The detection of prostate cancer growth-associated fusion gene in blood of prostate cancer patients

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Prostate cancer (PC) is one of the most common forms of cancers affecting men in the Western world. Androgens such as testosterone promote PC cell growth. During early stages of PC development tumor cells grow slowly within the prostate, PC can be treated efficiently by surgery or radiation therapy and the patient´s prognosis is good. During the PC progression tumor cells may spread to other parts of the body through the blood circulation and the respective tumor cells are called as circulating tumor cells (CTCs). The amount of CTCs vary between patients but usually they are very rare events in the blood; approximately 1 CTCs in million to billion of white blood cells. Currently there are no effective treatments available for the advanced (lethal) form of PC. The lethal form of PC is treated by withdrawal of androgens by endocrine therapy. However, cells can easily adapt to low levels of hormones leading to resistance against endocrine therapy.

Prostate specific antigen (PSA) is released from the prostate and it is currently the only reliable blood-based marker available that is used for PC detection. However, PSA is not only PC specific but also prostate specific marker and the PSA levels in blood can increase due to other factors such as inflammation of the prostate. Currently, the best predictor of PC survival is provided by the combination of PSA levels, clinical and pathological tumor stage and Gleason score (cell differentiation stage).

Different genetic aberrations are strongly involved in PC progression. It is known that the gene fusion between androgen regulated *TMPRSS2* (*transmembrane protease, serine 2*) gene and tumor growth stimulating *ERG* (*v-erythroblastosis virus E26 homolog avian*) gene is formed in 50% of PC cases. Moreover, the formation of respective gene fusion has been shown to occur early during the PC development. *TMPRSS2:ERG* gene fusions have been shown to be present only in the cancerous form of prostatic cell population and the frequency of respective gene fusions have been found to increase in advanced form of PCs. However, despite several studies the real functional role of respective gene fusion in PC development is still unclear.

In my study the sensitivity of three different gene expression detection methods was validated to detect the *TMPRSS2:ERG* status in fusion positive PC cell line. The main aims of my research were to study the occurrence of the fusion gene in 163 PC blood samples and to examine how the fusion gene occurrence affects patient outcome. In my study *TMPRSS2:ERG* gene fusion was found to be more often present in locally advanced and advanced forms of PC blood samples than clinically localized PC blood samples. However, according to different statistical analysis gene fusion status was not shown to be significantly associated either with patient´s clinicopathological data or outcome due to high variability of fusions detected in PC patients´ blood samples. Thus, the gene expression detection method used in my study cannot be used as clinical diagnostic method for PC.

In the future, it would be interesting to evaluate if the sensitivity of the gene expression detection method used in my study and the detection of *TMPRSS2:ERG* fusion positive PC cases could be improved by using different combination of blood-based biomarkers.

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