**Supplementary file 2**

**List of HGSNAT mutations implicated in MPS IIIC**

|  |  |  |
| --- | --- | --- |
| **Mutation** | **Total energy (kcal/mol)** | **Region of the protein** |
| G423W | 41.0 | LD-TMD interface  |
| G424V | 18.8 |
| G424S | 11.8 |
| G262R | 7.5 |
| C76F | 5.0 |
| N273K | -0.6 |
| G133A | -1.4 |
| P283L | 3.0 | Catalytic core |
| R344H | 2.0 |
| R344C | 2.0 |
| E471K | 1.4 |
| N258I | -0.1 |
| G486E | 17.9 | Scaffold domain |
| M482K | 3.2 |
| S518F | 2.5 |
| W403C | 2.2 |
| A489E | 1.1 |
| ***K523Q*** | 0.9 |
| S539C | 0.7 |
| S541L | -0.2 |
| ***V481L*** | -0.3 |
| L445P | 5.9 | Other regions |
| L113P | 4.9 |
| L137P | 3.4 |
| A54V | 2.9 |
| ***A615T*** | 2.3 |
| Y627C | 1.4 |
| D562V | 1.2 |
| ***P237Q*** | 0.1 |
| P571L | -0.2 |
| G173D | -0.4 |
| G173E | -0.9 |

FoldX web server was used to predict relative mutant stability (Schymkowitz *et al,* 2005). Positive total energy value indicates destabilization, with greater values meaning lower stability. Nonsense mutations indicated in the figure 4 as black were not included in FoldX calculations. Polymorphisms are italicized. All other mutants listed are missense mutations (Canals *et al,* 2011; Fan *et al,* 2006; Fedele & Hopwood, 2010; Feldhammer *et al,* 2009a; Feldhammer *et al,* 2009b; Hrebicek *et al,* 2006; Huizing & Gahl, 2020).