Munaweera K.H.S.

MODULATION OF RADIATION-INDUCED BREAST CARCINOGENESIS BY SYNTHETIC ESTROGEN EXPOSURE

Tutor: PhD, associate professor Dziarzhynskaya N.A.
Department of Radiation Medicine and Ecology
Belarusian State Medical University, Minsk

Research indicates women have higher radiation-associated cancer risks than men, particularly, breast and thyroid due to hormonal fluctuations throughout life in women (Biegon et al., 2022). Estrogen regulates breast epithelial proliferation and reproductive functions, affecting DNA damage responses and breast cancer risk. Early pregnancy and high pregnancy estrogen levels reduce risk, while prolonged exposure, obesity, and exogenous estrogen use increase vulnerability, highlighting estrogen's complex role in breast tissue and carcinogenesis (Hilakivi-Clarke et al., 2013).

The aim of this research is to know the hormonal modulation influencing the affect of ionising radiation-induced breast carcinogenesis, treatments and outcomes, improve knowledge in personalized radiation- based therapies.

Epidemiological data suggests, radiation increases breast cancer risk by inducing DNA damage and chromosomal abnormalities in breast cells, Misrepaired DNA and mutations in oncogenes or tumor suppressor genes allow abnormal cells to survive and accumulate further changes, eventually leading to malignancy. Latency periods of 10–12 years reflect the time for these changes to manifest, with susceptibility influenced by age and tissue developmental stage (Ronckers et al., 2004).

Estrogen are steroid hormones that help in reproduction and non-reproduction. Womens produce higher level due to ovarian and adipose tissue activity. Additionally, beside natural estrogen humans are also exposed to exogenous estrogen such as, pharmaceutical estrogens, xenoestrogens and phytoestrogens, which mimics natural estrogens binding to receptors and affecting cell proliferation, gene transcription, and DNA damage responses. Breast cancer risk can be increased by pharmaceutical estrogens and xenoestrogens and decreased by phytoestrogens. The effects depend on dose, timing, receptor expression, and tissue context (Malik & Mukherjee, 2025).

Immortalized human breast epithelial cell line, (MCF-10F) was exposed to doses of radiation and grown with or without endogenous estrogenic steroid hormone, 17β-estradiol. Analysis of differential gene expression shows Fibroblast growth factor 2 (FGF2), fibroblast growth factor-binding protein 1 (FGFBP1) was higher in the tumor cell line. Additionally, transforming growth factor alpha (TGFα) shown more in tumor cells than in non-tumorigenic lines.

Short-term exposure to estrogen and progesterone during critical stages of mammary development reduces tumor incidence and progression by decreasing cell proliferation, enhanced DNA damage responses, and alterations in the mammary stroma. Hormones modulate key oncogenic pathways, including tumor suppressor gene and proto-oncogene, which affects the survival and progression of radiation-damaged cells. These findings demonstrate that the body's hormonal milieu can significantly modulate the carcinogenic effects of ionizing radiation (Helm & Rudel, 2020).

Radiation-induced breast carcinogenesis can be managed by individualized treatments guided by molecular, genetic, and proteomic profiling, including hormonal and human epidermal growth factor receptor, HER2-targeted therapies (Sheva et al., 2024), and synthetic estrogen causes can be treated by using selective estrogen receptor modulators, aromatase inhibitors to prevent estrogen production, targeted therapies, lifestyle adjustments, and personalized radiation or chemotherapy (Hilakivi-Clarke et al., 2013b).