**S1 Table. Clinical and genetic data for the MPS IVA patients used in present study:** age, gender, genetic diagnosis, GALNS and beta-galactosidase (beta-Gal.) activity in leucocytes obtained using van Diggelen protocol [4.]. All the MPS IVA patients presented clinical symptoms consistent with MPS IV phenotype, while the carriers presented no clinical symptoms that indicated the presence of MPS IV.Sequence Reference for GALNS NM_000512.4.

| MPS IVA Patient | Age | Gender | Coding effect | cDNA change | Mutation type | Localization | PolyPhen-2 | Reference | Genotype | In vitro enzymatic test in leucocytes nmol MU/mg protein | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | GALNS[a] | Result GALNS enzymatic test | beta-Gal.[b] |
| patient 1 | 19 | female | p.(?) | c.759-3C>G | Splicing | intron 7 | | novel, CentoMD® | Homozygous | < 1 | pathologic | 861 |
| patient 2 | 4 | male | p.T312A | c.934A>G | Missense | exon 9 | probably damaging | Wang (2010) J HumGenet 55:534 | Homozygous | < 1 | pathologic | 490 |
| patient 3 | 10 | male | p.Y181C | c.542A>G | Missense | exon 5 | probably damaging | novel, CentoMD® | Homozygous | 3 | pathologic | 797 |
| patient 4 | 10 | male | p.G50R | c.148G>A | Missense | exon 2 | probably damaging | novel, CentoMD® | Homozygous | < 1 | pathologic | 520 |
| patient 5 | 6 | male | p.(?) | c.1482+1G>A | Splicing | intron 13 | | novel, CentoMD® | Homozygous | < 1 | pathologic | 313 |
| patient 6 | 4 | male | p.P498L | c.1493C>T | Missense | exon 14 | probably damaging | novel, CentoMD® | Homozygous | < 1 | pathologic | 890 |
| patient 7 | 6 | female | p.G340D | c.1019G>A | Missense | exon 10 | probably damaging | Tomatsu (2004) J Med Genet 41:e98 | Homozygous | < 1 | pathologic | 563 |
| patient 8 | 8 | female | p.G340D | c.1019G>A | Missense | exon 10 | probably damaging | Tomatsu (2004) J Med Genet 41:e98 | Homozygous | < 1 | pathologic | 405 |
| patient 9 | 6 | male | p.P498L | c.1493C>T | Missense | exon 14 | probably damaging | novel, CentoMD® | Homozygous | < 1 | pathologic | 476 |
| patient 10 | 8 | male | p.A107T | c.319G>A | Missense | exon 3 | probably damaging | Tomatsu (2004) J Med Genet 41:e98 | Homozygous | < 1 | pathologic | 620 |
| patient 11 | 5 | female | p.T100P | c.298A>C | Missense | exon 3 | probably damaging | novel, CentoMD® | Homozygous | 2 | pathologic | 830 |
| patient 12 | 9 | female | p.G340D | c.1019G>A | Missense | exon 10 | probably damaging | Tomatsu (2004) J Med Genet 41:e98 | Homozygous | < 1 | pathologic | 1063 |
| patient 13 | na | male | p.P179S | c.535C>T | Missense | exon 5 | probably damaging | Terzioglu (2002) Hum Mutat 20:477 | Homozygous | 5 | pathologic | 613 |
| patient 14 | na | male | p.P179S | c.535C>T | Missense | exon 5 | probably damaging | Terzioglu (2002) Hum Mutat 20:477 | Homozygous | < 1 | pathologic | 963 |
| patient 15 | 7 | male | p.P498L | c.1493C>T | Missense | exon 14 | probably damaging | novel, CentoMD® | Homozygous | < 1 | pathologic | 573 |
| patient 16 | na | male | p.P498L | c.1493C>T | Missense | exon 14 | probably damaging | novel, CentoMD® | Homozygous | < 1 | pathologic | 596 |
| patient 17 | 3 | male | p.Q29X | c.85C>T | Nonsense | exon 1 | | novel, CentoMD® | Homozygous | < 1 | pathologic | 777 |
| patient 18 | na | female | p.T312A | c.934A>G | Missense | exon 9 | probably damaging | Wang (2010) J HumGenet 55:534 | Homozygous | < 1 | pathologic | 810 |
| patient 19 | 8 | female | p.A392V | c.1175C>T | Missense | exon 11 | probably damaging | Tomatsu (2004) J Med Genet 41:e98 | Homozygous | < 1 | pathologic | 842 |
| patient 20 | 12 | male | p.F156L | c.466T>C | Missense | exon 4 | probably damaging | Morrone (2014) Mol Genet Metab 112:160 | Homozygous | < 1 | pathologic | 1034 |
| patient 21 | 4 | male | p.S287L | c.860C>T | Missense | exon 8 | probably damaging | Bunge (1997) Hum Mutat 10:223 | Compound | < 1 | pathologic | 1003 |
| | | | p.R386C | c.1156C>T | Missense | exon 11 | probably damaging | Ogawa (1995) Hum MolGenet 4:341 | heterozygous | | | |
| patient 22 | 6 | male | p.S287L | c.860C>T | Missense | exon 8 | probably damaging | Bunge (1997) Hum Mutat 10:225 | Compound | < 1 | pathologic | 920 |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | p.R386C | c.1156C>T | Missense | exon 11 | probably damaging | Ogawa (1995) Hum MolGenet 4:341 | heterozygous | | | |
| patient 23 | 8 | male | p.D39Y | c.115G>T | Missense | exon 1 | probably damaging | novel, CentoMD® | Other | < 1 | pathologic | 720 |
| | | | p.N204T | c.611A>C | Missense | exon 6 | probably damaging | novel, CentoMD® | complex | | | |
| | | | p.F226L | c.676T>C | Missense | exon 7 | benign | novel, CentoMD® | | | | |
| patient 24 | 11 | female | p.D39Y | c.115G>T | Missense | exon 1 | probably damaging | novel, CentoMD® | Other | < 1 | pathologic | 630 |
| | | | p.N204T | c.611A>C | Missense | exon 6 | probably damaging | novel, CentoMD® | complex | | | |
| | | | p.F226L | c.676T>C | Missense | exon 7 | benign | novel, CentoMD® | | | | |
| carrier 1 | 36 | female | p.N204T | c.611A>C | Missense | exon 6 | probably damaging | novel, CentoMD® | Other | na | na | na |
| | | | p.F226L | c.676T>C | Missense | exon 7 | benign | novel, CentoMD® | complex | | | |
| carrier 2 | 36 | male | p.D39Y | c.115G>T | Missense | exon 1 | probably damaging | novel, CentoMD® | Heterozygous | na | na | na |

na = data not available

[a]Normal values for GALNS activity in leucocytes are between 107-198 nmol MU/mg protein

[b]Normal values for beta -Galactosidase activity in leucocytes are between 119-65