

## Research Articles

# Microarray analysis identifies a death-from-cancer signature predicting therapy failure in patients with multiple types of cancer

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Activation in transformed cells of normal stem cells' self-renewal pathways might contribute to the survival life cycle of cancer stem cells and promote tumor progression. The *BMI-1* oncogene-driven gene expression pathway is essential for the self-renewal of hematopoietic and neural stem cells. We applied a mouse/human comparative translational genomics approach to identify an 11-gene signature that consistently displays a stem cell-resembling expression profile in distant metastatic lesions as revealed by the analysis of metastases and primary tumors from a transgenic mouse model of prostate cancer and cancer patients. To further validate these results, we examined the prognostic power of the 11-gene signature in several independent therapy-outcome sets of clinical samples obtained from 1,153 cancer patients diagnosed with 11 different types of cancer, including 5 epithelial malignancies (prostate, breast, lung, ovarian, and bladder cancers) and 5 nonepithelial malignancies (lymphoma, mesothelioma, medulloblastoma, glioma, and acute myeloid leukemia). Kaplan-Meier analysis demonstrated that a stem cell-like expression profile of the 11-gene signature in primary tumors is a consistent powerful predictor of a short interval to disease recurrence, distant metastasis, and death after therapy in cancer patients diagnosed with 11 distinct types of cancer. These data suggest the presence of a conserved BMI-1-driven pathway, which is similarly engaged in both normal stem cells and a highly malignant subset of human cancers diagnosed in a wide range of organs and uniformly exhibiting a marked propensity toward metastatic dissemination as well as a high probability of unfavorable therapy outcome.