

Online Table 1. List of pathogenic variants in known HTAD genes in 366 ESTAD cases

Gene	Aa change	mRNA accession#	Number of case	Reported
ACTA2	p.R179H	NM_001613.2	1	Yes
ACTA2	p.R198H	NM_001613.2	1	Yes
ACTA2	p.R314*	NM_001613.2	1	Yes
COL3A1	p.R326*	NM_000090.3	1	Yes
COL3A1	p.G360R	NM_000090.3	1	No
COL3A1	p.G420S	NM_000090.3	1	Yes
COL3A1	p.G909V	NM_000090.3	1	Yes
FBN1	p.L2842Pfs	NM_000138.4	1	No
FBN1	p.E2527G	NM_000138.4	1	Yes
FBN1	p.R2220*	NM_000138.4	1	Yes
FBN1	p.Y2149C	NM_000138.4	1	Yes
FBN1	p.C2096*	NM_000138.4	1	No
FBN1	p.C2038Y	NM_000138.4	1	No
FBN1	p.C1889Afs	NM_000138.4	1	No
FBN1	p.C1791Y	NM_000138.4	1	No
FBN1	p.C1719R	NM_000138.4	1	Yes
FBN1	p.P1521Qfs	NM_000138.4	1	No
FBN1	p.N1489K	NM_000138.4	1	p.N1489L
FBN1	p.E1366K	NM_000138.4	1	Yes
FBN1	p.D1238N	NM_000138.4	1	No
FBN1	p.R861*	NM_000138.4	2	Yes
FBN1	p.Q481*	NM_000138.4	1	No
SMAD3	p.L366Dfs	NM_005902.3	1	No
SMAD3	p.R368*	NM_005902.3	1	Yes
SMAD3	p.R287Q	NM_005902.3	1	Yes
TGFB2	p.Y341*	NM_003238.3	1	Yes
TGFBR1	p.P452Qfs	NM_004612.2	1	No
TGFBR1	p.R457Mfs	NM_004612.2	1	No
TGFBR1	p.R487Q	NM_004612.2	3	Yes
TGFBR2	p.R537C	NM_003242.5	1	Yes

Online Table 2. Rare VUSs in HTAD genes identified in 231 ESTAD-EA cases

Gene	Aa change	mRNA accession#	Number of cases
ACTA2	p.A140E	NM_001613.2	1
ACTA2	p.C376R	NM_001613.2	1
COL3A1	p.A1192T	NM_000090.3	1
COL3A1	p.K1313R	NM_000090.3	1
COL3A1	p.L734F	NM_000090.3	1
COL3A1	p.N76D	NM_000090.3	1
COL3A1	p.P686A	NM_000090.3	1
COL3A1	p.P892A	NM_000090.3	1
COL3A1	p.R1024Q	NM_000090.3	1
COL3A1	p.R271Q	NM_000090.3	5
FBN1	p.C2378R	NM_000138.4	1
FBN1	p.G2395V	NM_000138.4	1
FBN1	p.G2514R	NM_000138.4	1
FBN1	p.I2185T	NM_000138.4	1
FBN1	p.R1170H	NM_000138.4	2
FBN1	p.T619N	NM_000138.4	1
FBN1	p.V1765I	NM_000138.4	1
LOX	p.M233V	NM_002317.5	2
LOX	p.S247R	NM_002317.5	1
MYH11	p.A1101V	NM_001040113.1	1
MYH11	p.A1846V	NM_001040113.1	1
MYH11	p.H1208Q	NM_001040113.1	1
MYH11	p.I138F	NM_001040113.1	1
MYH11	p.I408T	NM_001040113.1	1
MYH11	p.I775V	NM_001040113.1	1
MYH11	p.K1263del	NM_001040113.1	2
MYH11	p.K1628del	NM_001040113.1	1
MYH11	p.L1247P	NM_001040113.1	1
MYH11	p.L1752inWRRS	NM_001040113.1	1
MYH11	p.M343V	NM_001040113.1	1
MYH11	p.R1336Q	NM_001040113.1	1
MYH11	p.R1542Q	NM_001040113.1	3
MYH11	p.R1765W	NM_001040113.1	1
MYH11	p.R676C	NM_001040113.1	1
MYH11	p.T1565M	NM_001040113.1	2
MYLK	p.A1826V	NM_053025.3	1
MYLK	p.D1682N	NM_053025.3	1
MYLK	p.E1446K	NM_053025.3	1
MYLK	p.N1324K	NM_053025.3	1
MYLK	p.P1431S	NM_053025.3	1
MYLK	p.V1213M	NM_053025.3	1
MYLK	p.W1378L	NM_053025.3	1

MYLK	p.Y1635C	NM_053025.3	1
SMAD3	p.C109G	NM_005902.3	1
TGFB2	p.R165W	NM_003238.3	2
TGFBR1	p.D290N	NM_004612.2	1
TGFBR1	p.L195W	NM_004612.2	1
TGFBR1	p.N478S	NM_004612.2	1
TGFBR1	p.V145G	NM_004612.2	1
TGFBR1	p.V153I	NM_004612.2	2
TGFBR1	p.Y282H	NM_004612.2	1
TGFBR2	p.D40N	NM_003242.5	1
TGFBR2	p.M373I	NM_003242.5	3
TGFBR2	p.S553T	NM_003242.5	1
TGFBR2	p.T421A	NM_003242.5	1
TGFBR2	p.S416G	NM_003242.5	1
TGFBR2	p.V387M	NM_003242.5	1
