

Scientists find genetic wrinkle to block suninduced skin aging

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Leigh Parkinson shows the device used to expose mice to ultraviolet light. Credit: Brian Kladko, UBC Faculty of Medicine

A scientific team at UBC and Providence Health Care have genetically engineered mice with less wrinkled skin, despite repeated exposure to wrinkle-inducing ultraviolet (UV) light.



The youthful-looking <u>mice</u> were bred without the gene that produces Granzyme B, an enzyme that immune cells use to destroy harmful pathogens. The UBC-Providence team, led by Professor David Granville and postdoctoral fellow Leigh Parkinson, found that Granzyme B also does harm: When produced and released by <u>skin</u> cells in response to UV light, it triggers the breakdown of collagen, a structural protein that makes skin firm.

The findings, published last week in *Aging Cell*, raises hope for a drug that would block the activity of Granzyme B in certain places, and thus prevent the aging and deterioration of tissues that depend on collagen - not just skin, but blood vessels and lung passages.

Granville, a professor in the UBC Department of Pathology and Laboratory Medicine and a principal investigator in the Centre for Heart Lung Innovation of UBC and St. Paul's Hospital, was investigating the role of Granzyme B in atherosclerosis and heart attacks. He and his team wanted to see if the blood vessels of mice lacking Granzyme B were more resistant to hardening and narrowing, which is a major cause of heart attacks in human. In the process, they discovered that such mice retained youthful-looking skin compared to the aged skin on normal mice.

Granville's team constructed an experimental "tanning bed" to simulate <u>sun exposure</u> on mice. Each mouse was put in a carousel that slowly turned under UV lamps, exposing them for three to four minutes, three times a week - enough to cause redness, but not to burn. After 20 weeks of repetitive exposure, it became clear that the skin of mice lacking Granzyme B had aged much less - and their collagen was more intact - compared to the control groups.

viDA Therapeutics, a company co-founded by Granville, is currently developing a Granzyme-B inhibitor based on technology licensed from



UBC. The company plans to test a topically applied drug within two years on people with discoid lupus erythematosus, an autoimmune disease worsened by sunlight that can lead to disfiguring facial scarring. (The musician Seal has such a condition.)

If the drug proves effective in preventing lupus-related skin lesions, there is potential for a cosmetic product to prevent the normal, gradual aging of the skin, which is mostly caused by sun exposure. But the drug might also be used for life-threatening conditions, such as aneurysms and chronic obstructive pulmonary disease, caused by the breakdown of collagen and other proteins that provide structure to <u>blood vessels</u> and lung passages.

More information: Granzyme B mediates both direct and indirect cleavage of extracellular matrix in skin after chronic low-dose ultraviolet light irradiation, <u>onlinelibrary.wiley.com/doi/10 ... /acel.12298/abstract</u>

Provided by University of British Columbia

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