

**Additional file 1: Non-pathogenic or unclassified variants identified by means of NGS panel diagnostics in the MFM-causing genes.**

| Pat.  | Gene        | Exon | Variant                      | SNP database               | Predicted as                  | Conservation status            | NHLB1  | 1000GP                            |
|-------|-------------|------|------------------------------|----------------------------|-------------------------------|--------------------------------|--|-----------------------------------|
| F13.1 | <i>ZASP</i> | 4    | c.664G>A,<br>p.Ala222Thr*    | rs139922045,<br>MAF <0.1 % | predicted<br>inconsistently   | AA highly,<br>Nt weakly        | 4/8596 (European<br>American<br>population)  | not found                         |
| F15.1 | <i>FLNC</i> | 21   | c.3721C>T,<br>p.Arg1241Cys   | rs146953558,<br>MAF 0,95%  | benign                        | AA highly,<br>Nt weakly        | 81/8433 (European<br>American<br>population) | 5/753<br>(European<br>population) |
| F17.1 | <i>FLNC</i> | 23   | c.4022G>A,<br>p.Arg1341Gln   | rs149641783,<br>MAF 0,18%  | predicted<br>inconsistently   | AA highly                      | 15/8425 (European<br>American<br>population) | 2/756<br>(European<br>population) |
| F19.1 | <i>FLNC</i> | 34   | c.5578C>T,<br>p.Arg1860Cys   | rs181067717,<br>MAF 0,62%  | probably/possibly<br>damaging | AA highly,<br>Nt<br>moderately | 52/8320 (European<br>American<br>population) | 3/755<br>(European<br>population) |
| F20.1 | <i>FLNC</i> | 40   | c.6595G>A,<br>p.Gly2199Arg   | rs368977589,<br>MAF 0,012% | predicted<br>inconsistently   | AA and Nt<br>highly            | 1/8357 (European<br>American<br>population)  | not found                         |
| F23.1 | <i>TTN</i>  | 343  | c.95297C>T,<br>p.Ser31766Phe | rs191484894,<br>MAF 0.2 %  | disease causing               | AA and Nt<br>highly            | 16/8334 (European<br>American<br>population) | 2/756<br>(European<br>population) |

Predicted as, here the results of the prediction programs PolyPhen-2 and Mutation Taster are shown; Conservation status, conservation of the changed amino acid (AA) and nucleotide (Nt) using data of Alamut; NHLB1, frequency of the variant according to the database of NHLBI exome sequencing project (ESP); 1000GP, frequency of the variant according to the database of the 1000 genome project. \*, the disease did not segregate in the family; MAF, minor allele frequency; predicted inconsistently, the mutation is predicted to be disease causing by one programme and predicted to be benign by the other; -, not performed; for abbreviations of genes see text.