

## People with rare longevity mutation may also be protected from cardiovascular disease

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Jaime Guevara-Aguirre (back left), Valter Longo (back right), and several of the Laron study participants at the USC Leonard Davis School of Gerontology in Los Angeles. Credit: Jaime Guevara-Aguirre and Valter Longo

A new study highlights possible cardiovascular health advantages in individuals with a rare condition known as growth hormone receptor



deficiency (GHRD), also called Laron syndrome.

GHRD, which is characterized by the body's impaired ability to use its own growth hormone and results in stunted growth, has been linked in mice to a record 40% longevity extension and lower risks for various agerelated diseases. However, the risk of <u>cardiovascular disease</u> in individuals with GHRD has remained unclear until now, leading to the speculation that in people, this mouse longevity mutation may actually increase cardiovascular disease.

The <u>study</u>, appearing in *Med* on April 26, 2024, is the latest product of an international collaboration spanning nearly 20 years between Valter Longo, professor of gerontology at the USC Leonard Davis School of Gerontology, and endocrinologist Jaime Guevara-Aguirre of the Universidad San Francisco de Quito, Ecuador.

Over the past two decades, Longo, Guevara-Aguirre and colleagues have examined the health and aging of people with the gene mutation that causes GHRD. This rare mutation—found in just 400 to 500 people worldwide—was identified in a group of Ecuadorians whose ancestors had fled Spain during the Inquisition more than three centuries ago. The mutation leaves them with ineffective growth hormone receptors and results in a type of dwarfism.

The team's previous research has indicated that while GHRD/Laron syndrome reduces growth, it also appears to reduce the risk of several age-related diseases. They also appear to have healthier brains and achieve better performance on tests of cognition and memory.

For the current study, the research team examined cardiovascular function, damage, and <u>risk factors</u> in GHRD subjects and their relatives. Researchers conducted two phases of measurements in Los Angeles and Ecuador, involving a total of 51 individuals, with 24 diagnosed with



GHRD and 27 relatives without GHRD serving as controls.

Key findings from the study included:

- GHRD subjects displayed lower blood sugar, <u>insulin resistance</u>, and <u>blood pressure</u> compared to the control group.
- They also had smaller heart dimensions and similar pulse wave velocity—a measure of stiffness in the arteries—but had lower carotid artery thickness compared to control subjects.
- Despite elevated <u>low-density lipoprotein</u> (LDL), or "bad cholesterol," levels, GHRD subjects showed a trend for lower carotid artery atherosclerotic plaques compared to controls (7% vs. 36%).

"These findings suggest that individuals with GHRD have normal or improved levels of cardiovascular disease risk factors compared to their relatives," said Longo, senior author of the new study.

"Although the population tested is small, together with studies in mice and other organisms this human data provide valuable insights into the health effects of growth hormone receptor deficiency and suggest that drugs or dietary interventions that cause similar effects could reduce disease incidence and possibly extend longevity."

**More information:** Normal or improved cardiovascular risk factors in IGF-I deficient adults with growth hormone receptor deficiency, *Med* (2024). DOI: 10.1016/j.medj.2024.03.022. www.cell.com/med/fulltext/S2666-6340(24)00134-X



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