ADA Gene Analysis in Autosomal Recessive Severe Combined Immune Deficiency (SCID)

Clinical Features:
ADA deficiency is associated with an autosomal recessive form of severe combined immune deficiency (SCID) in which B, T, and NK cells are deficient. Bacterial, viral and fungal infections are common and often life-threatening, but there is a wide range of severity and age of onset. Diminished red cell adenosine deaminase activity is diagnostic, correlating with deoxyadenosine toxicity in lymphocytes. Enzyme replacement, bone marrow/stem cell transplantation, and gene therapy have been used successfully for treatment.

Inheritance Pattern/Genetics:
Autosomal recessive

Test Methods:
Analysis is performed by bi-directional sequencing of the coding regions and splice sites of the 12 exons of the ADA gene. If sequencing identifies a variant on only one allele, focused array CGH analysis with exon-level resolution (ExonArrayDx) will be performed to evaluate for a deletion or duplication of one or more exons of this gene. Variants found in the first person of a family to be tested are confirmed by repeat analysis using sequencing, restriction fragment analysis or another appropriate method.

Test Sensitivity:
In T-B-NK- SCID or milder variants showing partial adenosine deaminase deficiency, most patients will have homozygous or compound heterozygous variants in the ADA gene. The approach used by GeneDx is expected to have a sensitivity of over 98% for all types of ADA variants.

Published variants in ADA are distributed throughout the gene. Missense, nonsense, and frameshift variants are predominant but deletions of several exons have been reported.

References: