

Pharmacogenomics predictions for breast cancer treatments' efficacy and toxicity

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Breast cancer is the major cause of death among Mexican women between 35 and 50 years of age. Among the most prescribed chemotherapeutic agents are Capecitabine, a precursor of 5-fluorouracil, which inhibits the synthesis of thymidine and DNA replication, and tamoxifen, a chemotherapeutic adjuvant that prevents recurrence in estrogen receptor positive patients that have undergone surgery. Capecitabine needs to be efficiently eliminated by dihydropyrimidine dehydrogenase (DPD) to avoid its accumulation and adverse effects. Tamoxifen is a prodrug that needs the P450 liver enzyme isoform CYP2D6 for conversion to its active form, endoxifen. Therefore, prediction of efficacy and toxicity in breast cancer chemotherapy depends on pharmacogenomics.

PHARMachip™ is a DNachip developed by Progenika Biopharma, SA (Bilbao, Spain) that consists of a microscopic slide carrying hundreds of oligonucleotides to screen for mutations and single nucleotide polymorphisms in genes of phase I, phase II, transporters, receptors and other enzymes and proteins with which drugs interact after entering the patient's body and metabolism. Among the genes present on this DNachip genotype are those for the P450 and pyrimidine metabolism enzymes described above.

We are using the PHARMachip to investigate its usefulness as a predictor of chemotherapy efficacy and toxicity in Mexican breast cancer patients. The first fifty genomic DNAs from these patients analyzed reveal that most (almost 85%) patients carry a genotype corresponding to a phenotype of normal to extensive metabolism of tamoxifen with no mutations in the DPD gene that would otherwise cause 5-Fluorouracil derivative accumulation.

Biography

The author completed his PhD at the age of 25 and is a distinguished alumnus from the University of Texas at Houston. His postdoctorate was at Louis Pasteur University in Strasbourg, France. He has created prestigious Molecular Biology Research and Graduate Programs and Centers in Mexico. He is the founder of Vitaxentrum, a premier Biotechnology and Genomics Consulting and Servicing Organization. He has published over 100 papers in prestigious journals and has served as reviewer of international journals and national academic committees. His team is recognized in Latin America as a pioneer and leader in molecular biology, DNA diagnostics, biotechnology, and gene therapy.