MedicalXpress

Gene variants found to affect human lifespan

February 4 2013

By broadly comparing the DNA of children to that of elderly people, gene researchers have identified gene variants that influence lifespan, either by raising disease risk or by providing protection from disease.

"This research is the first genome-wide, population-based study of copy number variations in children associated with human longevity," said study leader Hakon Hakonarson, M.D., Ph.D., director of the Center for Applied Genomics at The Children's Hospital of Philadelphia.

The study appeared Jan. 30 in the open-access journal PLOS ONE.

Copy number variations (CNVs) are losses or gains in DNA sequence that are usually rare, but which often play an important role in raising or lowering the risk of disease.

The study team compared the rates of CNVs in a sample of 7,313 young subjects, 18 years old and below, from the Children's Hospital network, to a group of 2,701 Icelandic subjects, 67 years old or above, recruited by the Icelandic Heart Association. The researchers used microchip arrays to perform the whole-genome CNV analyses.

"Our assumption was that CNVs appearing in children but not in the elderly were more likely to be disease-causing, while CNVs that were proportionately higher in older people were more likely to be protective, allowing them to live longer," said Hakonarson.

After performing a replication study in an independent U.S. cohort of

2,079 children and 4,692 older people and making statistical adjustments to address population stratification, the study team found seven significant CNVs. Three of the CNVs were deletions of DNA sequence, while four were duplications.

The genes impacted by the CNVs were disproportionately involved in alternative splicing. This is an important biological mechanism in which, instead of one gene simply expressing one protein, modifications to messenger RNA result in different protein products based on the same underlying DNA code in a given gene.

"Our results suggest that CNVs and other genetic variants may exert their effects through gene networks and pathways that regulate biological functions through mechanisms such as alternative splicing," said Hakonarson. "Possibly in a more global way than previously thought, some of these CNVs may have favorable effects, whereas others are bad for you and predispose you to diseases."

Although much work remains to be done, he added that the CNVs overrepresented in children may represent novel targets implicated in short lifespan. Eventually, added Hakonarson, if such CNVs are incorporated into early clinical screening tests, their presence could be prognostic markers indicating which patients should take individualized preventive health measures.

More information: "Copy Number Variations in Alternative Splicing Gene Networks Impact Lifespan," PLOS ONE, published online Jan. 30, 2013. dx.doi.org/10.1371/journal.pone.0053846

Provided by Children's Hospital of Philadelphia