Impact of genetic variations of Polymerase γ gene (*POLG*) on breast cancer patients

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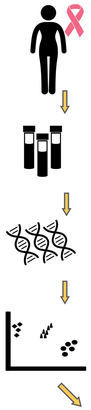
Background

- Breast cancer is the leading cause of cancer-related deaths among women.
- Variations in mitochondrial DNA (mtDNA) and nuclear DNA, coding for mitochondrial proteins or regulatory molecules, are seldom under consideration to be related to cancer.
- Polymerase gamma is important for mtDNA repair.
- It is also the only polymerase involved in mtDNA replication.

Aim

- Aassess POLG gene variations rs3087374, rs2307441, rs2072267, rs976072 and associations with tumor phenotype, disease outcome for 234 breast cancer patients.

Methods



- 234 breast cancer patients
- Blood samples
- DNA purification
- SNP analysis
- Statistical analysis

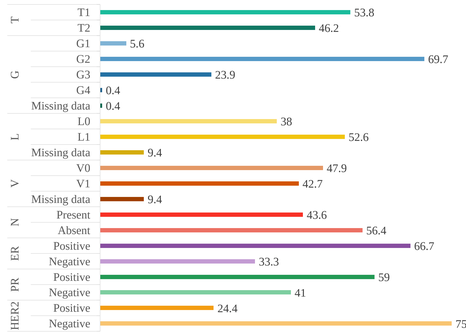
- Clinical data

Patients' clinical data collected and updated from patient's case history

Results

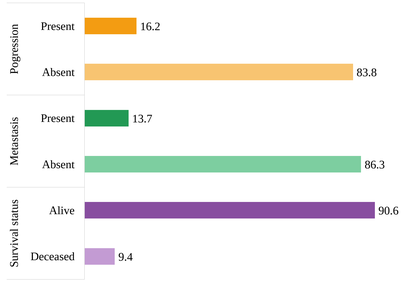
- Patients with rs2307441 TT and CT genotypes had a lower probability for tumor vascular invasion than CC genotype (OR=0.075; 95% CI 0.017-0.323; p=0.001)
- The carriers of the T allele in rs2307441 had a lower probability of tumor vascular invasion than non-carriers (OR=0.064; 95% CI 0.015-0.273; p=0.000)
- Patients with rs2072267 AG genotype were predisposed for disease progression compared with GG genotype (OR=3.386; 95% CI 1.262-9.086; p=0.015)
- The carriers of the A allele of rs2072267 had a higher probability of disease progression that the non-carriers (OR=3.197; 95% CI 1.237-8.261; p=0.016)

Tumor pathomorphological characteristics



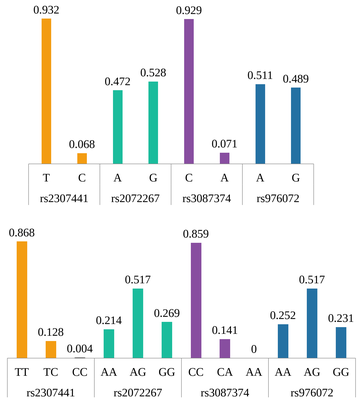
T - Pathological tumor size; G - Tumor differentiation grade; L - Lymphatic invasion; V - Vascular invasion; N - Lymph node involvement; ER - Estrogen receptors; PR - Progestin receptors; HER2 - Human epidermal growth factor receptor 2.

Clinical disease characteristics

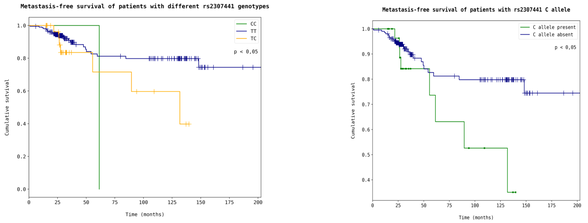


- Most of the patients presented without progression or metastasis and with deaths for only 9.4% of all patients.

POLG genotypes and alleles distribution



Survival analysis



- Patients with rs2307441 CT genotype presented with a tendency of shorter MFS when compared to the patients with TT genotype (p=0.051)
- The C allele holders had approximately 2.5 higher probability of shorter MFS than those without C allele (HR = 2.495; CI 1.114-5.587; p=0.026)

Conclusions

Our data indicate that nuclear DNA variations in POLG (rs2307441, rs2072267) gene play an important role for in breast cancer patients

Key words

POLG, SNV, breast cancer, tumor phenotype, outcome