Supplementary Table 5.1. Estimated electronic donor-to-acceptor coupling between adjacent redox centres on the electron path as calculated by the Pathways software (Balabin et al. 2012; Beratan et al. 1991) for wild-type SDH and mutants. The unit-less net decay calculated by Pathways is roughly proportional to the donor-to-acceptor coupling and appears in the "Coupling" columns as a relative indicator of electron transfer rates. The electronic coupling between adjacent redox centres is ranked, and the relative ranking appears in the Rank columns. An asterisk * denotes the electron path segment having the mutant residue between its redox centres. A breakdown of the jumps comprising each calculated electron path appears in Supplementary Tables 5.2 to 5.5.

Electron path segment	**wild-type**		**B:G99D**		**B:S100F**		**B:S100P**		**B:P197R**	
	Coupling	**Rank**	**Coupling**	**Rank**	**Coupling**	**Rank**	**Coupling**	**Rank**	**Coupling**	**Rank**
FAD - FES	1E-6	6	4E-6	5	2E-6 *	6	4E-6 *	5	3E-6	5
FES - SF4	3E-4	2	4E-4 *	2	1E-3	2	2E-4	2	8E-4	2
SF4 - F3S	2E-3	1	3E-3	1	3E-3	1	3E-3	1	3E-3	1
F3S - ubiquinone	7E-5	3	7E-5	3	6E-5	3	7E-5	3	2E-4 *	3
F3S - heme	5E-6	4	5E-6	4	5E-6	4	5E-6	4	5E-6	4
heme - ubiquinone	3E-6	5	2E-6	6	4E-6	5	3E-6	6	2E-6	6

Supplementary Table 5.2. Segments of the electron transfer path between iron-sulfur centres FES and SF4 for wild-type and mutant SDHB:G99D as calculated by the Pathways (Balabin et al. 2012; Beratan et al. 1991) software. The possible types of electron jumps are CB for covalent bond, HB for hydrogen bond, and TS for through space jumps. The wild-type is calculated to have a larger through space jump of 3.57 Å than the mutant, whose through space jump is 2.93 Å. The electron path distance of 23.57 Å for wild-type is longer than that of the mutant, which is 23.37 Å. Images of the jumps comprising the calculated electron paths appear in Supplementary Figure 2 entry Gly99Asp.

Electron donor		**Electron acceptor**		**Type of electron jump**	**Distance of this jump (Å)**	**Accumulated distance for this path (Å)**
Residue	**Atom**	**Residue**	**Atom**			
Wild-type						
FES	FE1	FES	FE2	CB	2.69	2.69
FES	FE2	C98	SG	CB	2.02	4.71
C98	SG	C98	CB	CB	1.81	6.53
C98	CB	C98	CA	CB	1.54	8.07
C98	CA	C98	C	CB	1.50	9.57
C98	C	G99	N	CB	1.35	10.92
G99	N	G99	CA	CB	1.44	12.36
G99	CA	C189	CB	TS	3.57	15.93
C189	CB	C189	SG	CB	1.80	17.73
C189	SG	SF4	FE4	CB	2.97	20.70
SF4	FE4	SF4	FE1	CB	2.87	23.57
				Average jump distance	2.14	
SDHB:G99D						
FES	FE1	FES	FE2	CB	2.69	2.69
FES	FE2	C98	SG	CB	1.94	4.63
C98	SG	C98	CB	CB	1.82	6.44
C98	CB	C98	CA	CB	1.54	7.98
C98	CA	C98	C	CB	1.51	9.49
C98	C	D99	N	CB	1.35	10.84
D99	N	D99	CA	CB	1.44	12.28
D99	CA	D99	CB	CB	1.52	13.80
D99	CB	C189	CB	TS	2.93	16.74
C189	CB	C189	SG	CB	1.81	18.54
C189	SG	SF4	FE4	CB	2.96	21.51
SF4	FE4	SF4	FE1	CB	2.87	23.37
				Average jump distance	2.03	

Supplementary Table 5.3. Segments of the electron transfer path between redox centres FAD and FES for wild-type and mutant SDHB:S100F as calculated by the Pathways (Balabin et al. 2012; Beratan et al. 1991) software. The possible types of electron jumps are CB for covalent bond, HB for hydrogen bond, and TS for through space jumps. Images of the jumps comprising the calculated electron paths appear in Supplementary Figure 2 entry Ser100Phe.

Electron donor		**Electron acceptor**		**Type of electron jump**	**Distance of this jump (Å)**	**Accumulated distance for this path (Å)**
Residue	**Atom**	**Residue**	**Atom**			
Wild-type						
FAD	N1	FAD	N5	TS	3.78	3.78
FAD	N5	FAD	C5X	CB	1.40	5.18
FAD	C5X	FAD	C6	CB	1.43	6.61
FAD	C6	FAD	C7	CB	1.55	8.16
FAD	C7	FAD	C8	CB	1.43	9.59
FAD	C8	FAD	C8M	CB	1.48	11.07
FAD	C8M	H99	NE2	CB	1.95	13.02
H99	NE2	H99	CD2	CB	1.38	14.40
H99	CD2	H99	CG	CB	1.36	15.76
H99	CG	H99	CB	CB	1.49	17.25
H99	CB	H99	CA	CB	1.53	18.78
H99	CA	H99	N	CB	1.43	20.21
H99	N	S98	N	CB	1.34	21.55
S98	C	S98	CA	CB	1.49	23.04
S98	CA	S98	N	CB	1.44	24.48
S98	N	R97	C	CB	1.35	25.83
R97	C	R97	O	CB	1.23	27.06
R97	O	C98	CB	TS	3.81	30.88
C98	CB	C98	SG	CB	1.81	32.69
C98	SG	FES	FE2	CB	2.02	34.71
FES	FE2	FES	FE1	TS	2.69	37.40
				Average jump distance	1.78	
SDHB:S100F						
FAD	N1	FAD	N5	TS	3.78	3.78
FAD	N5	A103	CA	TS	2.98	6.77
A103	CA	A103	N	CB	1.45	8.21
A103	N	A102	C	CB	1.35	9.57
A102	C	A102	CA	CB	1.51	11.07
A102	CA	I97	CD1	TS	3.27	14.35
I97	CD1	I97	CG1	CB	1.51	15.86

I97	CG1	I97	CB	CB	1.51	17.38
I97	CB	I97	CA	CB	1.48	18.86
I97	CA	I97	C	CB	1.52	20.37
I97	C	C98	N	CB	1.35	21.73
C98	N	C98	CA	CB	1.45	23.17
C98	CA	C98	CB	CB	1.54	24.71
C98	CB	C98	SG	CB	1.81	26.53
C98	SG	FES	FE2	CB	1.88	28.41
FES	FE2	FES	FE1	TS	2.68	31.09
				Average jump distance	1.94	

Supplementary Table 5.4. Segments of the electron transfer path between redox centres FAD and FES for wild-type and mutant SDHB:S100P as calculated by the Pathways software (Balabin et al. 2012; Beratan et al. 1991). The possible types of electron jumps are CB for covalent bond, HB for hydrogen bond, and TS for through space jumps. Images of the jumps comprising the calculated electron paths appear in Supplementary Figure 2 entry Ser100Pro.

Electron donor		**Electron acceptor**		**Type of electron jump**	**Distance of this jump (Å)**	**Accumulated distance for this path (Å)**
Residue	**Atom**	**Residue**	**Atom**			
Wild-type						
FAD	N1	FAD	N5	TS	3.78	3.78
FAD	N5	FAD	C5X	CB	1.40	5.18
FAD	C5X	FAD	C6	CB	1.43	6.61
FAD	C6	FAD	C7	CB	1.55	8.16
FAD	C7	FAD	C8	CB	1.43	9.59
FAD	C8	FAD	C8M	CB	1.48	11.07
FAD	C8M	H99	NE2	CB	1.95	13.02
H99	NE2	H99	CD2	CB	1.38	14.40
H99	CD2	H99	CG	CB	1.36	15.76
H99	CG	H99	CB	CB	1.49	17.25
H99	CB	H99	CA	CB	1.53	18.78
H99	CA	H99	N	CB	1.43	20.21
H99	N	S98	N	CB	1.34	21.55
S98	C	S98	CA	CB	1.49	23.04
S98	CA	S98	N	CB	1.44	24.48
S98	N	R97	C	CB	1.35	25.83
R97	C	R97	O	CB	1.23	27.06
R97	O	C98	CB	TS	3.81	30.88
C98	CB	C98	SG	CB	1.81	32.69
C98	SG	FES	FE2	CB	2.02	34.71
FES	FE2	FES	FE1	TS	2.69	37.40
				Average jump distance	1.78	
SDHB:S100P						
FAD	N1	FAD	N5	TS	3.78	3.78
FAD	N5	A103	CA	TS	2.98	6.77
A103	CA	A103	N	CB	1.45	8.21
A103	N	A102	C	CB	1.35	9.56
A102	C	A102	CA	CB	1.51	11.07
A102	CA	I97	CD1	TS	2.95	14.02
I97	CD1	I97	CG1	CB	1.51	15.54

I97	CG1	I97	CB	CB	1.49	17.05
I97	CB	I97	CA	CB	1.49	18.54
I97	CA	I97	C	CB	1.51	20.04
I97	C	C98	N	CB	1.35	21.39
C98	N	C98	CA	CB	1.44	22.83
C98	CA	C98	CB	CB	1.54	24.37
C98	CB	C98	SG	CB	1.81	26.19
C98	SG	FES	FE2	CB	1.76	27.95
FES	FE2	FES	FE1	TS	2.69	30.64
				Average jump distance	1.91	

Supplementary Table 5.5. Segments of the electron transfer path between redox centres F3S and ubiquinone for wild-type and mutant SDHB:P197R as calculated by the Pathways software (Balabin et al. 2012; Beratan et al. 1991). The possible types of electron jumps are CB for covalent bond, HB for hydrogen bond, and TS for through space jumps. Images of the jumps comprising the calculated electron paths appear in Supplementary Figure 2 entry Pro197Arg.

Electron donor		**Electron acceptor**		**Type of electron jump**	**Distance of this jump (Å)**	**Accumulated distance for this path (Å)**
Residue	**Atom**	**Residue**	**Atom**			
Wild-type						
F3S	FE1	F3S	FE4	CB	2.25	2.25
F3S	FE4	C196	SG	CB	2.99	5.24
C196	SG	C196	CB	CB	1.80	7.04
C196	CB	C196	CA	CB	1.53	8.57
C196	CA	C196	C	CB	1.50	10.08
C196	C	P197	N	CB	1.31	11.39
P197	N	P197	CA	CB	1.44	12.83
P197	CA	P197	CB	CB	1.53	14.36
P197	CB	Ubiquinone	C1	TS	4.34	18.71
Ubiquinone	C1	Ubiquinone	O1	CB	1.23	19.94
				Average jump distance	1.99	
SDHB:P197R						
F3S	FE1	F3S	FE4	CB	2.25	2.25
F3S	FE4	C196	SG	CB	2.98	5.23
C196	SG	C196	CB	CB	1.80	7.02
C196	CB	C196	CA	CB	1.53	8.56
C196	CA	C196	C	CB	1.50	10.06
C196	C	R197	N	CB	1.36	11.42
R197	N	R197	CA	CB	1.44	12.86
R197	CA	R197	CB	CB	1.54	14.40
R197	CB	R197	CG	CB	1.52	15.92
R197	CG	Ubiquinone	C2	TS	3.07	19.98
Ubiquinone	C2	Ubiquinone	C1	CB	1.46	20.44
Ubiquinone	C1	Ubiquinone	O1	CB	1.23	21.67
				Average jump distance	1.81	