Appendix S1. Judgement standard for next-generation-sequencing [reference genome version (HG19), dbSNP (v147)].

First, it was necessary to estimate the quality of sequencing, which resulted in: i) Coverage of the target region >98%; and ii) average sequencing depth on the target region >400X.

A pathogenic or suspected pathogenic variant was selected. If one of the following criteria were met, the variant was classified as a pathogenic variant: i) The variant has been reported as a disease-causing mutation and does not appear in publicly available population databases; ii) certain variants [frameshift, stop gain, stop loss, splicing (±1 or 2 splice sites) or start codon mutation] that do not appear in publicly available population databases; or iii) the site is classified as a pathogenic variant in the clinvar database. The ClinVar Augest 2015 XML file was used in the analysis (ftp://ftp.ncbi.nlm.nih.gov/pub/clinvar/vcf_GRCh37/archive_2.0/2015/).

If either of the following criteria were met, the variation was classified as a suspected pathogenic variation: i) The variant has been reported to be associated with cancer, with its minor allele frequency (MAF) >0.01, or it is absent in the publicly available population databases; ii) certain variants [frameshift, stop gain, stop loss, splicing (±1 or 2 splice sites), start codon variation] with an MAF >0.01 in standard human databases; or iii) predicted by multiple software as a pathogenic variant and does not appear in the publicly available population databases, or has an MAF >0.01 in the publicly available population databases.

Cluster analysis was performed and the variant was examined in more than one sample.