ROLE OF PPM1D IN PROSTATIC CARCINOMA: OVEREXPRESSION IN PROSTATE TUMORS AND REGULATION BY ANDROGEN

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Prostatic carcinoma stands out for its increasing rates of incidence and mortality all over the World. The CAGE-Cancer project searched for and identified several differentially expressed genes in prostatic carcinoma (Reis at al, 2004). One of the upregulated genes isolated was PPM1D, encoding a serine/threonine phosphatase which is upregulated by p53. PPM1D is associated with cell cycle progression through downregulation of several tumor suppressor genes, such as p38MAPK, p53, p16INK4[a] and p19ARF. To understand the physiological role of PPM1D in prostate cells, we analyzed its expression upon androgen treatment of LNCaP cells, and observed induction of PPM1D expression by a direct and dose-dependent mechanism. Furthermore, we demonstrated that PPM1D is regulated by androgen both *in vitro* and *in vivo,* its expression increasing during post-natal prostate development. PPM1D expression was also analyzed in several cell lines from five different tissues and, in all cases, we observed a higher expression in more transformed cell lines, suggesting that PPM1D may acts as an important oncogene in different tumours. We amplified and cloned the complete PPM1D cDNA into a mammalian lentiviral vector, generating PPM1D-overexpressing LNCaP cells. Infected cells showed a change in morphology and higher saturation density, indicating a more transformed phenotype.

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