Memorial Sloan-Kettering
Cancer Center

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Mr. Andrew B. Abramson
Treasurer/Co-Founder
Cure Breast Cancer Foundation, Inc.
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Dear Andy,

December closes another terrific year of progress in our understanding of breast and related cancers. I would like to take this opportunity to summarize for you some of the highlights of the work you have supported in part the year. I would also like to thank the Cure Breast Cancer Foundation for its steadfast generosity, contagious enthusiasm, and inspirational encouragement. These are the fuels without which forward progress would be impossible.

The self-seeding concept of cancer growth revealed the critical role for white blood cells in both supporting and inhibiting breast cancer growth. In collaboration with the Professor Robert Benezra and colleagues, Dr. Elizabeth Comen and I are studying the ability of a very particular kind of white blood cell—cytotoxic neutrophils—to kill cancer cells. We have found that these neutrophils and the molecules that stimulate them, called chemokines, are present in the blood of women with breast cancer but not in women without cancer. Exactly how these cells are stimulated and how their presence contributes to a good prognosis is the basis for ongoing work. Furthermore, we are looking onto the possibility that we can give medicines to raise the level of these neutrophils so that cancers can be more effectively treated. Immunotherapy is one of the most excited new approaches to cancer medicine, and we feel that this work will add a significant new weapon to our armamentarium in that regard.

A closely related project—involving the renowned hematologist Professor Ross Levine and pathologists Drs. Edi Brogi and Hannah Wen and their colleagues in addition to Dr. Comen and myself—is studying the molecular make-up of a type of white blood cell called a lymphocyte. These cells infiltrate cancers of the breast and many other organs and actually stimulate their growth. We have made a highly significant discovery in this project, which we are about to submit for publication soon. This discovery will likely enable not only diagnostic tools, but also open entirely new avenues of cancer therapy. In fact, this work connects with the project you are supporting at Soroka Hospital in Israel, which as reported to you separately has found that the status of the bones relates directly to breast cancer incidence. The connection is that white blood cells come from the bone marrow, so signaling between bone cells and blood cells in formation,

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that eventually travel to and infiltrate cancers, might be keys to breast cancer biology. We expect that will have a lot more to say about this relationship in the coming year.

We are involved in many projects with several laboratories in MSKCC as well as collaborations with Rockefeller University and the Scripps Research Institute regarding the distant-seeding aspect of breast cancer, commonly called metastasis. Three of these are especially notable. With Professor Jorge Reis-Filho, recently recruited to MSKCC from London, we are studying how cancers evolve in their primary site (the breast) and in metastatic sites. Cancers tend to get more abnormal over time, accumulating mutations and other changes in their DNA. These cells also move around, both between tumors and back to the tumor itself, the essence of self-seeding. By tracking the changes in DNA in individual cancer cells from several sites simultaneously in individual patients we plan to monitor such movement as well as define the molecular mechanisms that make the cancer cancerous. This will open up many opportunities in diagnosis, prognostication (predicting the course of disease), and eventually therapy too.

Dr. Comen and MSKCC radiologists are collaborating with the biophysicist Professor Peter Kuhn in California in developing a mathematical understanding of breast cancer metastasis. MSKCC has detailed records for many hundreds of female patients including PET and other imaging data. With great effort to protect the confidentiality of the patients (as we always do, per MSKCC policy and legal requirements) we are examining these data to map patterns of spread. Results so far confirm the seeding concept in that the patterns elucidated cannot be explained without incorporating self-seeding. It is evident that this work and the work of professor Filho are synergistic.

Lastly, we are working with the Dr. Sohail Tavazoie laboratory in Rockefeller University to assess the relationship between miRNAs and exosomes—molecules derived from cancer cells found in the blood –and the geometry of cancer cells as measured on microscope slides and radiographic images. Cancer seeding has a direct influence on geometry, since more seeding produces more disorganized and denser masses. The goal here is to be able do interpret blood tests along with mammograms and MRIs to better predict who has cancer and who requires therapy. We want to make sure that nobody has to undergo surgery or other cancer treatment who does not need it and that nobody is denied therapy who does need it. The key here is better diagnosis and prognostication and we feel that this research is an important step in that direction.

Again, thank you and all the donors to the CBCF for all you do to help initiate and sustain such projects. This is a profoundly exciting time in breast cancer research. The relationship between the CBCF and MSKCC and its collaborators is contributing considerably to this excitement, leading toward what we all now believe as well as hope will be the end of breast and all cancers.

With Appreciation,

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