNLOCK SECRET TO YOUTHFUL SKIN

Increasing levels of* PYCR1 *protein could reverse conditions that cause fast ageing and wrinkly skin

1. Scientists from Singapore and Germany have made a novel discovery that might lead to ways of reversing the effects of ageing and wrinkled skin. The international team of scientists led by Dr Bruno Reversade from A*STAR's Institute of Medical Biology (IMB) discovered that mutations in the *PYCR1* gene cause a rare genetic condition which results in premature skin ageing, known as "wrinkly skin syndrome". Their findings, which are published in the 1 Sep 2009 print issue of the prestigious journal *Nature Genetics*, provide insight into how some unexpected genes help maintain youthful skin. This research project involved collaborations with over 15 hospitals and research centres in 13 countries.

2. Using bioinformatics tools, Dr Reversade and his team analysed rare DNA samples collected from affected patients across the world who, at a young age, displayed signs of premature ageing. They identified the *PYCR1* gene on chromosome 17 of these patients to be defective and found specific mutations in the gene that led to conditions often seen in elderly people, such as loose skin, loss of bone density, hip dislocation and cataract. Furthermore, they determined that skin and bone were the two tissues most severely affected in patients. As skin and bone contain high levels of the PYCR1 protein under normal circumstances, developing therapies that could increase the activity of the PYCR1 protein could possibly reverse the process of ageing in affected individuals or slow it down in normal people.

3. The scientists also found that inside cells, the PYCR1 protein is located in the mitochondria – the "power houses" of the cell that provide energy for the cells'

consumption. In their experiments, they observed changes in mitochondrial morphology and cell death in the connective tissues of individuals with *PYCR1* mutations. They also conducted further investigations into the effects of reduced levels of PYCR1 protein by examining the growth of frog and fish models in which the *PYCR1* gene had been experimentally shut off. They noted that mitochondrial function in the skin of the animal models was altered and there was also an increased occurrence of cell death.

4. Said Dr Reversade, "Our findings confirm the significance of mitochondrial function in the ageing process. They also unexpectedly highlight the importance of metabolism as *PYCR1* is important in the synthesis of proline, a common amino acid involved in metabolism. Age-defying and anti-wrinkling treatments for common disorders related to ageing may also benefit from sustaining proline metabolism."

5. Professor Birgit Lane, a skin biologist and Executive Director of IMB, said, "We are excited by these findings of Bruno and colleagues, which open up new possibilities in the field of ageing and skin research. The study is a great example of scientific synergy – when clinicians and scientists from around the world come together to share their specialist skills and knowledge, they can discover new insights into complex medical conditions. Rare genetic disorders often provide surprising revelations. Pooling resources and targeting research to find new ways of combating disease – and benefiting people faster – is exactly what we try to do at IMB."

6. Dr Reversade, a developmental biologist who holds a Principal Investigator position at IMB and an adjunct faculty position at the National University of Singapore, has published papers in top journals such as *Cell* and *Nature Cell Biology*, several of which are landmark discoveries explaining how identical twins can be produced from a single embryo. He is a Fellow of the Branco Weiss Foundation and also the first recipient of an A*STAR Investigatorship, a programme which provides competitive and prestigious fellowships to support the next generation of international scientific leaders, offering them funding support for set-up costs and research staff, and access to state-of-the-art scientific equipment and facilities at A*STAR.

AGENCY FOR SCIENCE, TECHNOLOGY AND RESEARCH

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Notes to the Editor:

The research findings described in the press release can be found in the article titled "Mutations in *PYCR1* cause cutis laxa with progeroid features", published in the 1 Sep 2009 print issue of *Nature Genetics.*

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About the Institute of Medical Biology (IMB)

The Institute of Medical Biology is a member of the Agency for Science, Technology and Research (A*STAR). With its roots in the Centre for Molecular Medicine since 2004, it became the Institute of Medical Biology in 2007, with a mission to study mechanisms of human disease in order to discover new and effective therapeutic strategies for improved quality of life. IMB is developing internationally excellent research programmes working closely with clinical collaborators, targeting the challenging interface between basic science and clinical medicine, and aiming to promote increased and effective throughput of research from bench to bedside. Its growing portfolio of strategic research topics aims to promote translational research on the mechanisms of human diseases with a cell to tissue emphasis that can help identify new therapeutic strategies for disease amelioration, cure and eradication.
For more information about IMB, please visit www.imb.a-star.edu.sg.

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