Kayla Miller

CBIO GIDP

AGE Abstract

Current treatment modalities for cancer such as chemotherapy and radiotherapy, while effective, often lead to unwanted side effects and damage to surrounding normal, healthy tissue. healthy tissue. Fasting and short-term starvation prior to therapy has been shown to enhance the efficacy of cancer treatment while reducing side effects through the induction of differential stress resistance (DSR). DSR refers to the enhancement of the ability of healthy cells to resist the damaging effects of chemotherapy and radiotherapy, with simultaneous sensitization of cancer cells to these same stressors. Previous mouse research has demonstrated that fasting can enhance chemo- and radiotherapy efficacy, but the molecular mechanisms mediating this phenomenon have yet to be fully elucidated. Here, we investigate the role of FOXO transcription factors in fasting-induced DSR to tamoxifen, a commonly used breast cancer drug. FOXOs are essential transcription factors that control stress resistance, apoptosis, and metabolism in response to nutrient and stress signals. Distinct patterns of FOXO activation can result in either cell survival or apoptosis. Our preliminary data demonstrate both that tamoxifen activates FOXOs and that serum starvation can sensitize breast cancer cells to tamoxifen treatment. These findings implicate FOXOs as potential mediators of the benefits of fasting-induced DSR in breast cancer. Our objective in this work is to determine whether FOXOs mediate the ability of fasting to both sensitize cancer cells and desensitize normal cells to tamoxifen.