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Phytoalexin Glyceollin I Suppresses Viability in Her2+ Breast Cancer

For women worldwide, breast cancer (BC) ranks top 2 in both annual quantity of cases and deaths among cancers. Leading these statistics, developing new methods for combating breast cancer remains at the forefront of cancer research. Types of breast cancer are differentiated based on the presence of 3 receptors: estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor 2 (Her2). HER2+ BC targeted agents such as trastuzumab, pertuzumab, and lapatinib, alone or in combination with traditional chemotherapeutics, have become the standard of care for this BC subtype, significantly improving patient survival rates. However, the development of resistance to targeted therapy represents a major obstacle in the treatment of HER2+ breast cancer, highlighting a critical need to identify novel therapeutic targets to treat resistant HER2+ breast cancer.

Isoflavonoids, an important class of natural compounds produced from numerous plant sources including legumes, have been identified to be beneficial for human health. A member of the legume family, the soybean, maintains a high isoflavonoid content, specifically daidzein and stress induced derivatives called glyceollins. Recent studies have demonstrated glyceollin activity against ER+ breast cancer due to inhibition of ER and its associated pathways. To date the impact of glyceollins on other breast cancer subtypes has not been fully explored. Here, we utilized a panel of Her2+ breast cancer cell lines (HCC 1954, Au565, SKBR3), as well as derived trastuzumab-resistant variants (Herceptin resistant SKBR3), to evaluate the effects of glyceollin treatment, alone or in combination with other targeted agents, on cell viability and clonogenicity. Additionally, we analyzed changes in downstream gene expression using qRT-PCR profiler array for Human Cancer Pathways to define potential glyceollin-targeted pathways involved in the regulation of Her2 breast cancer cell biology.

Results demonstrated that glyceollin was able to decrease cell survival and colony formation across cell lines. Further glyceollin suppressed expression of pro-oncogenic genes in Herceptin resistant SKBR3 cell lines. Our preliminary findings provide support for a novel approach using isoflavonoids in the development of targeted therapy for Her2+ BC.