Memorial Sloan-Kettering Cancer Center

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Andrew B. Abramson
Cure Breast Cancer Foundation, Inc.
1122 Clifton Avenue
Clifton, NJ 07013

Dear Mr. Abramson,

I am delighted to update the Cure Breast Cancer Foundation on the ongoing work that the Foundation has supported. There are three projects, overseen by Dr. Norton, which relate to the self-seeding hypothesis. As a testament to the breadth of our collaboration, our team consists of clinician-scientists (Dr. Norton and myself), select laboratories (the Robert Benezra laboratory, the Joan Massagué laboratory, and the Ross Levine laboratory), as well as bio-mathematicians, statisticians, and physicists.

1. One of the key aspects of the self-seeding hypothesis is understanding not just the "seed" or cancer cells but also how cancer cells move throughout the body. In this respect, the microenvironment surrounding cancer cells or the "soil" is as important as the seed itself. In particular, other cells such as those associated with the immune system or blood vessel growth have been shown to critically determine how cancers spread. Groundbreaking research by the Robert Benezra laboratory at the Sloan-Kettering Institute demonstrated that a type of white blood cell, called "neutrophils," can be "trained" by a primary breast tumor to actually inhibit cancer spread to other vital organs. Despite experiments in the lab and in mice, little is known about how neutrophils function in cancer patients. We were the first to demonstrate a critical difference in neutrophils from patients versus healthy volunteers. Neutrophils isolated from the blood of newly diagnosed breast cancer patients were able to kill breast cancer cells in the laboratory whereas those from healthy volunteers were not. Our preliminary data was the first to show the potential power of neutrophils in decreasing metastasis; now, we aim to change the natural history of breast cancer by discovering the unique stimulants that drive neutrophil activation in breast cancer patients. We are working now to isolate the mechanisms by which neutrophils are activated to kill cancer cells by evaluating key components in the serum of breast cancers patients versus healthy women. This works lays the foundation for the stimulation of a patient's neutrophils to kill cancer cells as a means for preventing and/or treating metastasis. Ultimately, this project is the first step towards meaningfully manipulating the immune system as an effective barrier against breast cancer metastasis.

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2. As an additional step towards understanding how the immune system acts as either a fertile or inhospitable environment for cancer growth, we are also evaluating the relationship between select white blood cells that infiltrate primary breast cancers. Research conducted in the Ross Levine laboratory demonstrated novel genetic mutations associated with white blood cells in certain blood disorders and leukemias. We are now the first group to investigate whether some of these same mutations can play a role in the interplay between breast cancer and the immune system.

3. Lastly, as part of an exciting new collaboration, Dr. Norton and I are working with Charles Swanton, PhD (London Research Institute) and Peter Kuhn, PhD (Scripps Research Institute), to build new mathematical models to understand the complexity of tumor growth and self-seeding. Dr. Swanton is a world-renown expert in the heterogeneity of breast cancer and Dr. Kuhn is a bio-mathematician who builds unique models of cancer growth. Together, we are using images collected over time from over 400 breast cancer patients to understand where and how breast cancer spreads. We are using these images to build a predictive model of breast cancer growth—much like the way a Google search engine provides "top hits"—by which doctors and scientists may be able to foresee what organs, if any, a particular breast cancer may spread to next. Such a model would help guide research into the prevention of breast cancer spread to certain organs. In this way, by better understanding the trafficking of breast cancer, we hope to one day stop the spread of cancer in its tracks.

Thank you again for you ongoing support.

Sincerely,

Elizabeth Comen

Elizabeth Comen, MD