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R462Q Mutation in Prostate Cancer Specimens

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Dear Editor,

We read with interest the article of Seidabadi et al. titled "R462Q Mutation in Prostate Cancer Specimens" in the previous issue of "Gene, Cell and Tissue" (1). In this study, the authors reported that the genetic variant R426Q within the RNASEL gene is not associated with the risk of prostate cancer in a population from Iran. Prostate cancer is a major cause of morbidity and mortality in Iran, yet there are few studies examining risk factors specific to the Iranian context (2). Therefore, the present study is of particular interest. A family history of prostate cancer is beside age and race the only established risk factor of prostate cancer pointing to the strong genetic background of the disease (3). RNase L, expressed by the RNASEL gene, plays a central role in innate immunity, apoptosis, cell growth and differentiation by regulating cellular RNA stability and expression. Default in its activity leads to increased susceptibility to virus infections and to tumour development. Genetics studies suggest that mutations in RNASEL predispose men to an increased incidence of prostate cancer, which in some cases reflect more aggressive disease and/or decreased age of onset compared with non-RNASEL linked cases (4).

Several studies have investigated the association between RNASEL R426Q polymorphism and prostate cancer susceptibility providing, however, inconclusive results so far. Most studies could not confirm a significant association between R426Q and prostate cancer risk (5). Notably, prostate cancer risk varies between ethnicities, probably due to genetic and lifestyle differences (6). Therefore, impact of the R426Q polymorphism on prostate cancer risk may differ between different populations also. Indeed, a significant association between R426Q and prostate cancer has been reported mainly in Africans, but not in Europeans and East-Asians (7). The present report of Seidabadi et al. is the first study investigating the association between R426Q polymorphism and prostate cancer risk in an Iranian population. Therefore, this study makes a valuable contribution to the evaluation of genetic risk factors of prostate cancer in this population. Despite the assumed role of RNase L in the manifestation of prostate cancer (4, 8), results of the study suggest that RNASEL R426Q polymorphism is not a prostate cancer risk factor of clinical relevance. These findings are in line with current collective knowledge about R426Q and prostate cancer risk in other populations (5, 7). However, association between R426Q and clinical parameters of prostate cancer patients is less investigated and the study of Seidabadi et al. would have benefit from correlating clinical parameters (e.g. prostate-specific antigen levels, Gleason score, etc.) with the genetic variant, particularly since clinical data were available from included subjects. It should be further noted, that compared to other genetic-epidemiological studies in the field of cancer research, number of included subjects appears small, particularly with regard to reported null-association between R426Q and prostate cancer risk. Therefore, it cannot be excluded that association between R426Q and prostate cancer risk may have reached statistical significance with a larger population. Nethertheless, reporting negative results may prevent future meta-analysis from publication-bias and, thus, contributes to the determination of the true association between genetic factors and disease development. Future studies are warranted to further define the pathologic role of the RNASEL R426Q variant in prostate cancer development, especially in populations of the middle-east.

Authors' Contributions

Axel Muendlein drafted the manuscript; Alois H. Lang critically revised the manuscript.

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