

The study of GSTP1 Ile105Val polymorphism among normal, cancer and cancer stem cells, in a wide spectrum of human tumors

Die Forschung der GSTP1 Ile105Val Polymorphismus unter normalen, Krebs und Krebs-stammzellen in einem breiten Spektrum von menschlichen Tumoren

Apostolou P.¹, Toloudi M.¹, Chatziioannou M.¹, Ioannou E.¹, Kourtidou E.¹, Vlachou I.¹, Papasotiriou I.¹

¹ Research Genetic Cancer Centre Ltd. (R.G.C.C. Ltd). 115 M.Alexandrou str, 53070 Filotas, Florina, Greece

Introduction: The Glutathione S-transferase P enzyme (GSTP1) is involved in phase-2 detoxification. It catalyzes the conjugation of hydrophobic compounds with glutathione. Although there are many polymorphisms of this protein, the Ile105Val may have the maximum magnitude. This single nucleotide polymorphism (SNP) is correlated not only with xenobiotic metabolism, but it is said that it is also implicated in susceptibility to cancer and nervous system diseases. The present study aims to examine the above polymorphism among breast, colon and lung cancer, including normal, cancer and cancer stem cells populations.

Results: The non-cancer sample was homozygote for allele 2 (normal-VIC). Among cancer cells, MCF-7 and COLO699N cells were heterozygote while HCT-116 cells were homozygote for allele 1 (mutant-FAM). Among cancer stem cells there was no detection for both probes. The ERCC1 gene expression levels were higher for HCT-116 cell line and CSCs but lower for the rest cell lines (data not shown).

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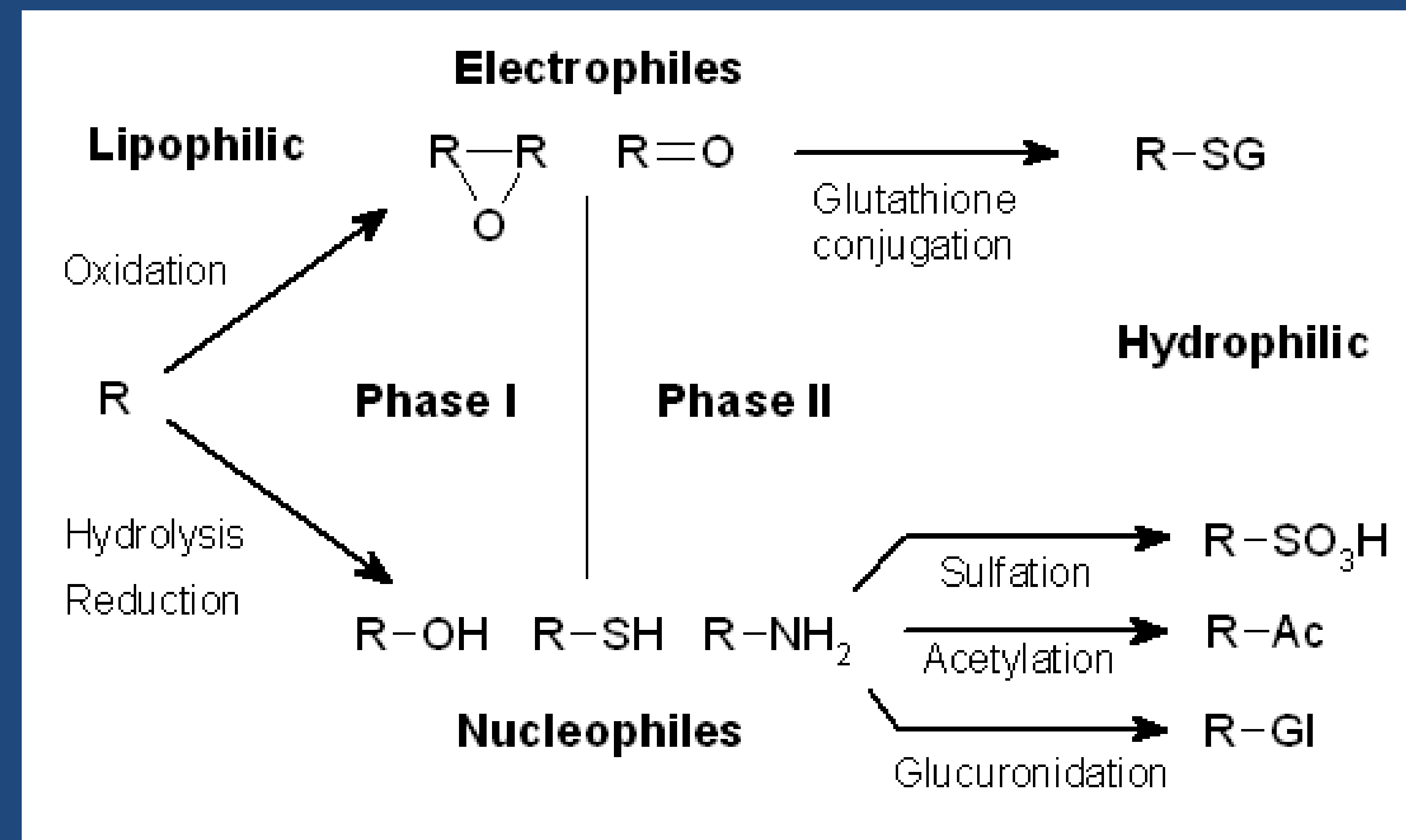


Figure 1 : Xenobiotic Metabolism (Wikipedia)

Materials & Methods: Genomic DNA was extracted from human established cancer stem cell lines, representing breast, colon and lung cancer, provided by CelProgen and the MCF-7 (breast), HCT-116 (colon) and COLO699N (lung) cancer cell lines, provided by ECACC. The allelic discrimination was evaluated by performing qPCR assays by using Custom TaqMan® probes for each allele. Non-cancer genomic DNA was used as control. All experiments were performed in triplicates. The resistance to platinum compounds was tested by extracting RNA and by performing RT-qPCR for ERCC1 gene in cancer cell lines.

Selected References:

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Conclusion: The polymorphism Ile105Val of GSTP1 seems to play an important role in cancer susceptibility and response to drugs. The different alleles among cancer cell lines explains the different sensitivity of each type in platinum compounds and taxanes, which was confirmed by qPCR assays. It is noteworthy that none allele was detected for cancer stem cells, even at DNA level. The lack of phase 2 detoxification mechanisms, could be considered one of the reasons for drug resistance of cancer stem cells.

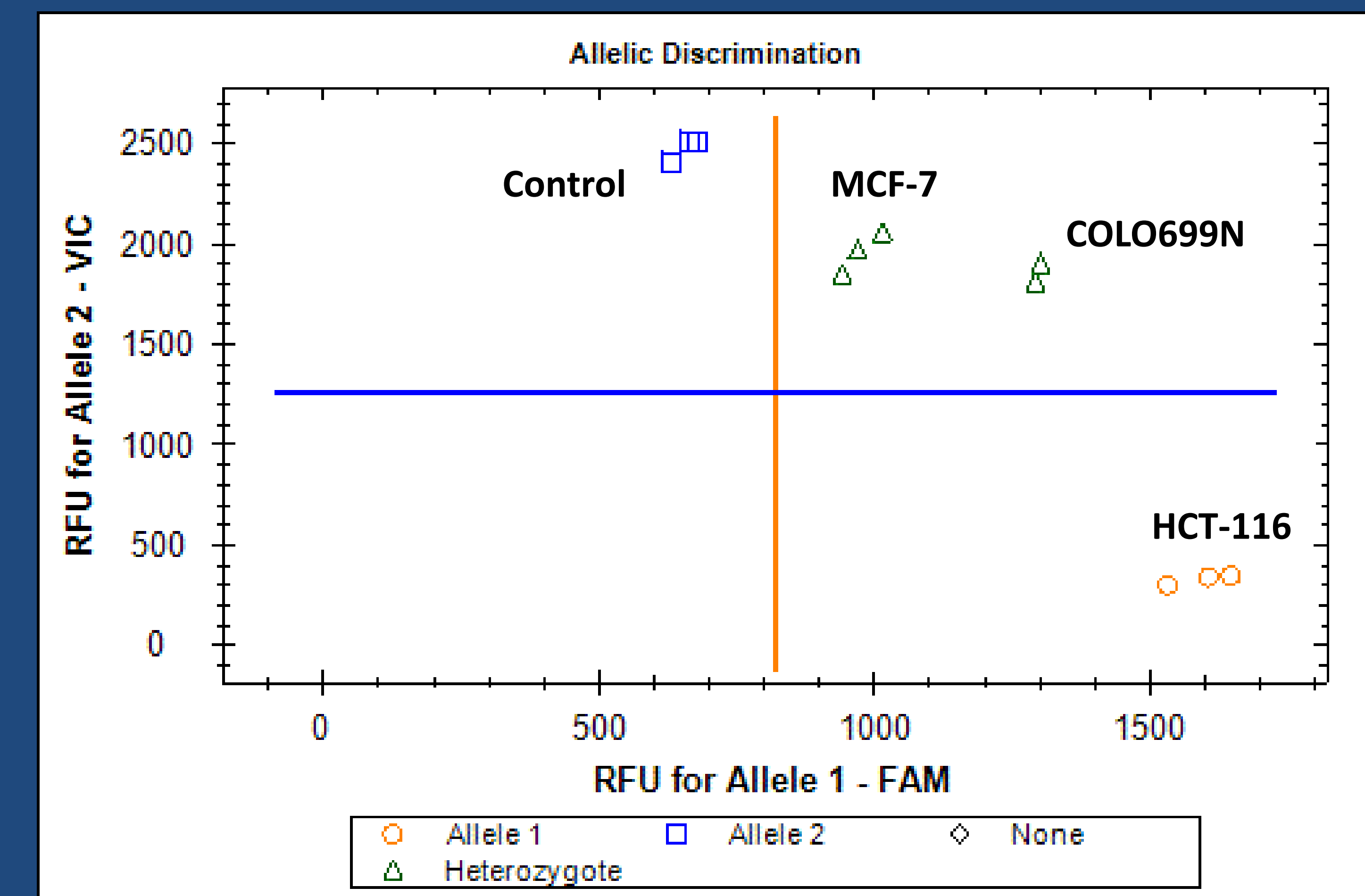


Figure 2 : Allelic discrimination for Ile105Val (rs1695) polymorphism

Disclosure of Potential Conflicts of Interest

None of the authors of the above study has declared any conflict of interest

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