# Genomics-Based Cancer Drug Response Prediction through the Adaptive Elastic Net

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Personalized cancer treatments promise drastic improvements in clinical benefit over traditional therapies. To develop individualized treatments, accurate models to predict drug response from patient genomics are needed, but traditional machine learning algorithms overfit and yield large predictive errors when trained on dimensionally imbalanced genomics datasets. I designed a machine learning framework based on Zou and Zhang's adaptive elastic net algorithm to address this problem. While the current state-of-the-art algorithm for drug response prediction—the traditional elastic net—trains on each drug independently, the adaptive elastic net takes advantage of related response variables—in this case, chemotherapeutics with related mechanisms of action—through differential shrinkage. When modeling drug response based on the same genomic dataset, the adaptive elastic net, applied through the "gcdnet" package, yielded a mean 10-fold cross-validated error 24.1% lower than the error of the traditional elastic net. Moreover, my framework correctly identified known biomarkers of drug response as well as known sensitivity-inducing biological pathways, confirming its biological validity. Finally, based on the models generated by the adaptive elastic net, I also identified novel associations between drug response and genomic features and pathways of tumors. Thus, my work can improve accuracy of genomics-based cancer drug response prediction and open new avenues of investigation by uncovering previously unknown relationships between biological mechanisms and drug response. Future studies could utilize my methods to prioritize in vitro screening of cancer treatments, reposition drugs, or identify putative mechanisms of drug sensitivity and resistance for further research.