PROJECT TITLE

A novel therapeutic strategy to target cancer cell survival and metastatic spread in breast cancer

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PROJECT SUMMARY

Treatment of breast cancer with surgery, radiation, chemotherapy, drugs designed to block specific cancer cell processes, or agents promoting anti-cancer immunity have improved outcomes for patients, but often fail to cure them because of the emergence of treatment-resistant cancer and metastatic spread to other organs, including the lungs, bone and brain. Treatment-resistant cancer emerges through adaptative changes in small subsets of cancer cells that allow them to survive therapeutic challenges. Even more dangerous, these adaptive changes often coincide with an enhanced ability of the surviving cancer cells to spread to other parts of the body. We have identified a protein that promotes both drug resistance and metastasis of breast cancer cells. This protein physically interacts with another protein which is also abundantly expressed in a subset of cancer cells which display increased drug resistance and metastatic potential.

Our research suggests that physical interaction between these two proteins is essential for cellular processes that promote cancer cell survival in response to chemotherapy as well as the metastatic spread of cancer cells. Furthermore, high levels of both proteins in tumors correlates with more aggressive disease and shorter survival in breast cancer patients. This leads to the hypothesis that drugs capable of blocking the physical interaction between these two proteins will prevent cancer cell resistance to chemotherapies and suppress their metastatic properties. We have developed a strategy to identify small molecules capable of blocking the interaction between these two proteins and develop one of these into a drug suitable for clinical use. Our preliminary work suggests that a drug that can effectively block the interaction of these two proteins in cancer cells will sensitize them to chemotherapies and suppress their metastatic potential, thereby enhancing the efficacy of currently used therapies when used in combination with them (e.g., chemotherapy and immunotherapy). This combinatory treatment strategy should improve treatment outcomes for breast cancer patients.