Presentation Abstract Submission

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Research Title	Pathway-based analysis and artificial intelligence reveals metabolic subtypes of clinical relevance in breast cancer

Abstract:

Pathway-based personalized analysis and machine learning reveals metabolic subtypes of clinical relevance in breast cancer Mohammad Askandar Iqbal et al Thumbay Research Institute of Precision Medicine, Gulf Medical University, Ajman, UAE Metabolic reprogramming is a cancer hallmark with immense biological and translational significance. However, emerging evidence suggest that cancer metabolism may be heterogenous, highlighting the need of systematic stratification of patients to identify and exploit subtype-specific metabolic liabilities. Here, we interrogated multiomics data from breast cancer patients and identified three metabolic subtypes in breast cancer. These subtypes exhibited different extents of deregulation of 90 metabolic pathways and were categorized as least, average, and most metabolically deregulated. Pathway analysis showed pyrimidine metabolism is the strongest predictor of metabolic deregulation. Genomic and clinicopathological characterization of metabolic subtypes revealed clinically relevant differences. For example, tumor grade, gene-classifier, prognosis, recurrence, and immune infiltration were found to be significantly correlated with metabolic deregulation. Next, we employed sophisticated machine learning pipeline to identify signature of each metabolic subtype. These signatures successfully predicted the metabolic subtype of a random sample with more than 80% precision and accuracy. In addition, cell lines representing each metabolic subtype were identified using this signature and in vitro metabolic inhibition of subtype-specific pathways revealed cell line sensitivities to be consistent with metabolic subtypes. Further, we identified FDA approved and other drugs which are more likely to benefit patients belonging a particular metabolic subtype. Unexpectedly, no cell lines were predicted to represent the least deregulated metabolic subtype which comprise over 50% of all samples, suggesting a caveat not known earlier. Overall, this study highlights metabolic stratification of breast cancer patients and demonstrates its clinical utility.