

## **Clonal Diversity Revealed By Morphoproteomic And Copy Number Profiles Of Single Prostate Cancer Cells At Diagnosis**

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Tumor heterogeneity is prevalent in treatment-naïve prostate cancer (PCa) as well as end-stage metastatic prostate cancer. This observation may contribute to the broad range of clinical presentation, treatment response, and disease progression. To characterize molecular heterogeneity associated with de novo metastatic PCa, multiplatform single cell profiling was performed using High Definition Single Cell Analysis (HD-SCA). HD-SCA enabled morphoproteomic and morphogenomic profiling of single cells from touch preparations of tissue cores (prostate and bone marrow biopsies) as well as liquid samples (peripheral blood and bone marrow aspirate). Although peripheral blood was examined, circulating tumor cells were not definitively observed. Targeted proteomics of PTTP, BMTP, and MTCs revealed cell lineage and luminal prostate epithelial differentiation associated with PCa. Hallmark PCa copy number alterations, including PTEN and ETV6 deletions and NCOA2 amplification, were observed in cells within the primary tumor and bone marrow biopsy samples. This case demonstrates that real-time molecular profiling of cells collected through prostate and bone marrow biopsies is feasible and has the potential to elucidate the origin and evolution of metastatic tumor cells. Altogether, biological and genomic data obtained through longitudinal biopsies can be used to reveal the properties of PCa and can impact clinical management.

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