Supplementary Table 1. SDHB mutations for which a structure homology model was created and analysed to predict biological consequence. Those for which a construct was made and analysed *in vitro* are marked as biologically assessed. Detailed presentation of predicted consequences appears in Supplementary Figure 2. Mutations not associated with disease were analysed for control purposes.

SDHB Mutation	Disease-associated	Biologically assessed	Predicted structural consequence
R27X	Yes	Yes	Truncation mutation – missing protein chain abrogates SDH assembly
K40E	Yes	No	Mutation having no obvious consequence and located in a disease-associated mutation hot-spot – non-peripheral residue may compromise assembly factor binding
A43P	Yes	Yes	Mutation having no obvious consequence and located in a disease-associated mutation hot-spot – peripheral residue may compromise assembly factor binding
R46G	Yes	Yes	Mutation having no obvious consequence and located in a disease-associated mutation hot-spot – peripheral residue may compromise assembly factor binding
R46Q	Yes	Yes	Mutation having no obvious consequence and located in a disease-associated mutation hot-spot – peripheral residue may compromise assembly factor binding
R46X	Yes	No	Truncation mutation – missing protein chain abrogates SDH assembly
G53R	Yes	No	Mutation having no obvious consequence and located in a disease-associated mutation hot-spot – peripheral residue may compromise assembly factor binding
P56L	Yes	No	Mutation having no obvious consequence and located in a disease-associated mutation hot-spot – peripheral residue may compromise assembly factor binding
L65P	Yes	No	Mutation having no obvious consequence and located in a disease-associated mutation hot-spot – non-peripheral residue may compromise assembly factor binding
K80Q	Yes	No	Mutation disrupting macromolecular assembly - affecting SDHB binding to subunit A
R90Q	Yes	No	Mutation disrupting macromolecular assembly - affecting SDHB binding to subunit A
R90X	Yes	Yes	Truncation mutation – missing protein chain abrogates SDH assembly
R94K	Yes	No	Mutation disrupting macromolecular assembly - affecting SDHB binding to subunit A
G96D	Yes	No	Mutation affecting electron pathways – may result in lost electrons and generation of reactive oxygen species
C98R	Yes	No	Mutation breaking electron pathways – due to loss of iron-sulfur centre
G99D	Yes	No	Mutation affecting electron pathways – may result in lost electrons and generation of reactive oxygen species
S100F	Yes	No	Mutation affecting electron pathways – may result in lost electrons and generation of reactive oxygen species
S100P	Yes	No	Mutation affecting electron pathways – may result in lost electrons and generation of reactive oxygen species
C101Y	Yes	Yes	Mutation breaking electron pathways – due to loss of iron-sulfur centre
I127S	Yes	Yes	Mutation having no obvious consequence and located in a disease-associated mutation hot-spot – non-peripheral residue may compromise assembly factor binding
Y150X	Yes	No	Truncation mutation – missing protein chain abrogates SDH assembly
P197R	Yes	Yes	Mutation affecting electron pathways – may result in lost electrons and generation of reactive oxygen species
R230G	Yes	No	no obvious effect – peripheral residue may compromise assembly factor binding
R230H	Yes	No	no obvious effect – peripheral residue may compromise assembly factor binding

R242H	Yes	Yes	Mutation disrupting macromolecular assembly – compromises SDHD assembly
H57R	No	No	No obvious effect – Is a non-disease-associated control mutation
G69V	No	No	No obvious effect – Is a non-disease-associated control mutation
L87S	No	No	No obvious effect – Is a non-disease-associated control mutation
G96S	No	No	No obvious effect – Is a non-disease-associated control mutation