Ambry Genetics® | Ambry Classifi™

Ambry Genetics® Gene-Disease Validity Scheme

The Ambry Classifi™ program is the way we actualize our promise to provide genetic test results of unparalleled quality. A cornerstone of the Classifi program is the Ambry Genetics Gene-Disease Validity Scheme, which is a points-based framework that allows for a clear understanding of gene disease characterization. Ambry is dedicated to routinely updating our Gene-Disease Validity Scheme to reflect published recommendations and scientific data to drive accurate gene associations to deliver high-confidence variant classifications.

Classification Score					
Disputed <0 points	No Evidence 0 points	Limited >0 to 7 points	Moderate 8 to 12 points	Strong 13 to 16 points	Definitive ≥17 points

	Point Range	Criteria
GENETIC	1.00 to 18.00	**Case-Control Studies** (significant disease association)
	0.1 to 18.00	**Case-Level Data** (Proband count weighted by *de novo,* functional, and segregation evidence)
	3.00 to 7.00	**Cohort Studies** (significant enrichment)
	0.5 to 1.00	**Protein Regional Evidence** (Missense constraint, hotspot, recurrent *de novo*)
	0.1 to 3.00	**Publication Count** (with case-level data)
EXPERIMENTAL	1.00 to 2.00	**Gene Function** (function, expression, interaction)
	1.00 to 2.00	**Gene Disruption** (relevant altered protein function in appropriate assay(s))
	1.00 to 2.00	**Model Organism** (relevant phenotype with appropriate genotype)
GENETIC	-18.00 to -1.00	**Case-Control Studies** (demonstrated insignificant disease association)

The Gene-Disease Validity Scheme is not intended for the interpretation of epigenetic factors including genetic modifiers, multifactorial disease, or low-risk disease association alleles and may be limited in the interpretation of diseases confounded by incomplete penetrance, variable expressivity, phenocopies, triallelic or oligogenic inheritance.

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