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Research Project: Genetic analysis of idiopathic scoliosis clinical subgroups

Background: Scoliosis is a medical condition in which a person's spine is curved from side to side. Although it is a complex three-dimensional deformity, on an X-ray, viewed from behind, the spine of an individual with scoliosis may look more like an "S" or a "C" than a straight line. Scoliosis is typically classified as congenital (caused by vertebral anomalies present at birth), idiopathic (cause unknown, sometimes subclassified as infantile, juvenile, adolescent, or adult, according to age at onset), or neuromuscular (having developed as a secondary symptom of another condition, such as spina bifida, cerebral palsy, spinal muscular atrophy, or physical trauma). This condition affects approximately 7 million people in the United States. Adolescent Idiopathic Scoliosis (AIS) is the most common type in all scoliosis patients; it has 5 subtypes according to surgical classifications. Genetic heterogeneity is apparent in IS; nevertheless our team has identified IS candidate genes using targeted and genome-wide association (GWA) methods. Reducing heterogeneity or otherwise identifying important endophenotypes for IS is an important goal in IS research. We will perform subtype analyses of our existing GWAS data to discover genes that may correlate with features such of the AIS such as age at onset, curve pattern, severity, etc.

Progress: We have completed a clinical review of 419 patients for whom GWAS data are available. Clinical parameters that were assessed include curve pattern (e.g. right or left thoracic, lumbar, etc.), gender, age at onset, cobb angle (a measure of spinal curve severity) prior to treatment, requirement for surgery, family history (paternal or maternal) etc. We next conducted genome-wide tests of allelic association according to different subtypes. For this we are using statistics available in PLINK. Positive results will be assessed in an independent validation cohort of 283 patients. Clinical review of this second cohort is also in progress.