

P021 The role of the PTEN in the development of hormone refractory prostate cancer.

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PTEN is a negative regulator of Akt a downstream protein in the PI3K cascade. Inactivating PTEN mutations are commonly found in prostate cancer and in the current study we investigate the role of PTEN deletion (fluorescent in situ hybridisation) and expression (immunohistochemistry) in the development of hormone refractory prostate cancer using matched hormone sensitive and insensitive tumours from 68 prostate cancer patients.

A significant rise in the rate of PTEN loss in the transition from hormone sensitive to hormone refractory disease was observed (23% vrs 52%, $p=0.044$). In addition, those patients with low cytoplasmic ($p=0.017$) and/or low nuclear ($p=0.014$) PTEN expression in their hormone sensitive tumours relapsed significantly quicker than those with high PTEN expression and this translated to shorter disease specific survival ($p=0.011$, 7.55 (6.53-8.57) years vrs 4.3 (2.36-6.36) years).

Nuclear PTEN may be a surrogate marker of PTEN activation as *in vitro* studies demonstrate that following phosphorylation, PTEN is released from the membrane bound scaffolding proteins and enters the nucleus. In support of this we report a correlation between membrane and nuclear PTEN expression ($p<0.001$, R_s 0.669). However, nuclear PTEN is also reported to be involved with nuclear import of PKC and accumulation of cells in G1 phase. In summary, results from this study demonstrate a role for both cytoplasmic and nuclear PTEN in progression of prostate cancer to the hormone refractory state.