Author’s response to reviews

Title: Genome-wide analysis of three way interplay between gene expression, cancer cell invasion, and anti-cancer compound sensitivity

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Dear Editor,

On behalf of my collaborators, I am submitting a manuscript “Genome-wide analysis of three way interplay between gene expression, cancer cell invasion, and anti-cancer compound sensitivity” for publication in BMC Medicine.

Chemosensitivity and tumor metastasis are two main topics in cancer management. Cancer cells often exhibit a wide range of sensitivity to anticancer compounds. To gain insight on the associated genetic mechanisms of drug sensitivity, a powerful approach was to employ the panel of 60 human cancer cell lines used by National Cancer Institute (NCI-60) for extensive drug screening. Cancer cells also show a wide range of invasion ability. However, a genome-wide portrait about the contributing molecular factors to the invasion heterogeneity is lacking.

Here we presented the first tumor invasion profiling on NCI-60 cell lines. We further proceeded with a series of bioinformatics analysis to characterize gene expression patterns associated with both tumor invasion heterogeneity and compound-sensitivity. We validated a key finding of an 8-gene signature with additional drug-tests outside the NCI-60 panel. Applying to two adjuvant chemotherapy cohorts, one on breast cancer and other one on lung cancer, the same 8-gene signature predicted distant relapse-free survival in both cases. This is remarkable because lung cancer and breast cancer are known to show great patho-clinical difference; for example, overall, the 5 year survival rate is around 15% for lung cancer but is higher than 75% for breast cancer.
In summary, this work provides the first glimpse of the three way interplay between gene-expression, drug-sensitivity, and tumor-invasion at the genome-wide level. Augmenting the NCI-60 model with *in-vitro* characterization of important phenotypes like invasion potential is a cost-effective approach to power the genomic chemosensitivity analysis.

We appreciate very much your consideration of our work, which we believe to have a wide interest for the reader of BMC Medicine.

Sincerely yours,

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