Gene mutation responsible for premature skin aging disease identified

August 31 2009

In the new print issue of *Nature Genetics,* scientists in Singapore and Germany report that mutations in the PYCR1 gene cause the rare genetic condition that results in premature skin aging and that is known as "wrinkly skin syndrome."

Their findings not only suggest that increasing levels of the PYCR1 protein could reverse conditions that cause fast aging and wrinkly skin but also provide insight into how some unexpected genes help maintain youthful skin.

Bruno Reversade, Ph.D. of Singapore's Institute of Medical Biology (IMB) led the international research team that involved collaborations with over 15 hospitals and research centres in 13 countries.

Using bioinformatics tools, Dr. Reversade and his team analyzed DNA samples collected worldwide from patients who, at a young age, displayed signs of premature aging. 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.

They also determined that skin and bone were the two tissues most severely affected in patients with wrinkly skin syndrome. Since 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 aging in

affected individuals or slow it down in normal people.

The scientists found that the PYCR1 protein is located in mitochondria, the cell's "power house," providing energy for the cell's consumption. In their experiments, they observed changes in mitochondrial morphology and cell death in the connective tissues of individuals with PYCR1 mutations.

To determine the effects of reduced levels of PYCR1 protein, the scientists studied the growth of frog and fish models in which the PYCR1 gene had been experimentally shut off. They found that the mitochondrial function in the animal models' skin was altered, and there was also an increased occurrence of cell death.

"Our findings confirm the significance of mitochondrial function in the aging process," said Dr. Reversade. "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."

"We are excited by these findings of Bruno and colleagues, which open up new possibilities in the field of aging and skin research," added Birgit Lane, Ph.D., a skin biologist and Executive Director of IMB, one of the research institutes sponsored by Singapore's A*STAR (Agency for Science, Technology and 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," said Dr. Lane. "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."

More information: "Mutations in PYCR1 cause cutis laxa with progeroid features," published in the 1 Sept. 2009 print issue of Nature Genetics.

Source: Agency for Science, Technology and Research (A*STAR)