Abstract form

Title: Impact of Point Mutations in the Androgen Receptor identified in clinical samples of Prostate Cancer.

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Abstract

The androgen receptor (AR) is a hormone-activated transcription factor that regulates genes involved in the cell cycle of prostate cells. Alterations in AR activity have been reported in clinical prostate cancer. Such alterations occur through a number of mechanisms, one of which is somatic point mutations, which can occur throughout the AR gene and have been identified mostly in androgen-independent prostate cancers. The aim of this study is therefore, to study the impact that specific mutations in the AR- N-terminal domain (NTD) identified in clinical prostate cancer, have on its function and structure.

Twelve point mutations were introduced into the AR-cDNA of an expression vector for transformation into mammalian cells together with a luciferase reporter gene so as to analyse the alterations in activity brought about by each point mutation as compared to the wild-type AR.

Experimental data on this regard could not be obtained; however, using data obtained from literature, we were able to speculate on the results that were expected. Secondary structure predictions were carried out and indicate that three point mutations (P269S, P340L and P504L) would give an increase in ordered structures (α-helix and β-sheets) while one mutation (E198G) caused a decrease in α-helix structures. Such alterations could have significant repercussions on the stability, binding affinities and activity of the AR.

Elucidating the functional impacts of these point mutations and their contribution to enhancing the potential for proliferation in prostate cancer is imperative towards understanding the pathways controlling this disease. This is ultimately required for the development of targeted treatment, aimed at inhibiting the activity of dysfunctional AR mutants.