Analysis of mutations affecting the KLK15 gene in prostate cancer

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Abstract

Prostate cancer is the most common form of non-skin cancer affecting men between the ages 45 to 60 years old. Diagnosed as the 4th most common cancer worldwide, this disease affects millions of men around the world, especially patients from developed regions. It has a low mortality rate and an ever-increasing rate of being cured if caught in the early to mid-range phases of the disease. This type of cancer is characterised by an aberrant and uncontrolled growth of abnormal cells in the prostate gland, which can be detected by blood tests, MRI, digital screening and prostate biopsy. One of the leading factors which has been disputed as causative of prostate cancer is the genetic aspect. These alterations include, but are not limited to mutations affecting the PTEN and Tp53 gene, fusion of the TMPRSS2 gene with the ETS genes, HOXB gene and lately as a novel indicator of prostate cancer, the KLK15 gene. Human kallikreins (KLK) proteins serve for a variety of functions in the human body ranging from immune responses, formation of the teeth enamel, peeling of skin and liquefying the semen. Higher expression of this gene could lead to the occurrence of pathological conditions of the aforementioned functions. Being a novel predictor gene, our focus was to elucidate the point mutations affecting this gene and their potential damage resulting in cancer. Twenty-five-point mutations were analysed via in silico methods to understand and elucidate the role these mutations have in the KLK15 gene in the prostate. To assess the role of these mutations and their possibility of being involved in the disease, 4 predicting algorithms were used (SIFT, PolyPhen-2, FATHMM and SNPs&GO). To predict the secondary structure, surface accessibility and protein stability we used NetSurfP3.0 and I-Mutant 2.0. Four mutations were found to be damaging to the KLK15 gene, I164M, D231Y, C242F and Y244S, with high deleterious effect causing significant structural and functional changes in the protein. These predictions help identify novel and potential point mutations, their uncharacterised function in the gene and possibility to be targeted by pharmaceutical drugs to counteract the effects of prostate cancer.

References

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