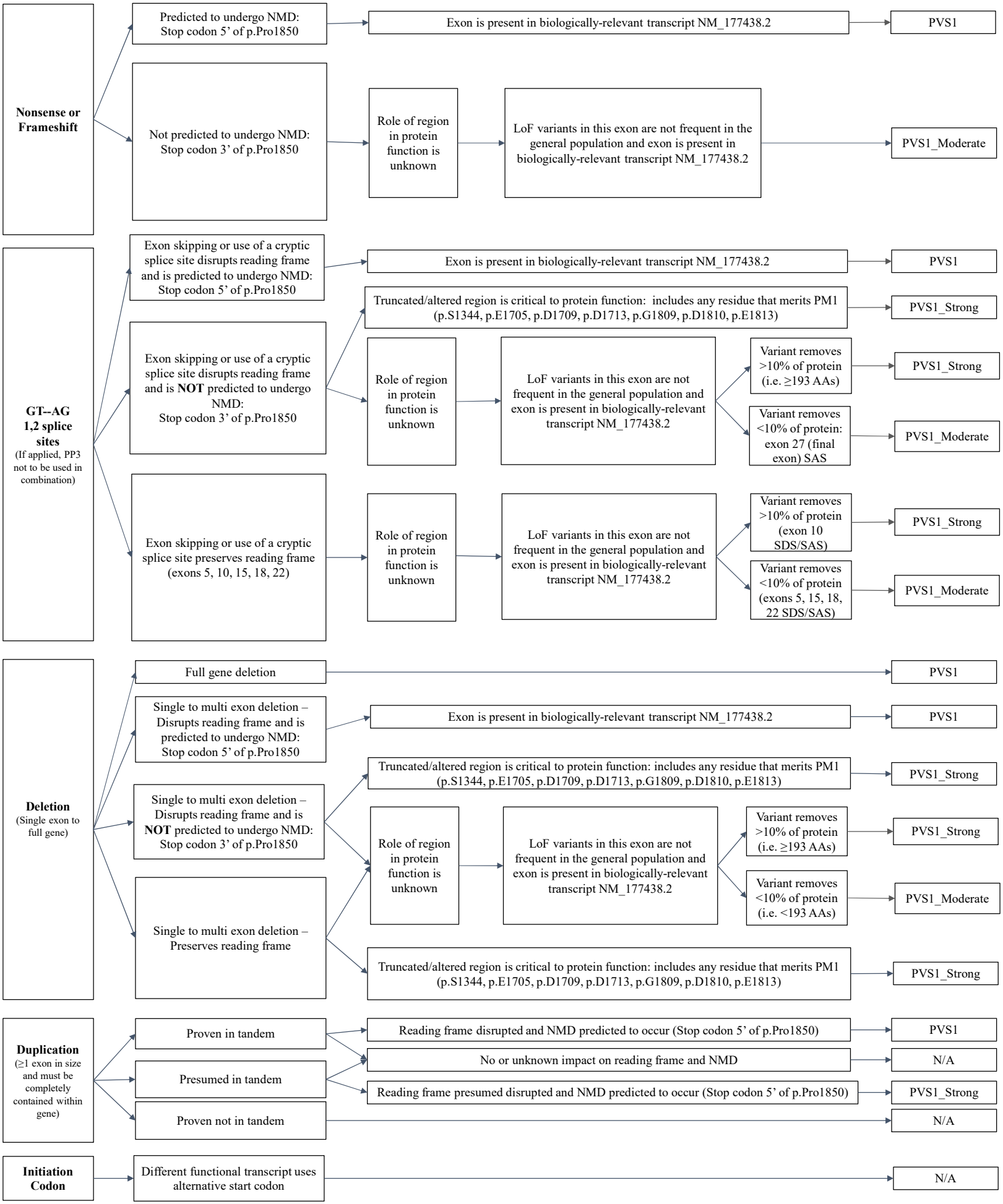
Nonsense or Frameshift
Predicted to undergo NMD: Stop codon 5' of p.Pro1850
Exon is present in biologically-relevant transcript NM_177438.2
PVS1
Not predicted to undergo NMD: Stop codon 3' of p.Pro1850
Role of region in protein function is unknown
LoF variants in this exon are not frequent in the general population and exon is present in biologically-relevant transcript NM_177438.2
PVS1_Moderate
GT--AG 1,2 splice sites
(If applied, PP3 not to be used in combination)
Exon skipping or use of a cryptic splice site disrupts reading frame and is predicted to undergo NMD: Stop codon 5' of p.Pro1850
Exon is present in biologically-relevant transcript NM_177438.2
PVS1
Exon skipping or use of a cryptic splice site disrupts reading frame and is NOT predicted to undergo NMD: Stop codon 3' of p.Pro1850
Truncated/altered region is critical to protein function: includes any residue that merits PM1 (p.S1344, p.E1705, p.D1709, p.D1713, p.G1809, p.D1810, p.E1813)
PVS1_Strong
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 NM_177438.2
Variant removes >10% of protein (i.e. ≥193 AAs)
PVS1_Strong
Variant removes <10% of protein: exon 27 (final exon) SAS
PVS1_Moderate
Exon skipping or use of a cryptic splice site preserves reading frame (exons 5, 10, 15, 18, 22)
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 NM_177438.2
Variant removes >10% of protein (exon 10 SDS/SAS)
PVS1_Strong
Variant removes <10% of protein (exons 5, 15, 18, 22 SDS/SAS)
PVS1_Moderate
Deletion
(Single exon to full gene)
Full gene deletion
PVS1
Single to multi exon deletion – Disrupts reading frame and is predicted to undergo NMD: Stop codon 5' of p.Pro1850
Exon is present in biologically-relevant transcript NM_177438.2
PVS1
Single to multi exon deletion – Disrupts reading frame and is NOT predicted to undergo NMD: Stop codon 3' of p.Pro1850
Truncated/altered region is critical to protein function: includes any residue that merits PM1 (p.S1344, p.E1705, p.D1709, p.D1713, p.G1809, p.D1810, p.E1813)
PVS1_Strong
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 NM_177438.2
Variant removes >10% of protein (i.e. ≥193 AAs)
PVS1_Strong
Variant removes <10% of protein (i.e. <193 AAs)
PVS1_Moderate
Single to multi exon deletion – Preserves reading frame
Truncated/altered region is critical to protein function: includes any residue that merits PM1 (p.S1344, p.E1705, p.D1709, p.D1713, p.G1809, p.D1810, p.E1813)
PVS1_Strong
Duplication
(≥1 exon in size and must be completely contained within gene)
Proven in tandem
Reading frame disrupted and NMD predicted to occur (Stop codon 5' of p.Pro1850)
PVS1
Presumed in tandem
No or unknown impact on reading frame and NMD
N/A
Reading frame presumed disrupted and NMD predicted to occur (Stop codon 5' of p.Pro1850)
PVS1_Strong
Proven not in tandem
N/A
Initiation Codon
Different functional transcript uses alternative start codon
N/A