Supplementary Data A

Functional and pathway enrichment analysis

To examine whether the prioritised genes were involved in processes or pathways relating to NESHIE pathogenesis, the Database for Annotation, Visualization, and Integrated Discovery (DAVID) bioinformatics resource was used to identify enriched biological process (BP), molecular function (MF) and cellular component (CC) GO terms and KEGG or Reactome pathways using the list of prioritised genes as input. GO or pathway enrichment was calculated using a stringent DAVID EASE score ≤ 0.05 with adjustment for multiple testing using the Benjamini method. GO terms and pathways were considered statistically significant if the Benjamini-adjusted p-value was ≤ 0.05.

Protein-protein interaction network analysis

The Search Tool for Retrieval of Interacting Genes (STRING) database tool v11.5 was utilised to construct a protein-protein interaction (PPI) network using the set of prioritised genes as input. The STRING database includes interaction information on more than 67 million proteins. Within the PPI network, nodes represent the proteins encoded by the genes and edges represent the interactions between those proteins. The network was constructed with a high level of confidence (≥ 0.7) using *Homo sapiens* as the target organism. Experimentally-determined evidence, known interaction sources from curated databases, predicted interactions from gene neighbourhood algorithms, gene expression and co-occurrence sources, and co-expression and protein homology data were included. Text-mining interactions were excluded due to a high likelihood of false positive results. A maximum of 10 directly-interacting proteins were included in the first shell, and a maximum of 50 indirectly-interacting proteins were included in the second shell. Cytoscape software v3.9.0 was utilised to visualise and analyse the PPI network.