Compound inheritance ID'd in cases of congenital scoliosis

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Image courtesy of Blausen Medical

(HealthDay)—In a case series of Han Chinese persons, compound inheritance of a rare null mutation and a hypomorphic allele accounted for a proportion of congenital scoliosis cases. These findings were published online Jan. 7 in the *New England Journal of Medicine*.

Nan Wu, M.D., from the Peking Union Medical College Hospital in China, and colleagues used comparative genomic hybridization, quantitative polymerase-chain-reaction analysis, and DNA sequencing to assess 161 Han Chinese persons with sporadic congenital scoliosis, 166 Han Chinese controls, and two pedigrees, whose family members had a 16p11.2 deletion. Tests of replication were conducted in 76 Han Chinese persons with congenital scoliosis and a multicenter series of 42 people with 16p11.2 deletions.

The researchers identified heterozygous *TBX6* null mutations in 11 percent of the 161 persons with sporadic congenital scoliosis; null mutations in *TBX6* were not observed in the controls. The null alleles included copy-number variants and single-nucleotide variants. In all 17 carriers of *TXB6* null mutations, the researchers identified a common *TBX6* haplotype as the second risk allele. This compound inheritance model was confirmed in replication studies involving additional persons with congenital scoliosis who carried a deletion affecting *TBX6*. The risk haplotype was suggested to be a hypomorphic allele in in-vitro functional assays.

"Compound inheritance of a rare null mutation and a hypomorphic allele of *TBX6* accounted for up to 11 percent of congenital scoliosis cases in the series that we analyzed," the authors write.

More information: Abstract
Full Text