ROGEL CANCER CENTER
UNIVERSITY OF MICHIGAN HEALTH

Accelerating Targeted Therapeutics in Breast Cancer Research

Think Pink Rocks Breast Cancer Research Fund

Prepared for Rich and Wendy Nelson

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Scientific breakthroughs are built on a foundation of relentless research and iterative trial and error. In the quest for knowledge, it is often one innovative idea, after countless attempts, that shifts the paradigm and leads to monumental advances. This is especially true in the realm of medicine, where every new discovery can mean the difference between despair and hope, between stagnation and cure. At the heart of these transformative moments is the dedication of scientists like Dr. Stephen Weiss and his team, whose pioneering efforts are pushing the boundaries of what is possible in the treatment of breast cancer.

Stephen J. Weiss, M.D. is an internationally recognized leader in cancer biology, serving as the E. Gifford and Love Barnett Upjohn Professor of Internal Medicine and Oncology and Research Professor at the Life Sciences Institute. An elected member of the National Academy of Medicine and former Editor-in-Chief of the Journal of Clinical Investigation, Dr. Weiss completed his training at the University of Michigan and has served in pivotal leadership roles, including Chief of Molecular Medicine & Genetics and Interim Director of the Life Sciences Institute. His groundbreaking research centers on how aggressive cancer cells breach tissue barriers and metastasize, a focus that recently culminated in a fundamental shift in how we view breast cancer survival. Today, with the support of Think Pink Rocks, the Weiss Lab is putting that expertise into action, starting with a breakthrough that upends decades of cancer biology.

THE BREAKTHROUGH: A NEW PARADIGM IN BREAST CANCER GROWTH

In science, the most significant leaps forward occur when we re-examine long-held beliefs. For decades, the field assumed that invasive breast cancer cells used molecular "scissors," a surface enzyme known as MMP14, merely to cut a physical path through tissue scaffolds, clearing the way to metastasize throughout the body. While the debris left behind in these microscopic tunnels was historically dismissed as inert waste, Dr. Weiss and his team uncovered a major paradigm shift: breast cancer cells do not just destroy their environment — they harvest it. The cells actively internalize and metabolize these cut tissue fragments, utilizing them as a vital fuel source to sustain rapid growth even under severe nutrient stress. This unexpected vulnerability fundamentally transforms our understanding of tumor bioenergetics. By revealing how cancer weaponizes its own destructive pathway for sustenance, this discovery opens up entirely new therapeutic avenues to disrupt tumor metabolism, cut off its supply chain, and ultimately halt the spread of metastatic disease.

TRANSLATING DISCOVERY INTO ACTION

Understanding this survival mechanism has fundamentally redirected our research focus, opening targeted avenues that were previously invisible to the scientific community. Armed with new support, our laboratory is actively pursuing three critical objectives to turn this discovery into therapeutic strategies:

- **Decoding the Metabolic Pipeline:** We are mapping the precise biochemical pathway cancer cells use to internalize and process the cut matrix fragments, identifying how these structural proteins are successfully converted into cellular fuel.
- **Evaluating Blockade Efficacy:** We are testing the impact of interrupting this process, analyzing how starving cancer cells of their self-generated fuel source affect overall tumor growth and halts progression.
- **Targeting Secondary Vulnerabilities:** We are investigating what happens to cancer cells when their molecular "scissors" are disabled, seeking to exploit the resulting stress to discover new ways to selectively eliminate the vulnerable cells.

THE FUTURE OF CARE: REDEFINING METASTATIC BREAST CANCER TREATMENT

Looking ahead, this research holds profound promise for transforming how we manage advanced disease. Beyond unraveling the basic biology of metastasis, this work will provide critical, new insights into how breast cancer cells adapt, survive, and maintain rapid growth at distant metastatic sites. Most importantly, our findings aim to address one of oncology's greatest challenges: drug resistance. By mapping this novel metabolic pipeline, we expect to uncover therapeutic vulnerabilities that can be targeted using clever combinations of existing, FDA-approved drugs. Rather than waiting years to develop entirely new compounds, this strategy offers a faster, safer, and more direct pathway to clinical translation, giving new hope to patients whose tumors have proven resistant to current standard-of-care treatments. Through this crucial work, we are not just advancing scientific understanding; we are pioneering smarter, multi-pronged therapies designed to outsmart cancer's adaptability and ultimately save lives.



CREATING A LANDSCAPE OF HOPE

Every breakthrough in cancer biology, every new therapeutic avenue opened, and every patient impacted by the work of dedicated researchers like Dr. Weiss and his team brings us closer to a future where a breast cancer diagnosis no longer carries the fear of untreatable metastasis. Your commitment is not just accelerating scientific discovery, it is offering tangible hope and new possibilities to patients and their families. By exposing how aggressive cancer cells feed and survive, this work is forging new paths toward targeted treatments that cut off the disease at its source.

Philanthropic support is the cornerstone that bridges the gap between a revolutionary idea in the lab and a life-saving therapy in the clinic. It enables the Weiss Lab to push the boundaries of science, test bold hypotheses, and turn unexpected biological discoveries into clinical solutions. With your investment, Think Pink Rocks is contributing to a legacy of innovation, turning the promise of smarter, safer breast cancer treatments into a reality.

Your generosity can propel breast cancer research to new heights, enabling us to launch the next phase of critical discoveries. By thinking boldly and broadly, we can create a lasting impact that will benefit generations to come.

Thank you for the opportunity to explore the possibilities of this partnership. Together, we can lead the charge in shaping the future of healthcare, working toward a day when cancer no longer devastates the lives of individuals and families.

Together, we will find the answers and make a difference.