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# Association of *CASP3* Genetic Polymorphisms rs1049216, rs2705897 and rs4647603 with the Risk of Prostate Cancer in Galicia (NW Spain).

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**Abstract**

Malfunction of apoptosis plays a key role in carcinogenesis. Previous studies have reported that polymorphisms in caspase genes could lead to poor apoptotic signaling, thus facilitating the onset of several human cancers. The aim of this study was to evaluate the association between three polymorphisms (rs1049216, rs2705897 and rs4647603) of the *CASP3* gene and the risk of prostate cancer (PCa) in Galicia (NW Spain).The relationship between these single nucleotide polymorphisms (SNPs) and PCa in European populations has yet to be studied. To test this hypothesis, we carried out a case-control study on a total of 243 patients with PCa and 191 healthy individuals, genotyping all polymorphisms using the matrix assisted laser desorption ionization time-of-flight (MALDI-TOF) method. Overall, none of the polymorphisms were clearly associated with the risk of PCa. Nevertheless, the results drawn from this study suggest that genetic variability in the *CASP3* gene, in combination with lifestyle and environmental factors may influence the predisposition to develop PCa in the Galician population. Specifically, the results of study seem to hint at a higher risk of PCa in smokers of up to 20 pack-years (PY) and carriers of both the *CASP3*-rs1049216 GG genotype and the G allele (OR = 3.61, p = 0.044; OR = 1.71; p = 0.018). In addition, the GG and AG genotypes showed increased predisposition to PCa in overweight individuals (OR = 4.43, p = 0.040; OR = 2.00; p = 0.022). Finally, the *CASP3*-rs4647603 CT genotype and T allele were associated with a higher susceptibility to PCa in obese individuals ($OR_{CT/TT}$ = 4.30, p = 0.003; $OR_{T/C}$ = 3.58, p= 0.004). Further replication studies in other populations are required to assess these findings.

**Keywords:** *CASP3*· prostate cancer· polymorphism · haplotype · risk factors.

**Abbreviations:** PCa, prostate cancer; BMI, body mass index; PY, pack-years; OR, odds ratio; CI, confidence interval; SNP, single nucleotide polymorphism; PARP, poly-ADP ribose polymerase; CASPs, caspases; MALDI-TOF, matrix assisted laser desorption/ionization-time of flight; LD, linkage disequilibrium; LFT, lowest frequency threshold; SAP, shrimp alkaline phosphatase; SBE, single base extension.

## 1. Introduction

Prostate cancer (PCa) is the second most frequently diagnosed cancer among men worldwide (31.1 cases/100,000 males) and the fifth leading cause of death by cancer (7.8 deaths/100,000 males). In western countries, PCa is the second most prevalent form of cancer and its incidence rates vary by over 7-fold throughout different European regions, being higher in northern/western countries and lower in southern/eastern ones (Ferlay et al., 2015; Bray et al., 2013). The incidence of PCa in Galicia (northwestern Spain) is one of the highest in Europe, with 143 cases/100,000 males (Sousa-Escandón et al., 2006).

As in most human cancers, PCa is a complex disease resulting from the interaction of both environmental and genetic factors. Well-known risk factors for PCa are old age, a family history of the disease, and belonging to certain population groups. Potential risk factors have been identified as lifestyle