Phytoestrogen coumestrol as a cytotoxic therapy against triple negative and HER2 amplified inflammatory breast cancer

Inflammatory Breast Cancer (IBC) is an aggressive and lethal disease with a low overall 5- year survival rate of 30-60%. The poor prognosis for patients with IBC emphasizes the need to better understand the molecular signature of this disease. Around half of diagnosed IBC cases are classified as triple negative breast cancer (TNBC) because it lacks the expression of estrogen receptor alpha (ER-α), progesterone receptor (PR) and amplification of growth factor receptor HER2. In addition, TNBC cells express alternate estrogen receptors such as ERα-36 which can promote the activation of ERK and AKT downstream signaling via estrogen non-genomic signaling pathway. Coumestrol (Cou), a phytoestrogen structurally similar to estradiol (E2), is a natural compound found in plants, specifically soybeans. Recent studies have shown that ER positive and ER negative breast cancer cell lines' proliferation and migration would be inhibited by Cou. The effects or mechanisms of Cou in IBC cell lines and its effects on estrogen non-genomic signaling has not yet been reported. **We hypothesized that the molecular mechanism of Cou anti-cancer action involves the inhibition of estrogen non-genomic signaling and the induction of apoptosis in IBCs.** The objective of this treatment is to characterize the cytotoxic activity of Cou against IBC and based on this data, test if treatment with Cou impairs the formation or invasion properties of IBC tumor emboli. Our long-term goal is to identify novel effective targeted therapeutics against IBC that could be used as monotherapy or in combination with other drugs.