

Supplementary Tables

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Table S1. PCR conditions of rs5370 polymorphism of *EDN1*

Gene	rs ID	Primer Sequence	Cycling Conditions	Product size, bp
EDN1	rs5370G/T	F 5'- GACCATGAGAAACAGCGTCA- 3'	I95°C 5', D95°C 30", A60°C 40", E72°C 40", 35cy, FE72°C 10'	201
		R 5'- AGAGGATGCTCCTGCTCTGA-3'		
		IP 5'- CTAGGGTTCGACTTTCCGTT-3'	I96°C 3', D96°C 10", A50°C 5", E60°C 30", 32cy, 4°C 10'	

A, annealing; cy, cycles; D, denaturation; E, extension; F, forward; FE, final extension; I, initial denaturation; IP, internal primer; R, reverse; bp, base pair.

Table S2. qRT-PCR conditions of *EDN1*

Gene	Primer sequences	Cycling conditions	Product size (bp)
<i>EDN1</i>	F 5' - AGCTGTCCAAGTCAGACGC - 3' R 5' - GCCCAAGTGCCCTTTTAACG - 3'	I 94°C 10', D94°C 15", A60°C 60", 40 cy	84

A, annealing; cy, cycles; D, denaturation; E, extension; F, forward; FE, final extension; I, initial denaturation; IP, internal primer; R, reverse; bp, base pair.

Table S3. Clinical characteristics of the HAPE-f, HAPE-p and, HLs

	HAPE-f	HAPE-p	HLs	HAPE-f vs. HAPE-p	HAPE-f vs. HLs	HAPE-p vs. HL
				<i>P</i> values		
n	310	310	310			
Age	29.5±6.2	29.2±8.5	37.5±11.2	0.65	7.37E-22	1.49E-19
BMI, Kg/m²	22.1± 3.2	22.9± 13.1	21.20± 3.5	0.30	3.85E-04	0.02
SaO₂, %	87.7± 4.4	48.6± 13.5	87.7± 9.9	4.71E-77	8.77E-24	3.92E-65
PR, rate/min	84.2± 20.4	102.8± 21.9	75.4± 10.6	6.38E-09	7.44E-05	5.76E-18
MAP, mmHg	92.8± 7.8	95.6± 10.7	93.2± 6.91	0.02	0.85	0.02

Data are presented as mean ± SD and are compared by unpaired Student's *t*-test. n, number of subjects; BMI, body mass index; SaO₂, arterial oxygen saturation; %, per cent; PR, pulse rate; MAP, mean arterial pressure.

Table S4. System characterization for parameters after 100-ns simulation.

Type	Average RMSD (Å)	Average RMSF (Å)	Radius of gyration (nm)	Average SASA (nm ²)	Average no. of Hydrogen bonds
<i>EDN1</i> wild-type	2.81	0.93	2.97	130.63	110
<i>EDN1</i> variant-type	2.05	0.91	3.20	129.28	114

Variant, K198N; Å, Angstrom; nm, nanometer; nm², nanometre square; SASA, solvent-accessible surface area.

Supplementary Figure S1:

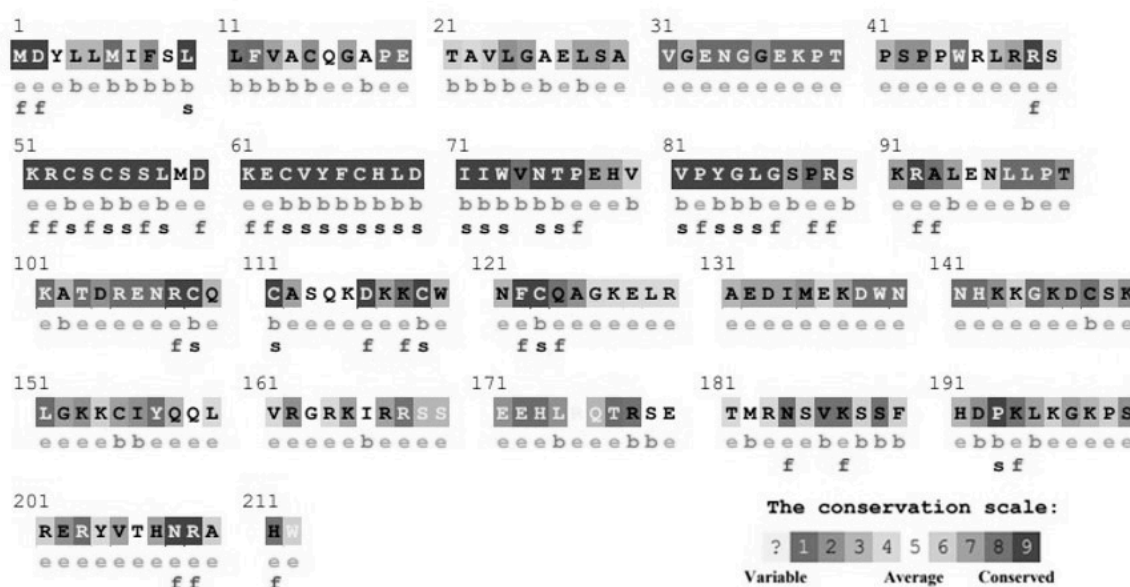


Figure S1. ConSurf analysis plot. The plot revealed residual conservation of the *EDN1* sequence. The rs5370 residue was located in the variable region.

Supplementary Figure S2:

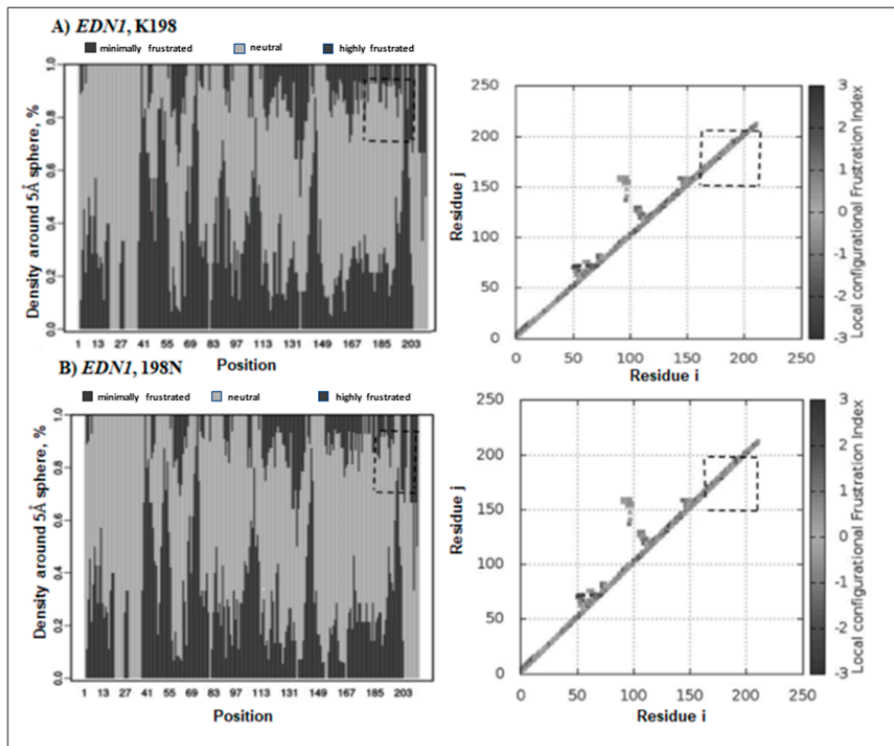


Figure S2. Frustration and configurational loss and gain contacts in K198N region. (A) Panel shows density and covariances matrices of *EDN1* K198. (B) Panel depicts *EDN1* 198N density and covariances matrices type. Green shades represent minimally frustrated and red shades represent highly frustrated residues. Å, Angstrom; i and j, covariance matrix for residues; %, per cent.