Interimate risk prostate cancer is a current medical challenge since the patients in this group can either be stable or progress, and there is no predictor for individual risk. Stratifying these patients would spare the patients unnecessary treatment or indicate the start of treatment immediately without losing precious time. Currently, prostate specific antigen (PSA) is used as evidence for biochemical progression. A more sensitive biomarker is needed to detect disease progression earlier and more reliably.

We have isolated circulating tumor cells (CTCs) using a filtration-based device (ScreenCell (1, 2)). We subsequently performed the genetic characterization of the captured CTCs on a single cell basis (11). Using three-dimensional (3D) nuclear telomere imaging and quantitative analysis of 3D telomeric signatures of CTCs (1,2), we have characterized CTCs in the blood of the patients and have identified patient subgroups with one or more groups of CTCs (11). 380 samples of intermediate risk prostate cancer all revealed the presence of CTCs. However, the CTCs found were not genetically identical. Marked heterogeneity was seen, and three main groups of CTC profiles were defined based on Teloview™ software our group developed earlier (3) (fig. 3). Repeat tests taken every months intervals define stable, mildly changing and significantly altered 3D profiles indicative of disease stability vs. progression (fig. 3).

Materials and Methods

CTCs were found in 380 intermediate risk PCa samples. 175 samples were analyzed including 65 follow-ups.

1. Size-based ScreenCell Filter Isolation of CTCs: A non-antibody based enrichment that captures all CTC subpopulations (1,2).

2. 3-Dimensional Nuclear Telomere Hybridization (QFISH): The 3D telomere profiles of individual CTCs are examined.

3. 3-Dimensional Imaging Acquisition: Reconstructed 3D images allow for telomere size quantification.

Immunohistochemical CTC Confirmation: CTC epithelial cytoskeleton is stained green, nuclear DNA stained blue.

Quantitative Image Analysis with Teloview™: Telomere number, nuclear size, telomere aggregates are accessed.

Automated CTC Enumeration with Teloscan™: Clinically adaptable molecular CTC characterization.

Conclusions

- The different intermediate risk CTC subpopulations can be isolated and genetically characterized by non-antibody size-based ScreenCell filtration (fig 1A, 1B).
- Intermediate risk prostate cancer patients can be classified into different telomeric profiles which indicates the severity of the cancer (fig 2A, 2B, 2C).
- Enumeration and molecular characterization of CTCs can be combined for accurate prediction of disease progression (fig 1C).
- With simple blood tests, the progression of prostate cancer can be monitored for personalized management (fig. 3A, 3B, 3C).
- Response to therapy can be easily monitored with periodic telomeric profiling.
- Identification and molecular characterization of resistant CTC subpopulation can improve future drug design.

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