PubMed

Display Settings: Abstract

Proc Natl Acad Sci U S A. 2008 Mar 4;105(9):3438-42. Epub 2008 Mar 3.

Functionally significant insulin-like growth factor I receptor mutations in centenarians.

Suh Y, Atzmon G, Cho MO, Hwang D, Liu B, Leahy DJ, Barzilai N, Cohen P.

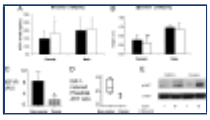
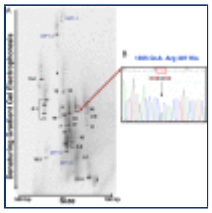
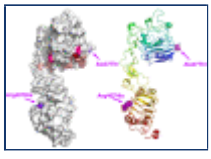
Departments of Medicine and Molecular Genetics, Albert Einstein College of Medicine, Bronx, NY 10461, USA.

Abstract

Rather than being a passive, haphazard process of wear and tear, lifespan can be modulated actively by components of the insulin/insulin-like growth factor I (IGFI) pathway in laboratory animals. Complete or partial loss-of-function mutations in genes encoding components of the insulin/IGFI pathway result in extension of life span in yeasts, worms, flies, and mice. This remarkable conservation throughout evolution suggests that altered signaling in this pathway may also influence human lifespan. On the other hand, evolutionary tradeoffs predict that the laboratory findings may not be relevant to human populations, because of the high fitness cost during early life. Here, we studied the biochemical, phenotypic, and genetic variations in a cohort of Ashkenazi Jewish centenarians, their offspring, and offspring-matched controls and demonstrated a gender-specific increase in serum IGFI associated with a smaller stature in female offspring of centenarians. Sequence analysis of the IGF1 and IGF1 receptor (IGF1R) genes of female centenarians showed overrepresentation of heterozygous mutations in the IGF1R gene among centenarians relative to controls that are associated with high serum IGFI levels and reduced activity of the IGFIR as measured in transformed lymphocytes. Thus, genetic alterations in the human IGF1R that result in altered IGF signaling pathway confer an increase in susceptibility to human longevity, suggesting a role of this pathway in modulation of human lifespan.

PMID: 18316725 [PubMed - indexed for MEDLINE] PMCID: PMC2265137 **Free PMC Article**

Images from this publication. See all images (3) Free text

Publication Types, MeSH Terms, Substances, Grant Support

LinkOut - more resources