

Validation of Progression Markers in Bladder Cancer using Tissue Microarray

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Background:

Bladder cancer is a common malignant disease. The prevalence is much higher than the incidence, making bladder cancer one of the most prevalent neoplasms, and therefore a major burden for health care systems. Despite treatment (TURB) and adjuvant therapy (BCG and Mitomycin), 70 % of the patients with non-muscle invasive bladder cancer will have more than 1 recurrent tumor, and up to 25 % will eventually develop the aggressive, muscle invasive disease. Patients with bladder cancer therefore have to be monitored thoroughly for disease recurrence and progression. Based on clinical and histopathological parameters is difficult to predict whether the disease will progress to a muscle invasive stage or not.

Hypothesis:

In an earlier study Dyrskjøl et. al have validated a gene expression signature which predicts outcome in patients initially diagnosed with non-muscle invasive bladder cancer. Our hypothesis is that the protein products of the genes from the progression signature can be used as prognostic markers for disease progression.

Materials & Methods:

This study is based on long-time follow up on prospectively collected data and tissue at Aarhus University Hospital. A tissue microarray (TMA) was constructed using 0.6 mm cores from each tumor, guided by an experienced pathologist. The TMA includes the following tumor material: 289 formalin fixed paraffin embedded urothelial tumors. 118 primary non-muscle invasive tumors, which all within the study progressed to muscle invasive bladder cancer. 171 primary non-muscle invasive tumors, of which none progressed to muscle-invasive bladder cancer. The latter group was followed for at least 5 years, and 80 % completed their control regime.

Through immunohistochemistry we aim at validating the previously identified gene expression changes on the protein level.

Results:

When >40 % of the tumor cells stain positive for Cathepsin E, the tumors malignant potential is low and prognosis is good, $P=0.041$.

Cathepsin E staining is an independent marker for progressive bladder cancer in pT1 primary tumors ($n=101$), $P=0,034$. Univariate Cox regression analysis of Cathepsin E staining in pT1 tumors showed an odds ratio of 2.04 ($P=0.042$). Univariate Cox regression analysis of tumor grade was not significant in the pT1 tumor group, and hence not included in the analysis.

Conclusions:

We have identified Cathepsin E as a marker for progression of bladder cancer on the protein level and are now in the process of examining the results of 3 other promising markers: Aurora Kinase B, Maspin and Survivin. Our hope is that the markers either independently or together will be able to single out the patients that need urgent treatment from those that do not.