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Harnessing the microbiome through probiotics administration to treat ER+ breast cancer

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Evidence has shown that breast tissue has a distinct microbiome, with different bacterial profiles existing between healthy women and those with breast cancer. Specifically, women with breast cancer have a higher relative abundance of E. coli and Staphylococcus bacterial species that cause DNA damage. Other studies have highlighted a reduction in beneficial probiotic Lactobacillus species in women with malignant breast cancer. Our group's preliminary data demonstrates that endocrine-targeted therapies, such as tamoxifen, also modulate the breast microbiome, suggesting specific bacterial species may potentiate the therapeutic responsiveness. Lactobacillus and Bifidobacterium, commonly found in over-the-counter probiotic supplements, may be useful in preventing breast cancer as well as potentially increasing tamoxifen efficacy. In addition, oral endocrine-targeting therapies in conjunction with probiotics may modulate breast tissue inflammation, a current risk factor for breast cancer. This study sought to determine the effects of probiotic conditioned media and 4-OHT (active metabolite of tamoxifen) on human ER+ breast cancer cell (MCF7 and ZR-75-1) and normal breast epithelial cell (S1) proliferation and protein expression. The effects of probiotic conditioned media on normal mammary cells mitochondrial respiration were also explored. In addition, immunohistochemistry (IHC) was performed on non-human primate mammary tissue to determine the correlation between breast probiotic bacteria abundance and immune cell infiltrate. Probiotic treatment was able to decrease breast cancer cell viability in a dose dependent manner. Higher doses (5-25%) lead to potent cell death responses in less than 24 hours, while lower doses (<1%) lead to a reduction in cell viability by 48 hours. IHC revealed differences in breast macrophage infiltration in tissues with higher probiotic bacteria abundance. Additionally, Seahorse assay showed alterations in mitochondrial function in normal mammary cells with Pro-CM treatment. Overall, these results demonstrate that probiotic conditioned media is able to reduce ER+ breast cancer, but not normal cell viability, as well as stimulate key anti-inflammatory immune responses in breast tissue. Moreover, probiotic conditioned media promoted mitochondrial respiration in normal breast epithelial cells suggesting key metabolic role of probiotic bacteria promoting breast health.