

Genetic Epidemiology of Glucose-6-Dehydrogenase Deficiency in the Arab World

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Supplementary Information

Supplementary Tables

Supplementary Table S1: Missense mutations in the *G6PD* gene along with *in silico* prediction and WHO classification.

Supplementary Table S2: Statistical evaluation of *in silico* prediction methods for the missense mutations in G6PD

Supplementary Table S3: Most common missense mutations in the Arab world for *G6PD* gene

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Supplementary Fig. S2: Results from Clustal Omega for Multiple Sequence Alignment

Supplementary Fig. S3: ConSurf results predicting the range of conservation of the amino acids in the G6PD protein sequence

Supplementary Tables

Supplementary Table S1

NCBI rs IDs	AA Change	Countries	WHO Severity /Class	SNPs&GO (Functional Effect & Reliability Index)	PolyPhen-2 (Functional Impact & score)	Mutation assessor (Functional Impact & score)	SNAP2 (Functional Effect & Reliability Index)	SIFT (Tolerance Index & score)	References
rs76645461	p.I48T	Algeria, Tunisia, Iraq, Jordan, Kuwait, Saudi Arabia & UAE	Mild/III	D(1)	PD(0.985)	L(1.365)	E(5)	IT(0.00)	1-18
rs1050828	p.V68M	Tunisia, Iraq, Comoros, Oman, Jordan, Kuwait, Palestine, Saudi Arabia & UAE	Mild/III	D(0)	PD(0.999)	M(3.365)	E(60)	IT(0.04)	1-6, 9, 12-17, 19, 21-26, 28, 34, 35, 39 & 40
rs1050829	p.N126D	Algeria, Tunisia, Comoros, Iraq, Jordan, Kuwait, Oman, Palestine, Saudi Arabia & UAE	Mild/III	N(3)	B(0.0)	N(0.535)	N(-26)	T(0.43)	1-6, 9, 12-17, 19, 21-26, 28, 29 & 39
NA	p.N135T	Egypt, Palestine & Jordan	NR	D(2)	PD(0.998)	M (2.83)	E(22)	IT(0.00)	9, 17 & 22
rs137852313	p.E156K	Algeria	Mild/III	N(1)	B(0.005)	N(0.49)	N(-89)	T(0.29)	32
NA	p.S179N	Palestine	NR	D(7)	*PD(0.9)	H (4.485)	E(17)	IT(0.00)	21,22
rs5030872	p.D181V	Algeria & Tunisia	Severe/II	N(6)	B (0.008)	N(-0.29)	N(-90)	IT(0.01)	1, 3, 29, 31 & 32
rs5030868	p.S188F	Algeria, Tunisia, Bahrain, Comoros, Iraq, Jordan, Egypt, Kuwait, Oman, Palestine, Saudi Arabia	Severe/II	D(5)	B(0.022)	M(3.42)	E(84)	IT(0.00)	1-6, 9, 12-17, 20-27, 32-35, 38 & 40-43

		& UAE							
NA	p.M212V	Saudi Arabia	Mild/III	D(3)	PD(0.986)	M (2.685)	N(-79)	IT(0.00)	7,8, 10, 11, & 37
rs137852328	p.R227L	Algeria	Mild/III	D(9)	PD(0.988)	H(4.2)	E(68)	IT(0.00)	30
NA	p.R246L	Tunisia	Severe/II	D(9)	PD(0.997)	H(4.65)	E(85)	IT(0.00)	1,3 & 34
rs137852318	p.D282H	Algeria	Mild/III	D(2)	PD(0.995)	M(2.57)	N(-9)	IT(0.00)	12
rs137852327	p.V291M	Saudi Arabia	Severe/II	D(7)	PD(1.00)	H (4.52)	E(32)	IT(0.00)	17
NA	p.Q307P	Tunisia	Severe/II	D(9)	*PD(0.951)	H(4.64)	E(88)	IT(0.00)	1, 3 & 12
rs76723693	p.L323P	Tunisia & Saudi Arabia	Mild/III	D(8)	B(0.249)	M(3.105)	E(93)	T(0.09)	1,3 & 36
rs5030869	p.A335T	Algeria, Iraq, Jordan, Kuwait, Oman & Saudi Arabia	Severe/II	D(1)	PD(0.961)	L(1.83)	E(89)	T(0.16)	2, 4-6, 9, 13-16, 24 & 32
rs137852321	p.R387H	Palestine	Severe/I	D(3)	PD(1.00)	M (2.46)	E(34)	IT(0.00)	22 & 41
NA	p.K407T	Tunisia	Severe/II	D(9)	PD(0.998)	H(4.64)	E(82)	IT(0.00)	1, 3 & 12
NA	p.S448G	Saudi Arabia	NR	D(4)	*PD(0.454)	M (2.77)	E(12)	T(0.44)	11
NA	p.R454C	Saudi Arabia & UAE	Severe/II	D(8)	PD(1.00)	H(3.655)	E(72)	IT(0.00)	7,8, 10, 11, 21, 25, 26, & 37
rs72554665	p.R459P	Algeria	Severe/II	D(8)	PD(0.979)	M(2.67)	N(-48)	IT(0.00)	17
rs72554665	p.R459L	Tunisia	Severe/II	D(5)	*PD(0.729)	L(1.7)	E(55)	IT(0.00)	1, 3 & 12
rs72554664	p.R463H	Tunisia	Severe/II	D(5)	PD(0.994)	M(3.25)	E(74)	IT(0.00)	1, 3 & 12

*D- Deleterious, N-Neutral, B- Benign, M-Mild, L-Low, H-High, E- Effect, *PD-Possibly Damaging, PD- Probably Damaging, IT- Intolerant, T-Tolerant, NA-Not applicable & NR-Not reported. The information for the above table was retrieved through a systematic search using 4 different databases: PubMed (<http://www.ncbi.nlm.nih.gov/pubmed>), Embase (<https://www.elsevier.com/solutions/embase-biomedical-research>), ScienceDirect (<http://www.sciencedirect.com/>) & Web of Science (<http://wokinfo.com/webtools/browsersearch/>)

Supplementary Table S2

Statistical parameters	SNPs&GO	PolyPhen-2	Mutation-assessor	SNAP2	SIFT
TP	14	12	11	11	13
TN	6	6	6	6	5
FP	3	5	6	6	4
FN	0	0	0	0	1
Total	23	23	23	23	23
PPV	0.82	0.70	0.64	0.64	0.76
NPV	1	1	1	1	0.83
Sensitivity/TP R (%)	1	1	1	1	0.93
Specificity/TN R (%)	0.67	0.54	0.50	0.50	0.55
FPR	0.33	0.45	0.50	0.50	0.45
FNR	0	0	0	0	0.07
ACC (%)	0.86	0.78	0.74	0.74	0.78
MCC	0.74	0.62	0.57	0.57	0.54

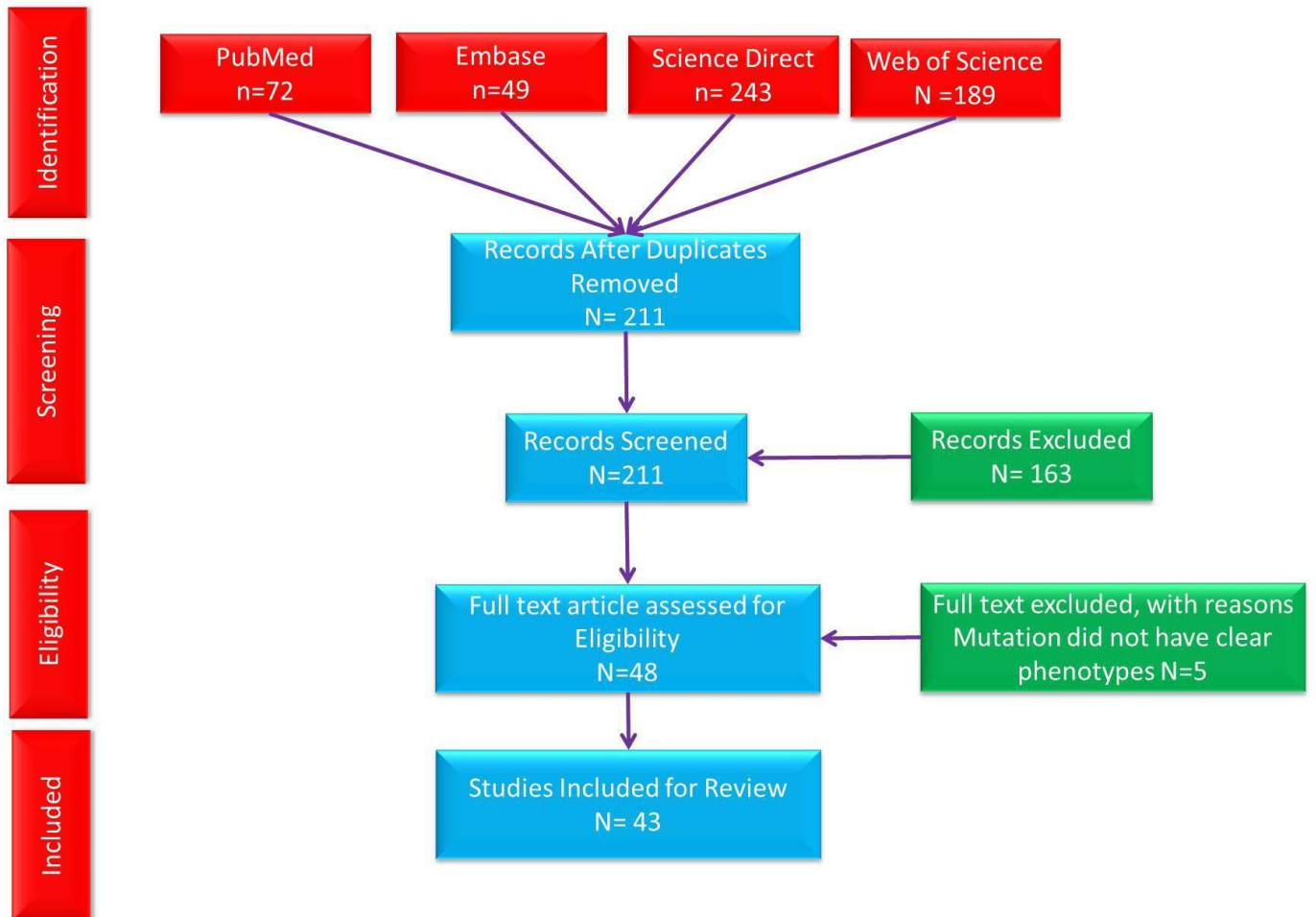
TP-True positive, TN-True negative, FP-False positive, FN-False negative, TPR-True positive rate, TNR-True negative rate, FPR-False positive rate, FNR-False negative rate, ACC- Accuracy, & MCC- Matthews correlation coefficient.

Supplementary Table S3

rs IDs	Nucleotide change	AA change	Exon	Origin	Frequency
rs5030868	c.563C>T	p.S188F	Exon 6	Mediterranean	56.80%
rs1050828	c.376G>A	p.N126D	Exon 5	Africa	10.03%
rs76645461	c.143T>C	p.I48T	Exon 3	Algeria	5.51%
rs1050828	c.202G>A	p.V68M	Exon 4	Africa	10 %

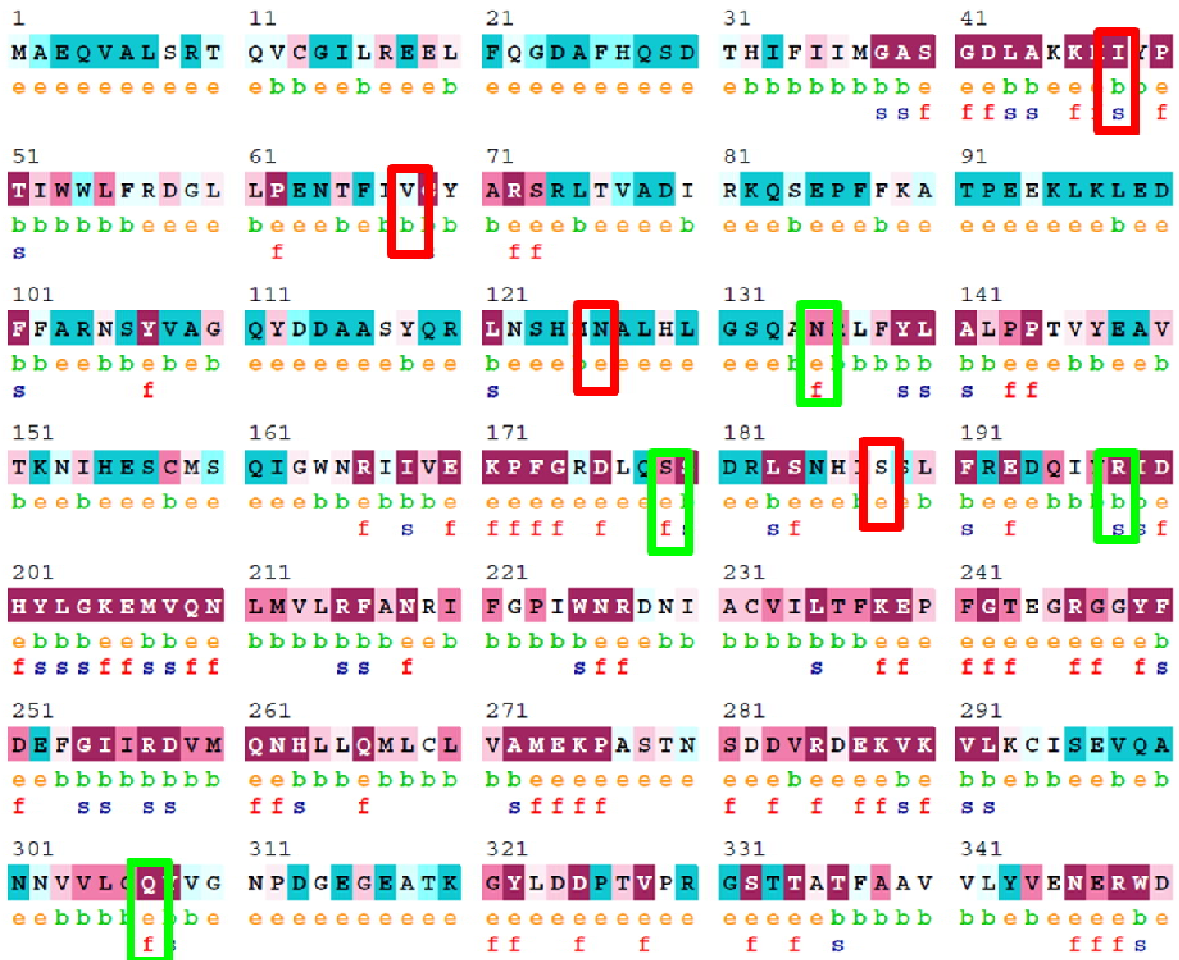
Supplementary Figures

Supplementary Fig. S1

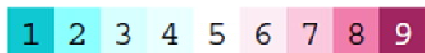


Supplementary Fig. S3

ConSurf Results



The conservation scale:



Variable Average Conserved

- e - An exposed residue according to the neural-network algorithm.
- b - A buried residue according to the neural-network algorithm.
- f - A predicted functional residue (highly conserved and exposed).
- s - A predicted structural residue (highly conserved and buried).

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