

Summary of gene mutations outcomes in parasitic disease

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Gene mutation may occur either in the parasite or in the host, which may be beneficial or harmful for each. In the era of parasitic diseases, the outcome of gene mutations includes 1) disease susceptibility and resistance, 2) drug resistance, 3) parasite virulence, 4) pathogenesis and host clinical presentations, 5) occurrence of malignancy, and 6) vector control. These categories were discussed in details in the previous issues [PUJ 2016; 9(2) and PUJ 2017; 10(1&2)], whereas objective of the following editorial is to summarize and tabulate all gene mutations incriminated in the outcome of the parasitic diseases.

Key Words: Gene mutations, parasites.

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Summary of host gene mutations and effect on parasitic diseases

Gene	Effect on parasitic diseases	Reference
<i>act1</i>	Increased susceptibility to cardiomyopathy in Chagas' disease	122
<i>adam12</i>	Susceptibility to Chagas' disease	79
<i>ank-1</i> (Ankyrin-1)	Susceptibility to malaria	52
<i>apobec3b</i>	Susceptibility to <i>P. falciparum</i>	56
<i>apoL-I</i>	Susceptibility to African trypanosomiasis	77
<i>bat1</i>	Protection against severe malignant malaria	114
<i>ccr5</i>	Increased susceptibility to cardiomyopathy in Chagas' disease	120
CD32 encoding gene	Susceptibility to severe malignant malaria	113
CD54 encoding gene	Increased severity of <i>falciparum</i> malaria	99
CD234 encoding gene (<i>fy</i>)	Resistance to <i>vivax</i> malaria	34
<i>cdkn2</i>	Susceptibility to cancer bladder in urinary schistosomiasis	83, 84
<i>chit</i>	Resistance to malaria	40
Cytochrome P450 encoding gene	Resistance to artemisinin therapy	136
<i>fas</i> in mice	Susceptibility to cutaneous leishmaniasis	67
<i>ftt4 & foxc2</i>	Increased susceptibility of lymphatic filariasis	119
<i>G6PD</i> encoding gene	Resistance to <i>vivax</i> malaria	44
	Protection against severe malaria	105-109
<i>Galactose binding protein (PpGalec)</i> encoding gene (transgenic mutation)	Decreased infection of sandflies with <i>Leishmania</i> spp.	135
<i>Glycophorins</i> encoding gene	Resistance to malaria	39
Hemoglobin mutant variants (sickle cell anemia & thalassemia)	Resistance to malaria	41-43
ICAM-1 encoding gene	Increased severity of <i>falciparum</i> malaria	99
IFN- γ receptor encoding gene	Increased susceptibility of peri-portal fibrosis in schistosomiasis	117, 118
<i>ikbl</i>	Increased susceptibility to cardiomyopathy in Chagas' disease	121
<i>il2ra</i>	Susceptibility to cutaneous leishmaniasis	70
<i>Kdr</i> in <i>A. gambiae</i> & <i>A. funestus</i> (transgenic mutation)	Increased resistance to DDT insecticide with Increased susceptibility to <i>P. falciparum</i>	124-130
<i>kras</i>	Susceptibility to cancer bladder in urinary schistosomiasis	88

Leptin receptor encoding gene	Susceptibility to amoebic cytotoxicity	74-76
<i>lpl</i> controlling lipoprotein lipase	High levels of triglycerides and high density lipoproteins→ susceptible to visceral leishmaniasis	65
<i>masp2</i>	Susceptibility to placental transmission of <i>Plasmodium</i> spp.	57
<i>mbl</i>	Increased severity of <i>falciparum</i> malaria	100, 104
<i>mbl2</i>	Susceptibility to placental transmission of <i>Plasmodium</i> spp.	57
	Resistance to visceral leishmaniasis	64
<i>mdr1a</i>	Susceptibility to cerebral malaria	51
	Ivermectin toxicity	132
<i>mmp2</i>	Susceptibility to Chagas' disease	79
Nitric acid encoding genes	Protection against severe malignant malaria	102, 103
<i>nramp1</i> in mice (codon 169)	Susceptibility to visceral leishmaniasis	59
<i>op/op</i> in mice	Susceptibility to visceral leishmaniasis	62
<i>p110δ</i> in mice	Resistance to visceral leishmaniasis	66
<i>p53</i>	No available codon	Susceptibility to cancer bladder in Egyptian urinary schistosomiasis
	codon 249	Susceptibility to hepatocellular carcinoma in intestinal schistosomiasis
Phospholipase A2 encoding gene (transgenic mutation)	Prevent invasion of <i>Plasmodium</i> ookinete	134
Pyruvate kinase (PK) (Gene encoding liver/erythrocyte-specific PK enzyme; PKLR)	Resistance to malaria	50
<i>slc11a1</i> in dogs (codon 145)	Susceptibility to visceral leishmaniasis	60
<i>slc7a2</i> in mice	Susceptibility to visceral leishmaniasis	61
<i>tep1</i> in mosquitos (transgenic mutation)	Decreased development of <i>Plasmodium</i> life cycle stages in mosquitos	133
Toll-like receptor 2 encoding gene	Protection against cerebral malaria	115
Toll-like receptor 4 encoding gene	Susceptibility to cutaneous leishmaniasis	69
Tumor necrosis factor-α encoding gene	Susceptibility to severe malignant malaria	111
Tumor suppressor genes (<i>p53, riz, cdc42, dffb&runx3</i>)	Susceptibility to cholangiocarcinoma in opisthorchiasis	93-95
<i>tyk2</i>	Susceptibility to toxoplasmosis	78

Gene abbreviations: *act1*: Gene encoding cardiac muscle alpha actin; *adam12*: Gene encoding placental expression enzymes; *ank-1*: Gene encoding ankyrin-1; *apobec3b*: Host gene involved in innate response; *apoL-1*: Gene controlling high-density lipoproteins, *bat1*: Gene regulating cytokines production; *ccr5*: Gene encoding chemokine (C-C motif) receptor 5; *cdkn2*: Tumor suppressor gene; *chit*: Gene controlling chitotriosidase; *fas*: Apoptosis gene; *flt4*: Gene encoding tyrosine kinase 4 receptor, *foxc2*: Gene encoding fork-head box protein C2 (Transcription factor); *ICAM-1*: Gene encoding intercellular adhesion molecule-1; *il2ra*: Gene controlling IL-2 pathway; *kras*: Tumor suppressor gene; *lpl* Gene controlling lipoprotein lipase; *masp2*: Gene encoding mannan-binding lectin serine peptidase 2; *mbl*: Gene encoding mannose-binding lectin protein; *mdr1a*: Gene encoding multi-drug resistance-1a; *mmp2*: Gene encoding placental expression enzymes; *nramp1*: Gene controlling innate immunity against intracellular parasites; *op/op*: Gene controlling macrophage colony stimulating factor, *p110δ*: Gene controlling hepatic stellate cells; *p53*: Tumor suppressor gene; *slc11a1*: Gene controlling parasite replication in the macrophage; *slc7a2*: Gene controlling arginine uptake by macrophages; *tep1*: Gene controlling immune response in mosquitos; *tyk2*: Gene encoding tyrosine kinase-2.

References are cited in “Gene mutations and parasitic diseases: Part I: Host gene mutations (PUJ 2016; 9: 65-79)”.

Summary of parasite gene mutations and effect on parasitic diseases

Gene		Effect on parasitic diseases	Reference
Single gene mutation			
<i>aqp2</i>		Melarsoprol/pentamidine resistance for <i>T. brucei</i>	181
		Antimonial drugs resistance for <i>Leishmania</i> spp.	193
<i>bat1</i>		Melarsoprol resistance for <i>T. gambiense</i>	177,179
		Diminazene aceturate resistance for <i>T. gambiense</i>	180
β-tubulin isotype-1 gene (Codons 167, 198)		Benzimidazole resistance for <i>A. caninum</i> in dogs	198
β-tubulin isotype-2 gene		Benzimidazole resistant for <i>E. granulosus</i> in human	199
<i>cg2</i>		Chloroquine resistance of <i>P. falciparum</i> <i>in vitro</i>	129
<i>crt</i>	Codon 76	Chloroquine resistance for <i>P. falciparum</i> in Brazil and several countries in Africa & Asia	96 & 100-107
		Increased severity of <i>falciparum</i> malaria	209
	Codons 72-76	Amodiaquine resistance <i>in vivo</i>	109
	Codons 76, 271, 326 & 371	Chloroquine resistance for <i>P. falciparum</i> in Yemen	111
<i>cyb</i>	No available codons	Antimycin A resistance for <i>Leishmania</i> spp.	189
		Atovaquone resistance for <i>Babesia gibsoni</i> in dogs	197
<i>cyt b</i>	No available codons	Atovaquone resistance for <i>P. berghei</i> <i>in vitro</i>	124
	Codon 268	Atovaquone-Pyrimethamine combined therapy resistance for <i>P. falciparum</i>	125-127
<i>dhfr</i>	No available codons	Atovaquone resistance for <i>T. gondii</i>	183
		Pyrimethamine resistance for <i>T. gondii</i>	184
	Codon 108 (serine→asparagine)	Pyrimethamine resistance for <i>P. falciparum</i> in Brazil, New Guinea & Tanzania	44-46
	Codon 108 (serine→threonine) + Codon 16 (alanine→valine)	Proguanil resistance for <i>P. falciparum</i> in Africa	43, 47
	Codons 51, 59 & 108	Pyrimethamine resistance for <i>P. falciparum</i> in India	71
	Codons 57, 58, & 117	Fansidar resistance for <i>P. vivax</i> isolated from widely separated countries from Asia and Africa	78
	Codons 58, 61 and 117	Pyrimethamine resistance for <i>P. vivax</i> in China	83
	Codons 36, 83 or 245	Different outcomes in the virulence of <i>T. gondii</i>	202
<i>dhps</i>	No available codons	Sulfonamide resistance for <i>T. gondii</i>	185
	Codons 436, 437 & 540	Sulphadoxine resistance for <i>P. falciparum</i> in India	71, 42
	Codons 540 & 588	Sulphadoxine resistance for <i>P. falciparum</i> in Indonesia	76
	Codons 57, 58, & 117	Sulphadoxine resistance for <i>P. vivax</i> isolated from malaria endemic countries	79
	Codon 382	Chloroquine resistance for <i>P. vivax</i> in Brazil	84
Ferredoxin gene		Metronidazole resistance in trichomoniasis	172
<i>fp2</i>		Artemisinin resistance for <i>P. falciparum</i>	151
<i>hrp2</i>		False diagnosis in <i>falciparum</i> malaria using rapid diagnostic tests	212-217
HSP70 encoding gene		Antimonial drugs resistance for <i>Leishmania</i> spp.	192
<i>kelch13</i>		Artemisinin resistance for <i>P. falciparum</i> in Bangladesh, China & Myanmar	155-159
<i>mdr</i>	Codon 86	Chloroquine, mefloquine & halofantrine resistance <i>in vitro</i>	85-89
		Increased sensitivity to Mefloquine & halofantrine in Gambia	97
	Codons 86 & 1246	Chloroquine resistance in India	90
<i>mrp2</i>		Quinolones (chloroquine, piperazine & mefloquine) <i>in vitro</i>	136

<i>ntr</i>	Benznidazole resistance for <i>T. cruzi</i>	201
Patatin-like protein encoding gene	Impaired replication of <i>T. gondii</i> in activated macrophages	204
<i>pgp</i>	Metronidazole resistance in amoebiasis, giardiasis & trichomoniasis	168-171
<i>pgpa</i>	Oxyanions resistance for <i>Leishmania</i> spp.	190
Proteophosphoglycan encoding gene	Impairment of <i>T. gondii</i> bradyzoite development	205
<i>ptr1</i>	Methotrexate resistance for <i>Leishmania</i> spp.	188
Regulators of chromosome condensation 1 (RCC1) (encoding gene)	Impairment of <i>T. gondii</i> growth and virulence	203
Transmembrane pellicle protein 1 (TPP1) encoding gene	Impairment of <i>T. gondii</i> virulence and invasion	206
Topoisomerase I gene	3,3'-Diindolylmethane (DIM) resistance for <i>Leishmania</i> spp.	191
Thymidine kinase (TK) encoding gene		
Uracil phosphoribosyl transferase (UPRT) encoding gene	Pyrimidine analogue 5-fluorouracil (5-FU) resistance for <i>L. infantum</i>	194
Uridine phosphorylase (UP) encoding gene		
Combined gene mutations		
	<i>crt</i> (Codon 76) + <i>mdr</i> (Codon 86 or 1246)	Amodiaquine resistance for <i>P. falciparum</i> in Burkina Faso, Nigeria & Colombia 65, 112, 113
	<i>crt</i> (Codon 72-76) + <i>mdr</i> (Codon 86)	Chloroquine & Amodiaquine resistance for <i>P. falciparum</i> in Angola 115
	<i>crt</i> (Codon 76) + <i>mdr</i> (Codon 86)	Chloroquine resistance for <i>P. falciparum</i> in India 116-118
	No available codons	Chloroquine resistance for <i>P. vivax</i> in Ethiopia 123
	<i>crt</i> (Codon 76) + <i>mdr1</i> (Codons 86 & 184)	Increased the severity of <i>falciparum</i> malaria 207
<i>crt</i> <i>nhe</i>	<i>crt</i> (Codon 76) <i>nhe</i> (No available codon)	Reduced quinine susceptibility for <i>P. falciparum</i> in Kenya, China & Viet Nam 131-133
	<i>dhfr</i> (Codons 51 & 108) + <i>dhps</i> (Codons 437 & 581)	Fansidar resistance for <i>P. falciparum</i> in Uganda and Venezuela 54, 55
<i>dhfr</i> <i>dhps</i>	<i>dhfr</i> (Codons 51, 59 & 108) + <i>dhps</i> (Codons 437 & 581)	Fansidar resistance for <i>P. falciparum</i> in Kenya, Cameroon, Nigeria, Ethiopia, Ghana, Sri Lanka & Tanzania 56-62
	<i>dhfr</i> (Codons 59 & 108) + <i>dhps</i> (Codons 436 or 437)	Fansidar resistance for <i>P. falciparum</i> in Iran 70,79
<i>dhfr</i> <i>mdr2</i>	<i>dhfr</i> (Codons 51 & 58 or 108) <i>mdr2</i> (Codon 423)	Pyrimethamine resistance for <i>P. falciparum</i> in Thailand 121

Gene abbreviations: *aqp2*: Gene controlling aquaglyceroporin transporter; *bat1*: Gene regulating cytokines production; *cg2*: A candidate gene for chloroquine resistance; *crt*: Chloroquine resistance transporter gene; *cyb*: Gene encoding mitochondrial apo-cytochrome b; *cyt b*: Gene encoding cytochrome b; *dhfr*: Dihydrofolate reductase gene; *dhps*: Dihydropteroate synthase gene; *fp2*: Gene encoding cysteine protease falcipain-2; *hrp2*: Gene encoding histidine-rich protein 2; *HSP*: Heat shock protein; *kelch13*: Gene encoding Kelch-domain 13; *mdr*: Multi-drug resistance-1a gene; *mrp2*: Multidrug resistance protein-2 gene; *nhe*: sodium hydrogen exchanger gene; *ntr*: A mitochondrial gene; *pgp*: P-glycoprotein-like gene; *pgpa* P-glycoprotein gene; *ptr1*: Gene encoding pteridine reductase 1.

References are cited in "Gene mutations and parasitic diseases: Part II: Parasite gene mutations (PUJ 2017; 10: 4-22)".