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Meta-analysis of transcriptional profiles in cancer for prognosis prediction and metastatic gene identification

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With thousands of cancer gene expression datasets deposited in public databases, we have developed a meta-analysis strategy called EXALT (EXpression AnaLysis Tool). It allows us to perform unique meta-analyses of gene-expression profiles that are independent of technology platforms and to discover recurrent and reliable gene expression signatures for cancer prognosis prediction and functional gene identification. We have clustered heterogeneous signatures from 223 public datasets containing 10,581 breast cancer samples. The signatures were systematically organized by their common data elements and assembled into a new signature data type called meta-signature. We identified a specific meta-signature consisting of 50 genes (BRmet50) that is robustly predictive of cancer prognosis in 6,011 breast cancer patients from 21 different breast cancer datasets as well as in other malignancies including lung and prostate cancer. These findings illustrate the value of BRmet50 in breast cancer prognosis. Furthermore, we have established a translational model by combining a meta-analysis of public cancer gene-expression profiles with functional validation approaches. From the candidate genes encoded in BRmet50, we identified SPARCL1 as a metastasis-suppressor. Loss of SPARCL1 expression was previously reported during the clinical progression of prostate cancer. We demonstrated that SPARCL1 reconstitution suppresses tumor cell migration and invasiveness *in vitro* and tumor metastatic growth *in vivo*, conferring improved survival in xenograft mouse models. Further investigations on SPARCL1 mechanisms, our results indicate that changes in the AKT signaling pathway correlates with SPARCL1 suppression of cancer cell invasion, and a truncated SPARCL1 mutant inhibits cancer cell invasion

Biography

Yajun Yi has completed his PhD from University Manitoba, Canada and postdoctoral studies from Northwestern University School of Medicine. He received Howard Temin Award from the National Cancer Institute. He has published more than 30 papers in peer-reviewed and obtained two patents.

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