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Breast Cancer Pharmacogenomics of Aromatase Inhibitors

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Abstract

Breast cancer is the most prevalent cancer in women, with more than 260,000 new cases each year in the US. In spite of the development of the treatment, still over 40,000 die from this disease each year. Among all breast cancer diseases, 70-80% patients have ER+ or hormonal receptor positive breast cancer which makes it the most common subtype. Hormonal therapies including SERMs (selective estrogen receptor modulators) as well as aromatase inhibitors (AIs) are the two major classes of drugs that are widely used to treat ER+ disease. Both of them are also FDA approved for the chemoprevention in women with high risk disease. However, in both treatment and prevention settings, response varies, ranging from undesirable side effect associated with these drugs to lack of efficacy even treated with standard doses of these drugs. Therefore, it is important to identify potential biomarkers. Both germline and tumor DNA can contribute to response to therapy. We have taken a genome wide association approach with clinical trial samples, in this case the largest phase III clinical trial, MA27 that is randomized to two AIs, exemestane and anastrozole to identify germline SNPs associated with AI efficacy as well as the most common side effect, muscular skeletal pain. In both cases, we identified common SNPs that might influence nearby gene transcription regulation in a drug dependent fashion, which opens a new area of research to study pharmacogenomics eQTL (expression quantitative trait loci) on gene expression regulation and drug response. Furthermore, we also identified unique SNP signals that differentially affect the response to exemestane and anastrozole, the two drugs that do not show clinical differences of efficacy in a population level. Our approach not only identify biomarkers to predict AI response, but also help to understand underlying mechanisms associated with these biomarkers that could have significant impact..

Biography:

Dr. Wang received MD from Fudan University Medical School, Shanghai China, followed by an PhD degree from the department of Pharmacology from Mayo School of Biomedical Science. She is currently Professor of Pharmacology at Mayo Clinic Rochester. Her research has been focusing on pharmacogenomics of cancer treatment with an emphasis on breast cancer and prostate cancer. She is using multiple omics approach to identify response biomarkers, followed by functional and mechanistic understanding of the biomarkers and their role in drug resistance. She has published over 180 publications with many in high impact journals such as Cancer Cell, Molecular Cell and JCI etc. She is a recipient of ASCPT (American Society of Clinical Pharmacology and Therapeutics) Leon Goldberg Young Investigator Awardee and a member of the honor society, American Society for Clinical Investigation (ASCI).

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