# STRATEGIES TO EVALUATE THE EFFECT OF CHEMOTHERAPEUTIC DRUGS AND CURCUMIN IN BREAST CARCINOGENESIS

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**Abstract:** Breast cancer is the most frequently diagnosed cancer in women, and one of the leading causes of cancer-related deaths worldwide. Breast carcinogenesis is a multistage process that involves mutations and phenotypic alterations attributed to exogenous environmental substances and endogenous agents as female hormones. The aim of this study was to evaluate genes that could be targeted by drugs and curcumin with strategies as 1) Epithelial-mesenchymal transition (EMT), 2) Migratory and invasive capabilities and 3) Analysis of microRNAs. We evaluated the effect of drugs and curcumin in a triple positive cell line for hormonal receptors, as MCF7 and a negative one, as MDA-MB-231 and in an *in vitro* model induced by radiation and estrogen. Such model was developed with a normal immortalized breast epithelial cell line, MCF-10F that was exposed to low doses of high LET (linear energy transfer) alpha particles (150 keV/μm) of radiation, and cultured in presence of 17β–estradiol. We used i) MCF-10F, ii) Alpha5, malignant and tumorigenic, and iii) Tumor2, derived from Alpha5 injected in nude mice. Previous results showed increased cell proliferation, anchorage independency, invasive capabilities and tumor formation in nude mice, and mutations of *c-Ha-ras* and *Rho-A* among others in Alpha5 and Tumor2. Drugs as 5-Fluorouracil (5-FU) is a widely used anticancer drug, a heterocyclic aromatic organic compound with a structure similar to that of the pyrimidine molecules of nucleic acids that inhibits thymidylate synthase and is incorporated into RNA and DNA, resulting in cytotoxicity and cell death. Curcumin is a natural polyphenolic compound, an antioxidant known as a dietary natural yellow pigment derived from the rhizome of the herb *Curcuma longa* that is widely used for medical, culinary and other purposes especially in India. EMT is a process involved in malignant progression inducing genes such as Slug, Axl and Twist1. Since such genes are aberrantly expressed in multiple tumor types and are known to favor metastasis. In this study we evaluated genes that could be targeted by several drugs and curcumin in relation to EMT. Results indicated that 5-FU and curcumin decreased expression of genes related with EMT as Axl, Slug, Twist1 as well as those related with metastasis such as c-Ha-ras, Rho-A, p53, Caveolin-1 and others and increased epithelial-related genes as E-Cadherin. Curcumin increased miR-34a expression, which in turn repressed several genes that are situated at the core of several signaling pathways known to mediate EMT. The migratory and invasive capabilities were decreased by drugs and curcumin. Thus, our studies showed that 5-FU and curcumin may prevent or the delay in cancer progression and dissemination through its ability to disrupt EMT. It can be concluded that 5-FU and curcumin influenced biochemical changes associated with EMT, and among microRNAs the miR-34a and its downstream genes Axl, Slug and Twist1 seems to promote such transition. Supported by Tarapaca University (GMC). (GMC).