Author's response to reviews

Title: An integrative approach to identify cancer chemoresistance-associated pathways

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Author's response to reviews: see over
Dear Editor,

Enclosed is a paper, entitled "An integrative approach to identify cancer chemoresistance-associated pathways". Please accept it as a candidate for publication in the BMC Systems Biology journal. Below are our responses to your submission requirements.

1. Title and the central theme of the article.

   Paper title: "An integrative approach to identify cancer chemoresistance-associated pathways". This study is anticipated to precipitate target identification for chemoresistant issue and highlights the interconnectivity of chemoresistant mechanism. The mechanisms that contribute to chemotherapy resistance are relatively unknown. This study elucidates the chemoresistance-associated pathways retrieved from the integrated biological interaction networks and identifies signature genes relevant for chemotherapy resistance. In summary, integrating pathway structure information with gene expression data provides a momentous systems biology implementation to identify system level responses by a comparative approach.

2. Which subject/theme of the Journal the material fits

   Systems Biology.

3. Why the material is important in its field and why the material should be published in the Journal?

   Although platinum-based chemotherapeutic agents are widely used for the treatment of endometrial, cervical and breast cancers, chemoresistance caused by molecular mechanisms still remains a major therapeutic difficulty. This approach elucidates the chemoresistance-associated pathway during large biological interaction networks. Likewise, genes deemed relevant for chemotherapy resistance are also determined. To reach these goals, an integrated metabolic interaction network is constructed and subsequently platinum-based chemoresistant pathways are identified by system algorithm. The strength of this approach lies in identifying modes’ action of chemosensitivity and chemoresistant by comparative studies which have been presented in the experimental results. This work is sufficiently flexible to accommodate various types of biological network information and experimental data. Moreover, this approach not only offers insights into the chemoresistant mechanisms but also provides the information of potential candidate target genes for future drug-development offers. We strongly believe the contribution of this study warrants its publication in the BMC Systems Biology Journal.
4. **Names, addresses, and email addresses of four experts in the subject of this paper**

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<th>Expert</th>
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Expertise: published a related paper (Modeling human cancer-related regulatory modules by GA-RNN hybrid algorithms) in *BMC Bioinformatics* 2007, **8**: 91-104.


Expertise: published a related paper (Transcriptional up-regulation of SOD1 by CEBPD: A potential target for cisplatin resistant human urothelial carcinoma cells) in *Biochemical Pharmacology* 2010, **80**: 21-33.

Expertise: Miss Chang provides her professional programming skills to help this work accomplished.

5. **Competing interests**

The authors report no competing interests.

Finally, this paper is our original unpublished work and it has not been submitted to any other journal for reviews.

Sincerely,

Shih-Yi Chao