

ETM/382 - Antiandrogen therapy in prostate cancer: impact of auto-regulation of the androgen receptor gene and receptor point mutations.

Cancer of the prostate is the most commonly diagnosed cancer in men, with ~ 3,000 new cases and 900 deaths reported in Scotland in 2011. The androgen receptor (AR) is required for tumour growth and a front line therapy in metastatic disease involves blocking AR action. However, treatment invariably fails resulting in a poor prognosis. It is known that genetic changes affecting gene copy number and mutations in the receptor occur in tumours, but the impact of these changes on the effectiveness of antiandrogen drugs is less well understood. Our previous studies showed that: (1) some mutations cause antiandrogens to switch on receptor activity; and (2) we identified a negative regulatory element that mediates down-regulation of the receptor expression in response to androgens. The aim of this project is to determine the mechanism (s) of repression of the AR gene by androgens and the impact of antiandrogen therapy and receptor point mutations on this auto regulation.