

Table S1 : Gene-Disease Validity Curation for Mosaic Variants

Gene:
Phenotype (ISSVA):
 also applies for ISSVA phenotypes:

1. Genetic evidence

1.1. Case-level data

1.1.1. Variant evidence

Reference PMID, case ID; internal data For internal data, refer to internal case-level data form	Variant cDNA protein	Reported as (specify phenotype designation according to reference, if applicable)	Mosaic Variant Basic Score: 0.5	Upgrade Pathogenicity: 0-1.5 Prediction weak: + 0; Prediction strong: + 0.5; Functional effect: + 0.5-1; Known LPATH: +1; Known PATH: +1.5	Clustering: 0-1 Second observation with same or other variant at same codon: + 1; Neighbouring codons (+/-2): + 0.5	Score given
			0			0
			0			0
			0			0
			0			0
			0			0
			0			0
			0			0
			0			0
			0			0
			0			0
			0			0
			0			0
			0			0
Total score (maximum score for genetic case level evidence: 12)						0

2. Experimental evidence

Select, if curation of experimental evidence was not or only partially done

Score only experimental evidence that applies for the given type of vascular anomaly (experimental evidence often applies for many/all types of vascular anomalies, unless the respective experiment is specific for one type of vascular anomaly)

Category	Evidence Type	Default Score (Range)	Description	Reference (PMID)	Score given
2.1. Function	Biochemical function	0.5 (0-2)			
	Protein interaction	0.5 (0-2)			
	Expression	0.5 (0-2)			
2.2. Functional Alteration	Patient cells	1 (0-2)			
	Non-patient cells	0.5 (0-1)			
2.3. Models	Non-human model organism	2 (0-4)			
	Cell culture model	1 (0-2)			
2.4. Rescue	Rescue in human	2 (0-4)			
	Rescue in non-human model organism	2 (0-4)			
	Rescue in cell culture model	1 (0-2)			
	Rescue in patient cells	1 (0-2)			

Total score 2.1. (maximum score for category: 2)
 Total score 2.2. (maximum score for category: 2)
 Total score 2.3. & 2.4. (maximum combined score for categories: 4)

3. Clinical Validity Summary Matrix

	Summary
Genetic evidence (0 to 12)	0
Experimental evidence (0 to 6)	0
Total points (sum of genetic & experimental evidence)	0
Replication over time: >2 publ. w/ convincing evidence over time (>3 yrs) (Y/N)	
Indicate PMID (replication 1)	
Indicate PMID (replication 2)	
Indicate PMID (replication 3)	
Calculated classification	NO EVIDENCE
Valid contradictory evidence (Y/N)	
if Y, list PMIDs for contradictory evidence	
if Y, describe contradictory evidence (if applicable)	
Curator classification	NO EVIDENCE
Final classification (to be entered manually after panel discussion)	

Commentary:

Select, if curation of experimental evidence was not or only partially done
 No scorable experimental evidence exists at the time of curation
 Experimental evidence exists but was not curated because of sufficient scores for genetic evidence
 Experimental evidence was only partially curated because of sufficient scores for genetic evidence