Inhibitor A: Targeting Therapeutically Resistant HER2+ Breast Cancer Tissues

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HER2 is a membrane bound protein receptor for cell proliferation. When present in excess, the cell divides uncontrollable and leads to cancer. This type of cancer is very prone to recurrence as it has two effective downstream pathways. Recurrent HER2+ tumors are often therapeutically resistant. Inhibitor A is hypothesized to overcome this resistance. This hypothesis was confirmed using Clonogenic Cell Survival Assays, Western Blots, and IHC of xenograft tumors. The clonogenic cell survival assay performed on the JIMT1 cell line, which has amplified HER2 oncogene and is therapeutically resistant to Trastuzumab and Pertuzumab, showed a 22% reduction in area coverage following treatment with Inhibitor A and a 100% reduction when treated with a combination of Inhibitor A and Lapatinib. Next, a western blot revealed that all treatments created PARP, a protein of apoptosis, but the combination treatment also created visible amounts of Cleaved-PARP. Finally, the IHC performed on JIMT1 xenograft tumors in nude mice revealed a decrease in Ki67 (protein for proliferation) of 39.2% for the tissue treated with Inhibitor A, and an increase in Cleaved-Caspase 3 (protein for apoptosis) of 1208%. The combination treatment had a decrease in Ki67 of 37.5% and an increase in Cleaved-Caspase 3 of 1275%. Combining this, the hypothesis is confirmed, but the combination treatment is revealed to limit proliferation and increase apoptosis more effectively than Inhibitor A alone. This can be continued in many ways, as clinical trials should begin soon.

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