**SDC Table 2.** *ATP8B1* individual participant gene mutation data.

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Patient number** | **Zygosity** | **Nucleotide change** | **Predicted amino acid change** | **Reference SNP cluster ID** | **CADD score (version 1.3)** | **AF**  **(gnomAD, all)** | **AF (gnomAD, population with highest frequency)** | **Mutation previously reported in literature?** |
| 1 - 10 | homozygous | c.923G>T | p.G308V | rs111033609 # | 31 | <0.0001 | <0.0001 | Yes (1,2) |
| 11 ^ | heterozygous | c.923G>T | p.G308V | rs111033609 # | 31 | <0.0001 | <0.0001 | Yes (1,2) |
| heterozygous | c.1982T>C | p.I661T | rs121909100 | 28.1 | <0.0001 | 0.00016 | Yes (1-5) |
| heterozygous | c.1220 G>A | [p.S407N](mailto:p.S407N@) | not found | 29.8 | Not reported | Not reported | No |
| 12 | heterozygous | c.1982 T>C | p.I661T | rs121909100 | 28.1 | <0.0001 | 0.00016 | Yes (1-5) |
| heterozygous | c.1804 C>T | p.R602\* | rs121909105 | 47 | <0.0001 | <0.0001 | Yes (4,6) |
| 13^^ | heterozygous | c.1982T>C | p.I661T | rs121909100 | 28.1 | <0.0001 | 0.00016 | Yes (1-5) |
| heterozygous | c.2097+2 T>C | splicing alteration | rs387906381 | 25.9 | <0.0001 | <0.0001 | Yes (1,2,4,7) |
| 14 | heterozygous | c.1982T>C | p.I661T | rs121909100 | 28.1 | <0.0001 | 0.00016 | Yes (1-5) |
| heterozygous | c.2674G>A | p. G892R | rs121909098 | 34 | <0.0001 | <0.0001 | Yes, (1,2,4,8) |
| 15 | heterozygous | c.1982T>C | p.I661T | rs121909100 | 28.1 | <0.0001 | 0.00016 | Yes (1-5) |
| heterozygous | c.2854C>T | p.R952\* | rs765889649 | 44 | <0.0001 | <0.0001 | Yes (4) |
| 16 - 18 | homozygous | c.1660G>A | p.D554N | rs121909101 | 31 | Not reported | Not reported | Yes (4,9) |
| 19 | homozygous | c.1697G>A | p.G566D | rs906857413 | 28.4 | Not reported | Not reported | No |
| 20 | homozygous | c.2558T>C | p.F853S | rs773092889 | 32 | <0.0001 | 0.0001 | Yes (4) |
| 21 | homozygous | c.3410C>G | p.S1137\* | rs74414989 # | 43 | Not reported | Not reported | No |
| 22 | homozygous | c.3531+1G>A | splicing alteration | rs753965947 | 26.2 | <0.0001 | 0.00055 | No |
| 23 | heterozygous | c.2081T>A | p.I694N | rs541474497 # | 33 | <0.0001 | 0.00038 | Yes (10,11) |
| heterozygous | c.2236T>C | p.C746R | not found (there is a different very rare missense at this same base, with  rs377461289) | 29.5 | Not reported | Not reported | No |
| 24 | heterozygous | c.2114C>A | p.A705D | not found | 33 | Not reported | Not reported | No |
| heterozygous | c.2572T>C | p.C858R | not found | 28.8 | Not reported | Not reported | No |
| 25, 26 | heterozygous | c.2699T>C | p.M900T | not found | 27.1 | Not reported | Not reported | Yes (2) |
| heterozygous | c.2989G>A | p.V997M | no rs ID, but variant present in gnomAD | 34 | <0.0001 | <0.0001 | Yes (2) |

# = 2 or more variants at this base, including the identified mutation, sharing the same 'rs' ID. 'rs' IDs do not uniquely identify a mutation, but rather, a location in the genome.

^This patient is heterozygous for three likely disease mutations, two of which are previously reported in a number of patients. Regarding phase, the p.I661T and p.S407N mutations were contributed by the same parent.

^^Participant 13 is compound heterozygous for p.I661T and another mutation previously reported in multiple participants, occurring at an invariant position in a splice junction (2097+2T>C). This patient is also heterozygous for a missense variant in *ABCB11*, c.2087G>A, resulting in p.R696Q. This *ABCB11* variant is rare in gnomAD (AF 0.00019 overall, occurring at highest frequency, 0.00089, in the African population) and may be functionally deleterious (CADD 1.3 score 25.1). Given that this patient carries two alleles bearing known disease mutations in *ATP8B1*, the variant in *ABCB11* is not necessary for disease in this patient. However, it may be possible that the *ABCB11* variant contributes to the disease phenotype.

Abbreviations: AF, allele frequency; CADD, combined annotation dependent depletion; gnomAD, genome aggregation database (<http://gnomad.broadinstitute.org/>); SNP, single nucleotide polymorphism.

**SDC TABLE 2 REFERENCES**

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