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Integrating genome and transcriptome data to predict functional driver mutation in breast cancer

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Accurate prediction of the functional effects of genetic variation in cancer is critical for realizing the promise of precision medicine. Due to a lack of statistically rigorous approaches and training data, differentiating driver mutations from passenger mutations remains a major challenge in cancer research. We develope a novel Bayesian method, xDriver that combines mutations and their sequence-derived functional features (such as GERP scores) with gene expression in a population of tumor samples to identify mutations that significantly alter gene expression landscapes. We demonstrate using 752 breast cancer samples in the cancer genome atlas that our integrative approach is able to significantly improve the accuracy of driver mutation identification over existing approaches that do not perform such integration. In particular, our approach is able to enhance the functional prioritization of so-called "tail" (rare) mutations and more accurately delineate cancer subtype specific mutations (such as PIK3CA mutants associated with lymph node negative patients). Importantly, scores generated by our model achieve the best agreement with *in vitro* functional cell viability data obtained from transfected Ba/F3 and MCF10A cell-lines, compared to predictions from other commonly used algorithms. Our results exemplify the importance of integrating gene expression in predicting candidate driver mutations. This integrative study has the potential to impact functional genomic experiments and is expected to link cancer genomic event to precision medicine.

Biography

Zixing Wang has completed his PhD degree in Genome Science and Technology at the University of Tennessee in 2011, with the thesis on the TGF-beta function in neuron development. After graduation, he moved on and switched to Bioinformatics and Computational Biology. Currently he is working as a Post-doc at MD Anderson Cancer Center, University of Texas. His main research interest focuses on data mining, machine learning, especially with their integration and application in cancer genomic and precision medicine. He has published 16 scientific papers in international well-recognized journals. He has been ACM SIG and ISMB member and also served as journal reviewer for many top-tier journals in the field of bioinformatics and systems biology.

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