STELLINGEN

Behorende bij het proefshrift
THE ROLE OF THE ANDROGEN RECEPTOR PATHWAY IN PROSTATE CANCER PROGRESSION

1. Androgen receptor modifications occur frequently in hormone-refractory prostate cancer, which shows that this pathway is instrumental in the progression of prostate cancer. (Newmark et al. (1992) Proc Natl Acad Sci U S A. 89(14):6319-23; Visakorpi et al. (1995) Nat Genet. 9(4):401-406; this manuscript)

2. The androgen receptor pathway is still active in most castration-resistant cell lines, indicating that current forms of androgen ablation and/or antiandrogen supplementation cannot completely shut-down androgen receptor signaling in the totality of prostate cancer cells. (this manuscript)

3. Since hormone-refractory prostate cancer cells can express key steroidogenic enzymes and produce androgens locally in the tumor itself, the combination of abiraterone acetate with new generation antiandrogens is a promising therapeutical approach for advanced prostate cancer. (Attard et al. (2009) Cancer Res. 69(12):4937-4940; Tran et al. (2009) Science 324(5928):787-790)

4. Androgen receptor overexpression results in a hyper-responsive receptor, which confers growth advantage under androgen deprived conditions but inhibits cell growth in the presence of physiologic concentrations of androgens. (this manuscript)

5. The androgen receptor-regulated expression profile is modulated in advanced metastatic prostate cancer, by up-regulation of proliferation related genes and selective inhibition of genes involved in cellular differentiation and maintenance of prostate functions. (Hendriksen et at. (2006) Cancer Res. 66(10):5012-5020; this manuscript)

6. Overexpression of VAV3 and TWIST1 proto-oncogenes or down-regulation of tumor suppressor DKK3 are possible mechanisms of androgen-independent growth. (this manuscript)

7. Gene fusions are not restricted to haematological malignancies and sarcomas, but also play a role in common solid carcinomas, as exemplified by the discovery of recurrent TMPRSS2:ERG and related gene fusions in prostate cancer. (Tomlins et al. (2005) Science 310:644-648)

8. The challenge of large-scale genomic analysis is to make sense of the nonsensical jungle of data collected from a microarray.

9. Legislation on animal testing is essential to control abuse of animal experimentation but it must not restrict researchers of reaching scientific and medical advances that cannot be achieved by other means.

10. The greatest danger for most of us is not that our aim is too high and we miss it, but that it is too low and we reach it. (Michelangelo)

11. According to the basic laws of aerodynamics, the bumble bee shouldn't be able to fly, but the bumble bee doesn't know it so it goes on flying anyway. (Mary Kay Ash)

Rute Marques, 2 September 2009