ASCO 2013 Abstract 5029

Evidence for a field effect in early prostate cancer (PCa): gene expression profiles in normal-appearing prostate tissue (NT) adjacent to tumor (T) are predictive of clinical outcome.

Eric A. Klein, Sara Moscovita Falzarano, Nan Zhang, Dejan Knezevic, Tara Maddala, H. Jeffrey Lawrence, Diana B. Cherbavaz, Robert J. Pelham, Carl Millward, Mark Lee, Cristina Magi-Galluzzi; Glickman Urological & Kidney Institute, Cleveland Clinic, Cleveland, OH; Pathology and Laboratory Medicine Institute, Cleveland Clinic, Cleveland, OH; Genomic Health, Inc., Redwood City, CA

Background: We previously identified genes whose expression predicts aggressive PCa (clinical recurrence (cR), prostate cancer death (PCD), adverse pathology) when assessed in histologically heterogeneous tumor foci and in biopsies (Klein ASCO 2012). These results enabled the definition of a multi-gene Genomic Prostate Score (GPS), which has been clinically validated (Cooperberg AUA 2013). There is interest regarding a possible field effect in PCa, i.e. molecular alterations throughout the gland that may influence PCa development. We conducted exploratory analyses to evaluate gene expression, including GPS, in adjacent normal-appearing tissue (NT) for prediction of cR and PCD. **Methods:** Cohort sampling was used to select 127 patients with and 374 without cR from 2,641 patients treated with RP for T1/T2 PCa. Expression of 732 genes was measured by qRT-PCR separately in T and NT (defined as > 3 mm from T) specimens. GPS (0-100 units) was determined using the genes and algorithm from the validation study. Analysis used Cox proportional hazards models and Storey's false discovery rate (FDR) control. **Results:** 410 evaluable patients had paired T and NT. Of the 405 genes which were predictive of outcome in T (FDR < 20%), 289 (71%) showed similar but weaker effects in NT. 47 genes were associated with cR in NT (FDR < 20%), of which 34 also concordantly predicted cR in T (FDR < 20%). GPS assessed in NT significantly predicted time to cR (HR/20 units = 1.8; 95% CI: 1.3-2.4; p< 0.001) and PCD (HR/20 units = 1.9; 95% CI: 1.2-3.0; p = 0.005) but was less predictive than GPS in T (HR/20 units = 4.8 for cR; 95% CI: 3.7-6.2; p < 0.001 and HR/20 units = 6.9 for PCD; 95% CI: 4.4-10.7; p < 0.001). The strongest components of GPS in predicting cR and PCD in NT were stromal response and androgen signaling genes (p < 0.05); proliferation and cellular organization genes did not consistently provide a significant contribution in NT. **Conclusions:** These data indicate that gene expression profiles, including GPS, can predict outcome in NT, albeit more weakly than in tumor. These findings suggest that there is an underlying field effect associated with the development of aggressive PCa.