

May 2009

Malaria

- Genotyping of drug resistance markers now available

To Health Care Providers:

A DNA sequencing method is now available at the Public Health Laboratory in Toronto for testing of malaria patients with *P. falciparum* infection. The method allows rapid genotyping of markers of drug resistance to commonly used anti-malarial therapies such as chloroquine, mefloquine, pyrimethamine-sulfadoxine, and malarone (atovaquone-proguanil).

This test will only be performed following discussion with the Medical Microbiologist, for cases where the clinician is concerned that the patient is not responding to standard anti-malarial therapy.

Genotyping is performed on the EDTA blood (purple top) specimen received as part of the routine malaria specimen submission.

The turn-around time is typically 48 hours. Results will be reported as “Research Purposes Only” as the genotypes have not been clinically validated and only provide an association with resistance or susceptibility at this time.

Discussion with the Medical Microbiologist is encouraged for interpretation guidance.

Below is a table that assists in the interpretation of mutations at specific codons. Each amino acid at a given codon position is associated with either resistance or susceptibility for a given drug. For example, in *P. falciparum* (Dhps codon 436 Serine) is associated with susceptibility to pyrimethamine-sulfadoxine.

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- **Genotyping of drug resistance markers now available (Continued)**

Interpretative Guide for Mutations Present in Genes:

Gene	Codon	Mutation		Malaria Drug Implicated
		Wild Type (Drug Susceptible)	Mutant Type (Drug Resistance)	
<i>Plasmodium falciparum</i> dihydropteroate synthetase (Dhps)	Codon 436	Serine	Alanine or Phenylalanine	Pyrimethamine-sulfadoxine
	Codon 437	Alanine	Glycine	
	Codon 540	Lysine	Glutamic acid	
	Codon 581	Alanine	Glycine	
	Codon 613	Alanine	Threonine or Serine	
<i>Plasmodium falciparum</i> chloroquine resistance transporter (Pfcr1)	Codon 72	Cysteine	Serine	Chloroquine
	Codon 74	Methionine	Isoleucine	
	Codon 75	Asparagine	Glutamic acid	
	Codon 76	Lysine	Threonine	
<i>Plasmodium falciparum</i> Cytochrome b (Cyt b)	Codon 268	Tyrosine	Serine or Asparagine	Atovaquone-proguanil
<i>Plasmodium falciparum</i> bifunctional dihydrofolate reductase-thymidylate synthase (Dhfr)	Codon 50	Cysteine	Arginine	Pyrimethamine-sulfadoxine
	Codon 51	Asparagine	Isoleucine	
	Codon 59	Cysteine	Arginine	
	Codon 108	Serine	Asparagine	
	Codon 164	Isoleucine	Leucine	
<i>Plasmodium falciparum</i> multi-drug resistance protein (Pfmdr)	Codon 86	Asparagine	Tyrosine	Any drug
	Codon 184	Tyrosine	Phenylalanine	
	Codon 1034	Serine	Cysteine	
	Codon 1042	Asparagine	Aspartic acid	
	Codon 1246	Aspartic acid	Tyrosine	

For Further Information:

- Dr. Dylan Pillai, Medical Microbiologist at **416-235-6548**
- Parasitology Laboratory at **416-235-5722**
- Public Health Laboratory Helpline **1-800-640-7221**
- For the Specimen Collection Guide and previous Lababstracts refer to the Ontario Agency for Health Protection and Promotion website: www.oahpp.ca