

CYP2D6 and IL-6 c-174G variants in schistosomiasis haematobia

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AIM

To study the polymorphic variants in CYP2D6 and the C-174G promoter polymorphism of the IL-6 gene on *S. haematobium* infected patients from an endemic area of Guinea Bissau.

BACKGROUND

- Our group has shown that schistosome egg associated catechol estrogens induce tumor-like phenotypes in urothelial cells. These estrogen metabolites might also be the cause of schistosomiasis associated infertility (Botelho et al, Trends in Parasitol, 2015).
- The cytochrome P450 (CYP) genes are oxygenases involved in estrogen biosynthesis and metabolism, generation of DNA damaging procarcinogens, and response to anti-estrogen therapies (Blackburn et al, Cancer Causes and Control, 2015).
- IL6 Interleukin-6 (IL-6) is a pleiotropic cytokine expressed in many tissues. This cytokine is largely expressed in female urogenital tract as well as reproduction organs. Very high or very low levels of IL-6 are associated with estrogen metabolism imbalance (Prins et al, J Reprod Immunol, 2012).

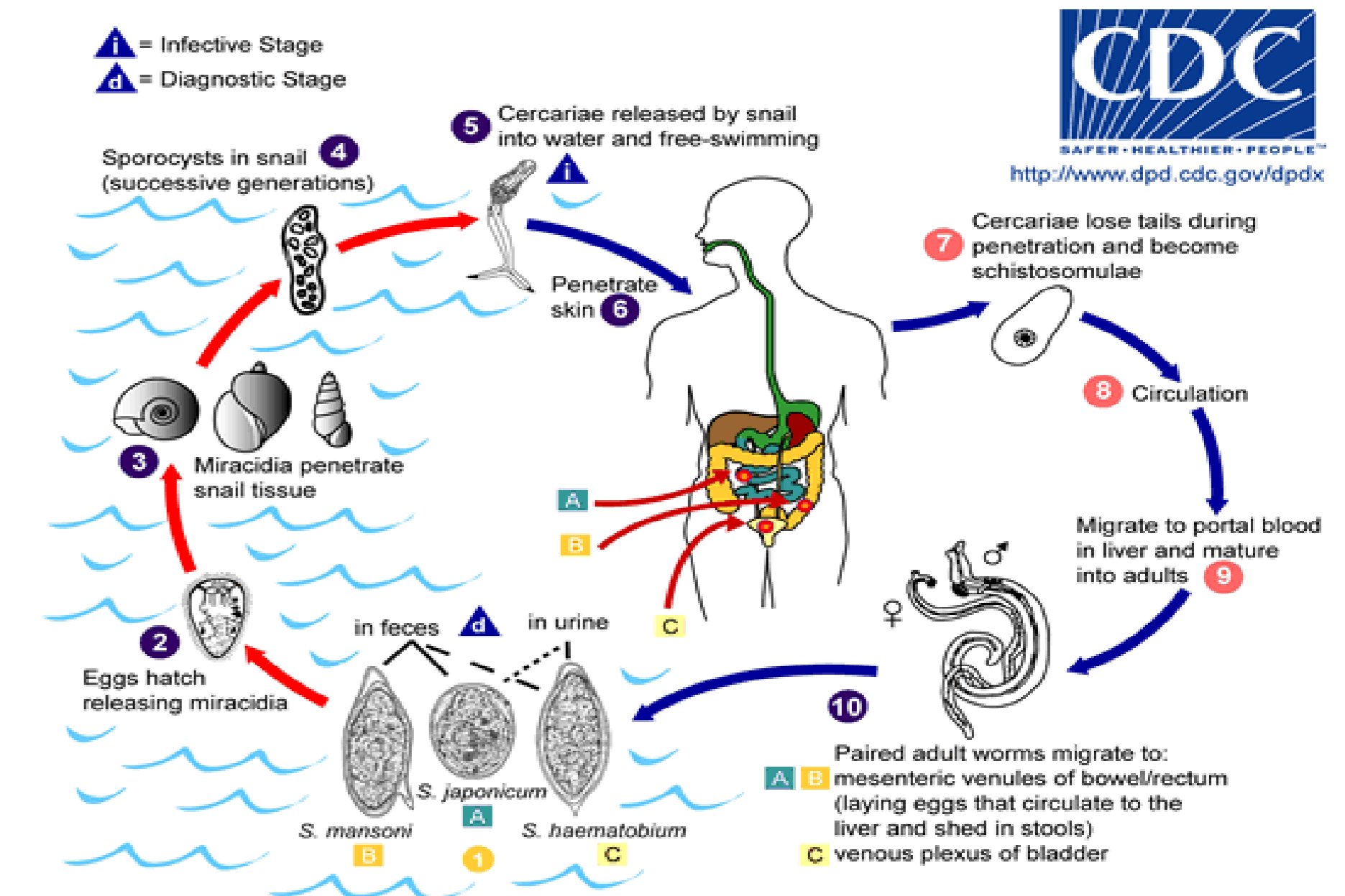


Fig. 1: *Schistosoma* spp. life cycle.

METHODOLOGICAL STRATEGY

1. 42 infected patients were targeted in this study.
2. DNA was extracted from urine sediments
3. LightMix Kit for the detection of CYP 2D6 alleles *3, *4 and *5/*5 and LightMix Kit for the detection of IL 6 G-174C were used with LightCycler 2.0 Instrument.

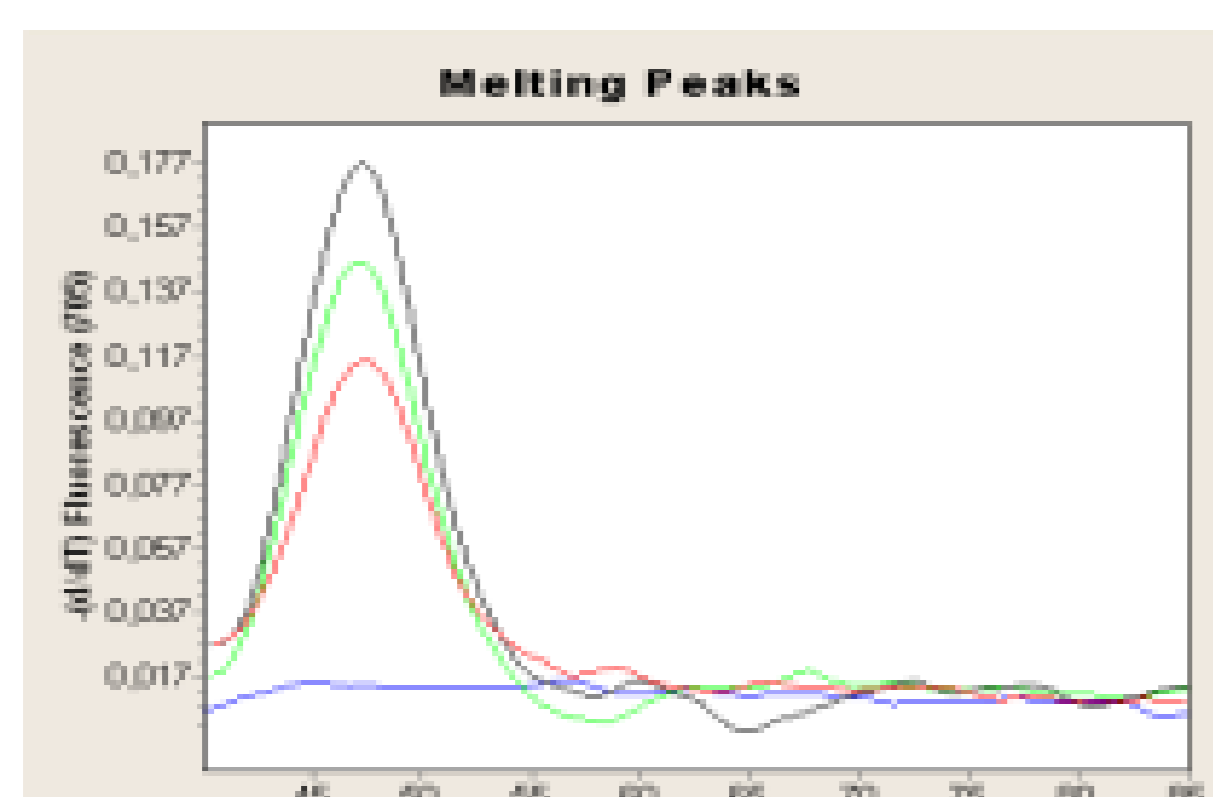


Fig.3: Control samples melting peak for CYP2D6*5 deletion

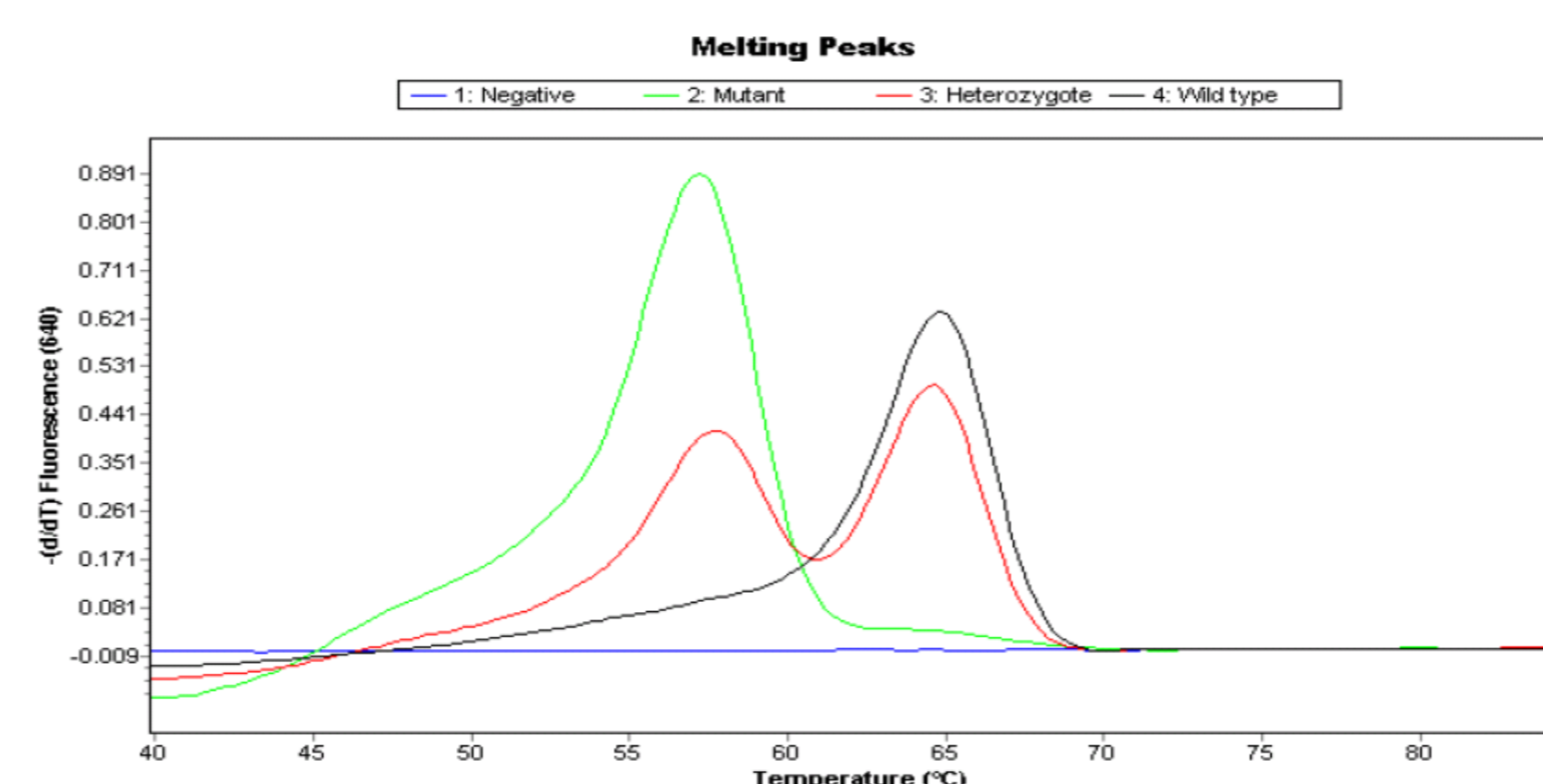


Fig. 4: Control sample melting peak for IL6 -174C mutant

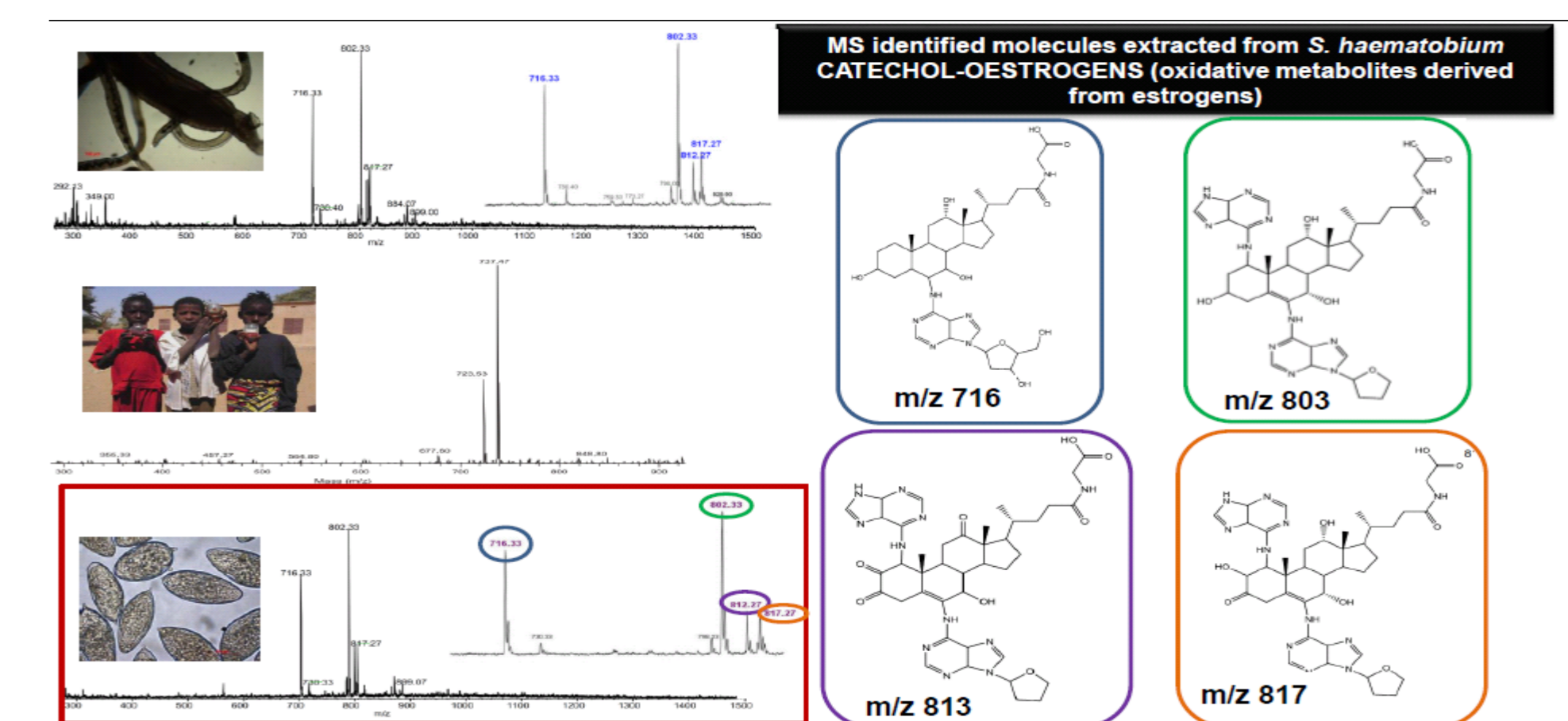


Fig. 2: Catechol-estrogens produced by *S. haematobium*.

RESULTS

1. We found that 25% of schistosomiasis haematobia infected patients are carriers of the inactivated allele CYP2D6*5 which is characterized by a deletion of the entire CYP2D6 gene. The frequency of this allele in a healthy population is 5% (Gaedigk et al, 1991).

2. In our study 6.25% of patients infected with *S. haematobium* have the IL6 -174C mutant where this variant is associated with lower IL6 secretion. The frequency of this variant in a healthy population is 0.4% (Fishman et al, J Clin Invest, 1998).

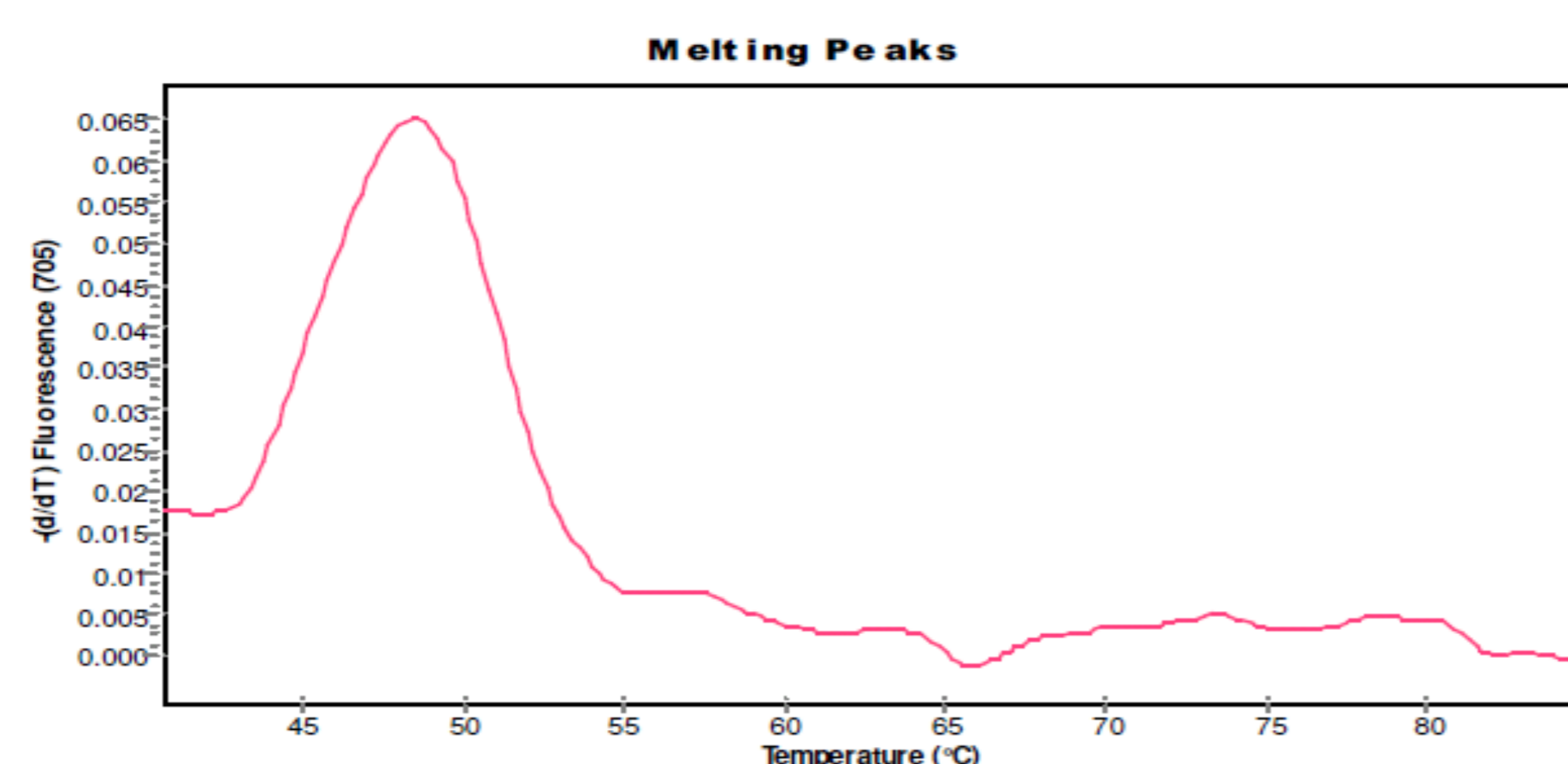


Fig. 5: Patient sample melting peak for CYP2D6*5 deletion.

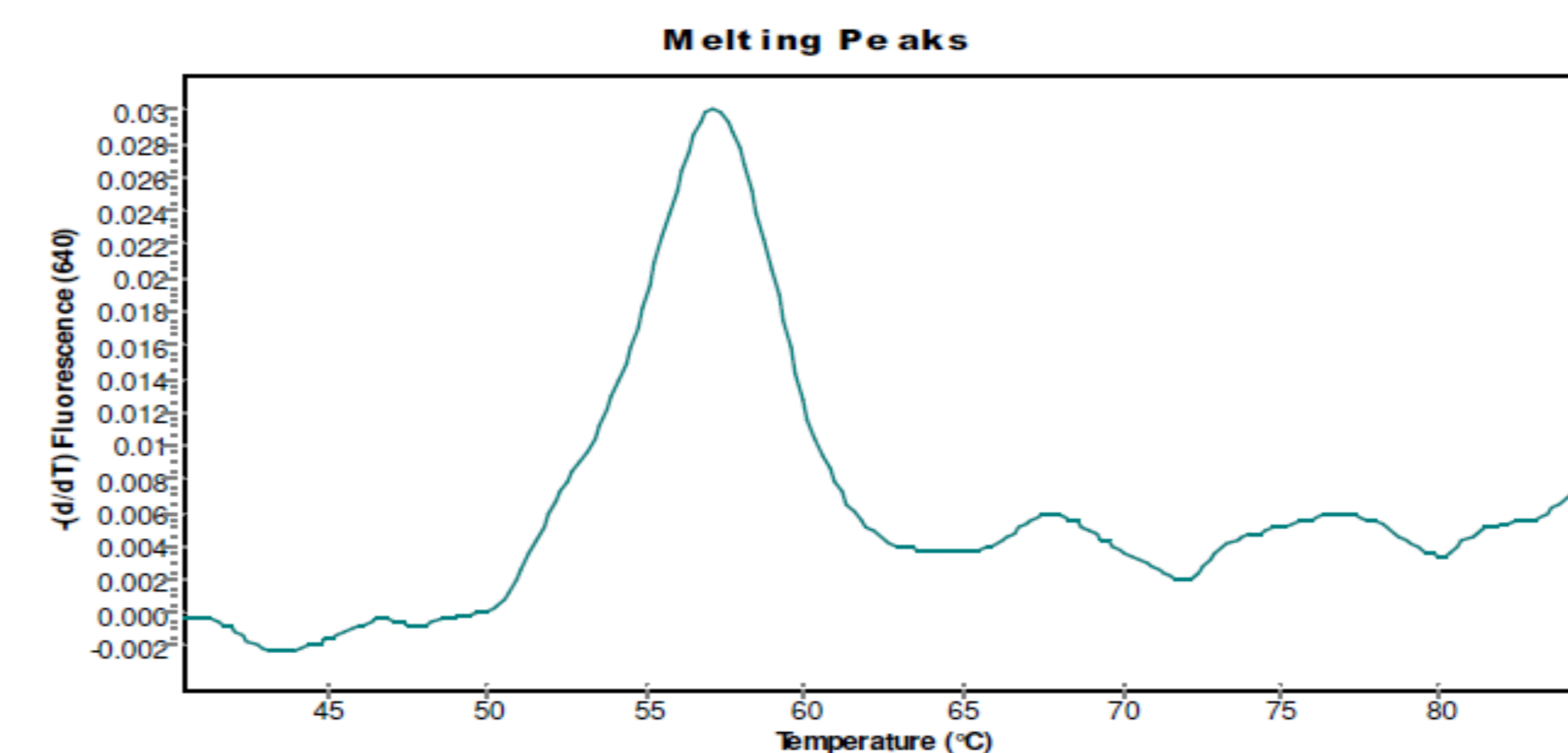


Fig. 6: Patient sample melting peak for IL6 -174C mutant.

CONCLUSIONS

1. This survey provides for the first time data on the frequency of inactivating alleles of CYP2D6 and IL6 G-174C polymorphisms in *S. haematobium* infected patients.
2. Allele CYP2D6*5 and IL6 -174C variant are associated with schistosomiasis haematobia infection and could explain schistosomiasis associated cancer and infertility.