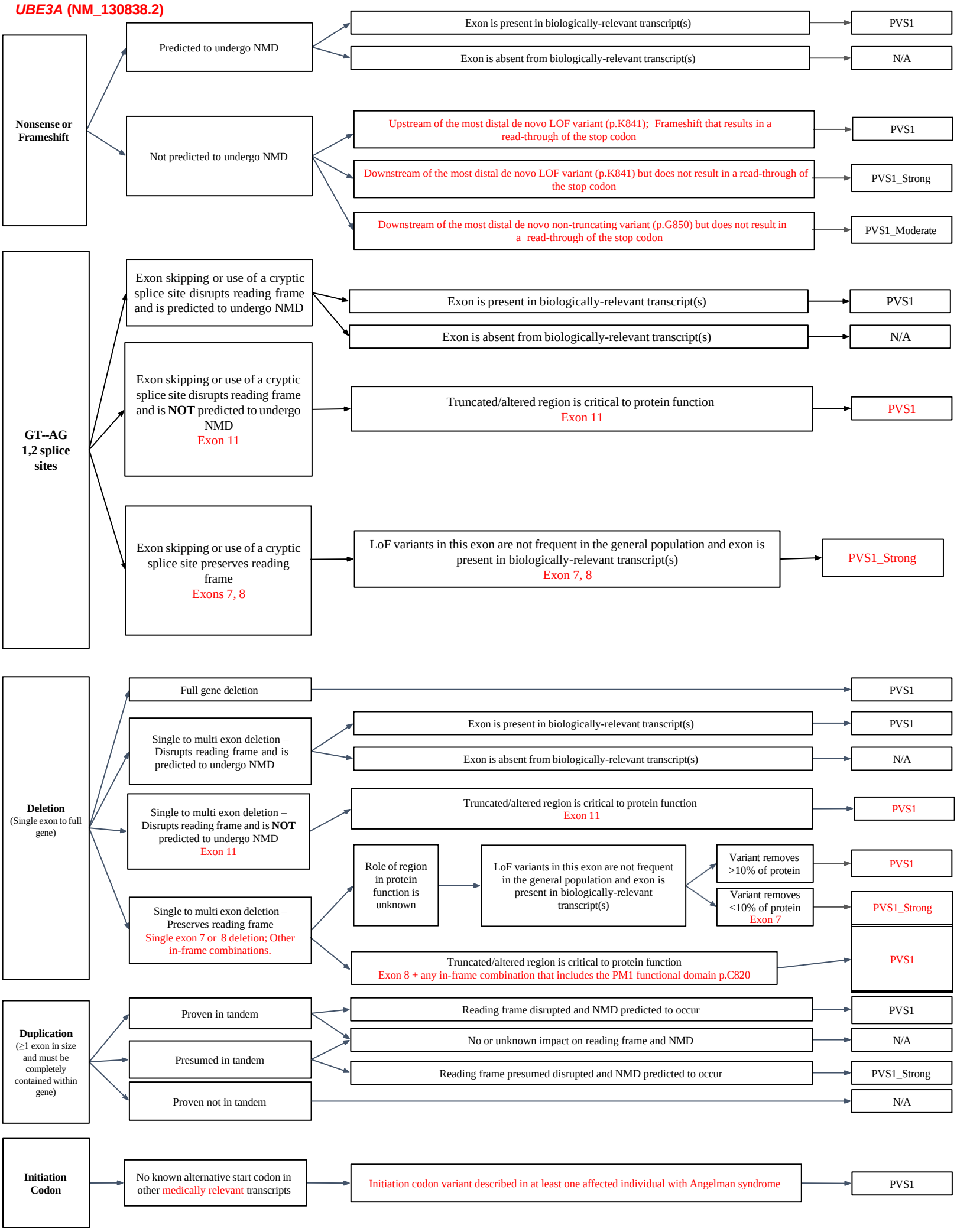
UBE3A (NM_130838.2)
Nonsense or Frameshift
Predicted to undergo NMD
Exon is present in biologically-relevant transcript(s)
PVS1
Exon is absent from biologically-relevant transcript(s)
N/A
Not predicted to undergo NMD
Upstream of the most distal de novo LOF variant (p.K841); Frameshift that results in a read-through of the stop codon
PVS1
Downstream of the most distal de novo LOF variant (p.K841) but does not result in a read-through of the stop codon
PVS1_Strong
Downstream of the most distal de novo non-truncating variant (p.G850) but does not result in a read-through of the stop codon
PVS1_Moderate
GT–AG 1,2 splice sites
Exon skipping or use of a cryptic splice site disrupts reading frame and is predicted to undergo NMD
Exon is present in biologically-relevant transcript(s)
PVS1
Exon is absent from biologically-relevant transcript(s)
N/A
Exon skipping or use of a cryptic splice site disrupts reading frame and is NOT predicted to undergo NMD
Exon 11
Truncated/altered region is critical to protein function
Exon 11
PVS1
Exon skipping or use of a cryptic splice site preserves reading frame
Exons 7, 8
LoF variants in this exon are not frequent in the general population and exon is present in biologically-relevant transcript(s)
Exon 7, 8
PVS1_Strong
Deletion
(Single exon to full gene)
Full gene deletion
PVS1
Single to multi exon deletion – Disrupts reading frame and is predicted to undergo NMD
Exon is present in biologically-relevant transcript(s)
PVS1
Exon is absent from biologically-relevant transcript(s)
N/A
Single to multi exon deletion – Disrupts reading frame and is NOT predicted to undergo NMD
Exon 11
Truncated/altered region is critical to protein function
Exon 11
PVS1
Single to multi exon deletion – Preserves reading frame
Single exon 7 or 8 deletion; Other in-frame combinations.
Role of region in protein function is unknown
LoF variants in this exon are not frequent in the general population and exon is present in biologically-relevant transcript(s)
Variant removes >10% of protein
PVS1
Variant removes <10% of protein
Exon 7
PVS1_Strong
Truncated/altered region is critical to protein function
Exon 8 + any in-frame combination that includes the PM1 functional domain p.C820
PVS1
Duplication
(≥1 exon in size and must be completely contained within gene)
Proven in tandem
Reading frame disrupted and NMD predicted to occur
PVS1
Presumed in tandem
No or unknown impact on reading frame and NMD
N/A
Reading frame presumed disrupted and NMD predicted to occur
PVS1_Strong
Proven not in tandem
N/A
Initiation Codon
No known alternative start codon in other medically relevant transcripts
Initiation codon variant described in at least one affected individual with Angelman syndrome
PVS1