

# Genetic variants of CYP2C9 and IL-6 on female infertility

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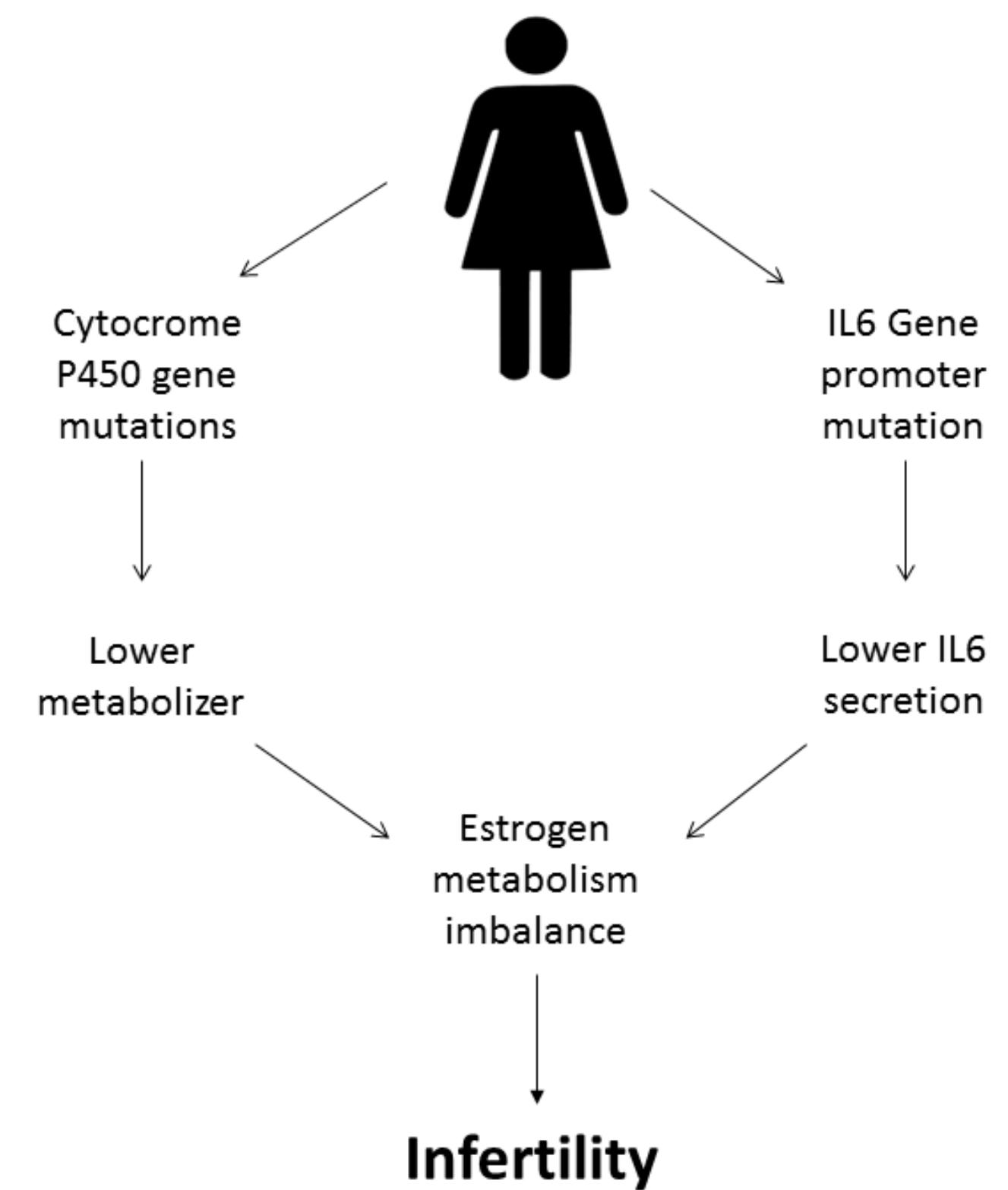
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## AIM

To study the polymorphic variants in CYP2C9\*2\*3 and the C-174G promoter polymorphism of the IL-6 gene on Infertile Women.

## BACKGROUND

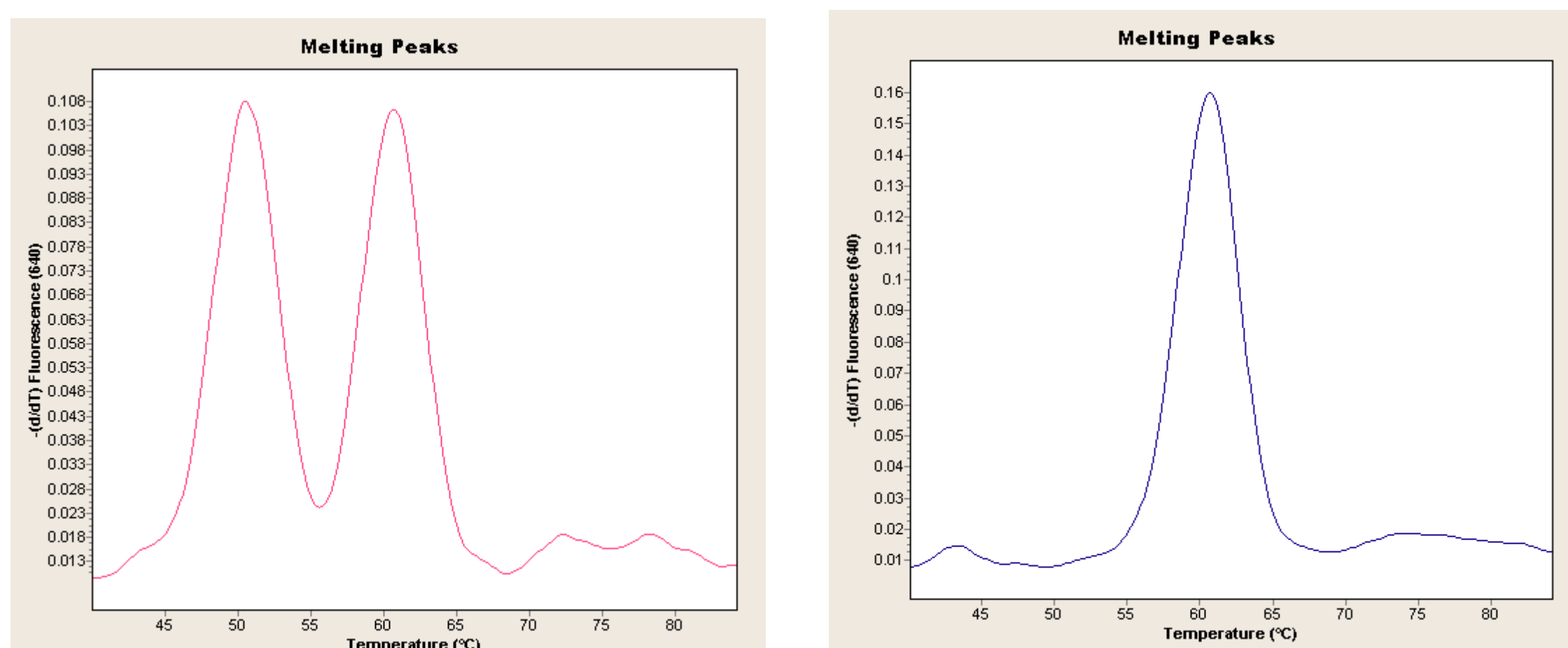
- Infertility affects 15-20% of couples worldwide. Within the past decades, there has been a steady rise in the treatment of female infertility with several drugs (Udell et al, CMAJ, 2017).
- The cytochrome P450 (CYP) genes are oxygenases involved in estrogen biosynthesis and metabolism, generation of 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).



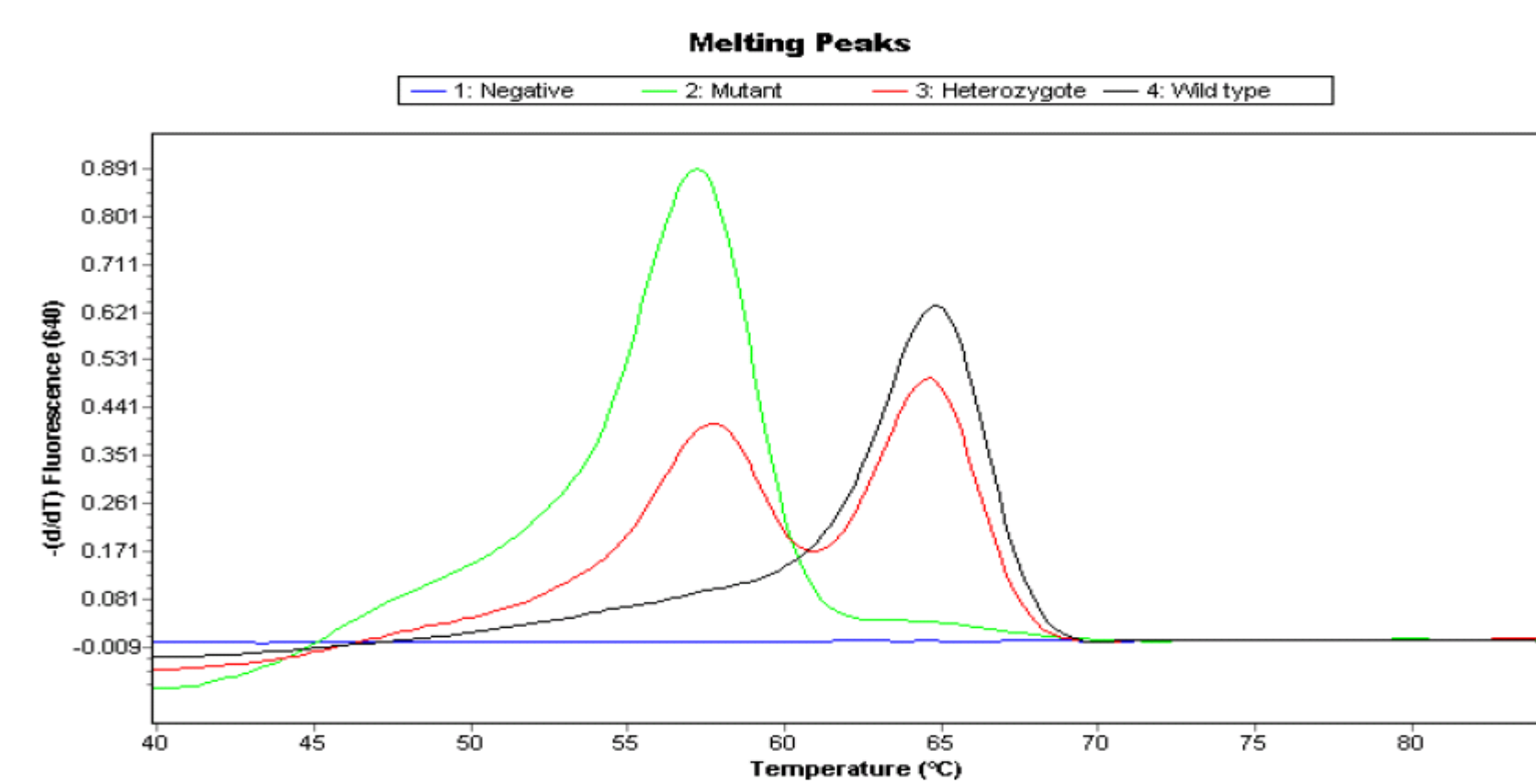
## METHODOLOGICAL STRATEGY

1. 10 infertile patients were targeted in this study.
2. DNA was extracted from urine sediments
3. LightMix Kit for the detection of CYP 2C9 alleles \*2, and \*3 and LightMix Kit for the detection of IL6 G-174C were used with LightCycler 2.0 Instrument.

*Fig. 1: Estrogen metabolism imbalance in infertility*



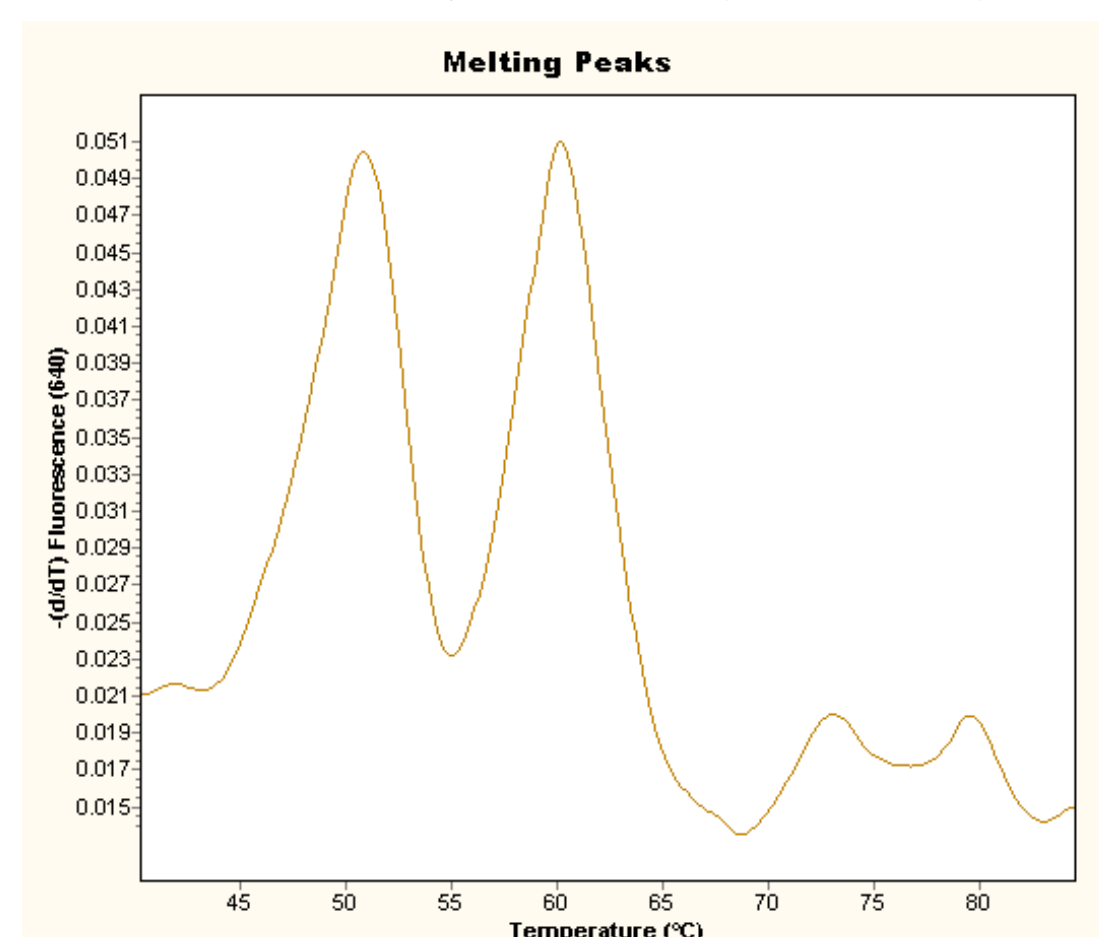
*Fig.2: Control samples melting peak for CYP2C9\*3 (left panel heterozygote; right panel mutant)*



*Fig. 3: Control sample melting peak for IL6 G-174C*

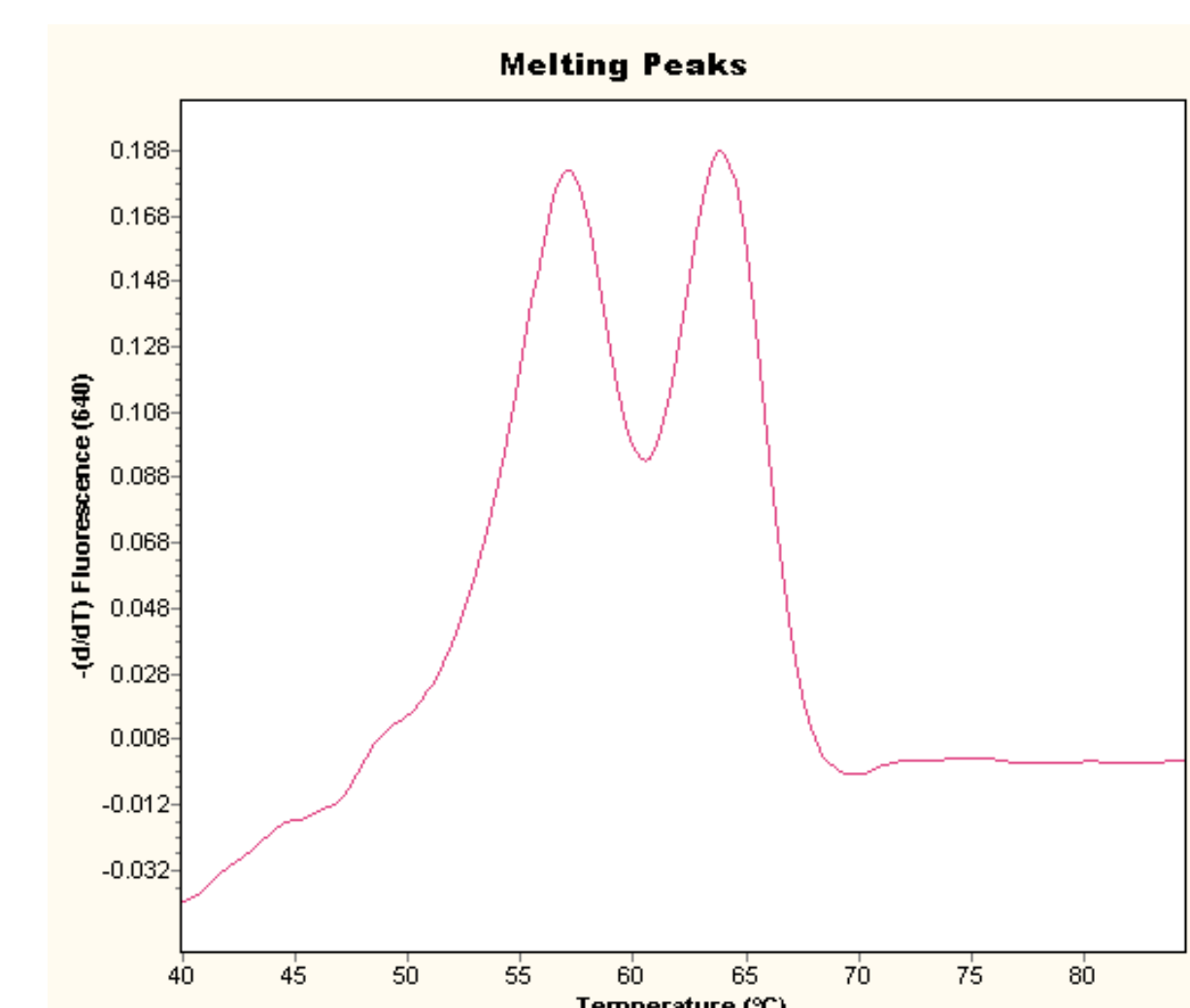
## RESULTS

1. Some samples did not amplified. To the CYP2C9\*2 allele we got amplification in 8 samples. All of them were WildType genotype (80%) Vs 77.6% in a control population. To the CYP2C9\*3 we got amplification in 5 samples. 60% were wildtype genotype (AA), 20% were heterozygotic (AC) and 20% were homozygous for the mutation (CC). The frequency of AC and CC genotypes in a control population are 12.1% and 0.45% respectively (Vasilyev, et al, Res Pharm Sci, 2016).



*Fig. 4: Heterozygotic patient sample melting peak for CYP2C9\*3*

2. Some samples did not amplified. IL6 - CC genotype was not found, IL6 - 174C/G genotype that is known to be associated with lower IL6 secretion was 80%. The frequency of GC genotype in a Caucasian control population is 44% (Fishman et al, J Clin Invest, 1998).



*Fig. 5: Heterozygotic patient sample melting peak for IL6 -174C/G*

## CONCLUSIONS

- CYP2C9\*3 C mutant and IL6-174C/G heterozygote genotypes may represent potential biomarkers for female infertility.
- On the other hand, they may have prognostic significance, namely regarding the metabolism of drugs used in infertility treatments, something which will need to be addressed in further studies.
- Their role in female infertility should be clarified using a larger group of infertile women.