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DRUG RESISTANT STEM CELLS IN CELLULAR MODELS FOR MOLECULAR SUBTYPES OF BREAST CANCER

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Study rationale global expression profiling of differentially expressed genes in breast cancer has provided scientifically robust rationales for molecular classification of breast cancer subtypes and for targeted treatment options. Chemo-endocrine therapy combined with pathway selective small molecule inhibitors represents common treatment of choice. However, this option is frequently associated with emergence of drug resistant stem cells that favor progression of therapy resistant disease. This limitation emphasizes development of cancer stem cell models that are capable of identifying testable therapeutic alternatives against drug resistant stem cells. Experimental approach experiments on cellular models for Luminal A, HER-2 enriched and triple negative breast cancer subtypes were designed to isolate and characterize stem cell phenotypes resistant to clinically relevant chemo-endocrine therapeutics and examine the mechanistic efficacy of natural products on drug sensitive and drug resistant phenotypes. Study outcome parental MCF-7 (Luminal A), 184-B5/HER (HER-2 enriched) and MDA-MB-231 (Triple negative) cells exhibited progressive growth in the presence of cytotoxic concentrations of Tamoxifen (TAM), Lapatinib (LAP) and Doxorubicin (DOX), respectively. Long-term treatment with these drugs favored emergence of drug resistant TAM-R, LAP-R and DOX-R phenotypes. These resistant cells exhibited up regulated expression of stem cell specific tumor spheroid formation and CD44 (cellular) and Oct-4 and NANOG (molecular) markers. Treatment of drug sensitive and resistant cells with select nutritional herbs, vitamin A derivative and natural terpenoid induced inhibition of tumor spheroid formation and down regulated expression of CD44, Oct-4 and NANOG. Study conclusions present cancer stem cell models provide a novel approach to identify natural products as testable alternatives for stem cell targeted therapy of chemo-endocrine therapy resistant breast cancer.

BIOGRAPHY

Nitin Telang obtained his PhD in Developmental Biology from University of Poona, India in 1974, followed by post-doctoral training in the USA during 1976-1985. He has served as attending Biochemist at Memorial Sloan-Kettering Cancer Center, New York during 1985-1991, as an Associate Professor at Cornell University Medical College, New York during 1991-2004, and as Senior Scientist and Director, Carcinogenesis a Prevention Laboratory at Strang Cancer Prevention Center, New York during 2004-2007. His research on preclinical models for genetically predisposed breast and colon cancer has been funded through US Department of Defense Breast Cancer Research Program and through US National Cancer Institute. His current research interests are in the fields of preclinical oncology, cancer stem cell biology and anti-cancer lead compound efficacy.

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