The genomic signature for in vitro-induced invasive growth is enriched in genes correlated with human cancer aggressiveness

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Motivation
Gene expression profiling has been extensively used to study human cancer and define gene signatures whose expression correlates with specific features of the tumor. However, such signatures generally lack biological insight, as gene selection is only based on correlation with clinical features of interest.
Methods
To build signatures with greater biological significance, we set-up a statistical procedure for metaanalysis of DNA microarray data named Signature Enrichment Analysis (SEA). SEA is aimed at assessing whether a gene expression signature defined in a given in vitro biological model (e.g. genes regulated by a growth factor) is significantly enriched in genes whose expression in tumours correlates with a specific clinical and/or pathological feature. If the enrichment is significant, such genes can be used to build a cancer signature encompassing both clinical relevance and biological meaning.
Results
We applied SEA to a signature composed of genes transcriptionally regulated in vitro during the induction of invasive growth by tyrosine kinase receptors for Hepatocyte Growth Factor (HGF) and Epidermal Growth Factor (EGF). This signature was tested against gene expression datasets of lung and prostate cancer. We found that the invasive growth signature is enriched in genes discriminating specific features of the cancers explored, and in particular: (i) lung cancer propensity to metastasize to brain or liver; (ii) Gleason score of prostate cancer; (iii) prostate cancer as opposed to normal prostate tissue. From this signature we derived and preliminarily validated a series of classifiers correlated with prostate and lung cancer aggressiveness. These results indicate that the genomic signature for in vitro-induced invasive growth captures a transcriptional program that can be reconstructed, albeit partially, in human cancer samples.

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