

Mutation of growth hormone receptor gene in men found to lengthen lifespan

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(Medical Xpress)—A team of researchers with member affiliations in the U.S., France and Israel has found that a mutation in a growth hormone receptor gene can make some men live longer. In their paper published on the open access site *Science Advances*, the group outlines their study of several different groups of men and the differences they found for those with the growth hormone receptor exon 3 deletion.

Growth hormones are molecules that connect to other molecules that reside on the surface of a cell—these growth [hormone](#) receptors then trigger signals telling the cell to speed up its growth or in some cases to release molecules known as growth factors. Prior research has shown that for some people, there is a genetic mutation that prevents the development of certain [growth](#) hormone receptors. Such people still have [receptors](#), but they are shaped differently. In this new effort, the researchers looked at mutation deletions in [growth hormone receptor](#) exon 3 and found that males who express it tend to live on average a decade longer, and also grow on average an inch taller.

The team first looked at a group (567 people) of Ashkenazi Jews over age 60 and at their children. They found that the mutation was present in 12 percent of men tested over the age of 100—a number that was three times higher than for men 70 years old. Men with the mutation lived on average 10 years longer than those without it. They found no difference for women. The team then tested other groups, such as those participating in the Cardiovascular Health Study, the Old Order Amish and the French Long-Lived Study.

The researchers report finding nearly identical results among all the groups. They suggest this indicates that exon 3 is clearly involved in longevity, though they readily acknowledge that it is almost certainly one of many agents involved in the overall process. But, they also note that their results suggest that further study should be conducted with larger groups to confirm their results. If others find the same thing, further research could explore the impact of mimicking the mutation to see whether it might be possible to extend the lifespan for males and perhaps to make them a little taller if they so choose.

More information: The GH receptor exon 3 deletion is a marker of male-specific exceptional longevity associated with increased GH sensitivity and taller stature, *Science Advances* 16 Jun 2017: Vol. 3, no.

6, e1602025, [DOI: 10.1126/sciadv.1602025](https://doi.org/10.1126/sciadv.1602025) ,
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Abstract

Although both growth hormone (GH) and insulin-like growth factor 1 (IGF-1) signaling were shown to regulate life span in lower organisms, the role of GH signaling in human longevity remains unclear. Because a GH receptor exon 3 deletion (d3-GHR) appears to modulate GH sensitivity in humans, we hypothesized that this polymorphism could play a role in human longevity. We report a linear increased prevalence of d3-GHR homozygosity with age in four independent cohorts of long-lived individuals: 841 participants [567 of the Longevity Genes Project (LGP) (8% increase; $P = 0.01$), 152 of the Old Order Amish (16% increase; $P = 0.02$), 61 of the Cardiovascular Health Study (14.2% increase; $P = 0.14$), and 61 of the French Long-Lived Study (23.5% increase; $P = 0.02$)]. In addition, mega analysis of males in all cohorts resulted in a significant positive trend with age (26% increase; $P = 0.007$), suggesting sexual dimorphism for GH action in longevity. Further, on average, LGP d3/d3 homozygotes were 1 inch taller than the wild-type (WT) allele carriers ($P = 0.05$) and also showed lower serum IGF-1 levels ($P = 0.003$). Multivariate regression analysis indicated that the presence of d3/d3 genotype adds approximately 10 years to life span. The LGP d3/d3-GHR transformed lymphocytes exhibited superior growth and extracellular signal-regulated kinase activation, to GH treatment relative to WT GHR lymphocytes (P

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