Memorial Sloan Kettering
Cancer Center

June 1st, 2016

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

Dear Andy:

With the generous support of the CBCF we have made significant progress in unraveling the enigma of cancer motivated by our discovery that cell movement is as important as cell division in malignant disease.

Drs. Comen, Kleppe, Reis Filho and Levine have established laboratory models to explore the impact of mutations in white blood cells that promote the growth of breast and other cancers. This laboratory is beginning to examine the mechanisms by which mutant white blood cells can stimulate the growth of cancer cells in contact with them. We have obtained samples from humans to further characterize the mutational status of cells other than cancer cells (with appropriate controls such as blood cells in circulation). We have a particular interest in patients who developed leukemia after breast cancer treatment, asking the question: did these leukemic cells pre-exist in the breast cancers before treatment?

Drs. Paty and Kolesnick are studying how to improve the killing of colorectal cancer stem cells by radiation so that more patients with rectal cancer can be cured by radiation and avoid rectal cancer surgery. Using stem cell technology they are able to grow human colorectal cancers from surgical specimens with a success rate of over 90%, and they can treat these tumor cultures with radiation. They have found that colorectal cancer stem cells from approximately 75% of patients are sensitive to radiation, whereas 25% are resistant for reasons that they are defining so that the resistance can be reversed.

An especially exciting discovery in this project is that the LGR5+ stem cell within the normal breast might well be the cell of origin for breast cancer. Using CRISPR/Cas9 genome editing technology they will determine if LGR5+ stem cells are the drivers of breast cancer metastases. This can well lead to new approaches to preventing breast cancer as a serious disease.

Dr. Hazan has made significant progress on defining the relationship between p21CIP1 expression and breast cancer stem cells and metastases. Involved are critical pathways for cancer cell mobility such as Wnt/β-catenin signaling , a gene called Frizzled 7 and other important molecules such as Axin, TCF4 and LEF1. Based on the results,

she plans to design inhibitors of the Wnt cascade to block p21 agonistic effects on Wnt signaling and thereby obliterate metastases.

The CBCF continues to support the study of bone integrity and breast cancer at the Soroka Hospital in Israel. In addition, this July the CBCF is holding an international think tank at a major meeting on human genetics in Haifa with a focus on the topic; "Should all people be tested for BRCA1 and BRCA2 mutations regardless of family history?" Obviously, the deliberations of this group could have a significant impact on public health in the area of breast and ovarian cancer prevention.

I emphasize—as I have in the past—that the support of the CBCF is essential in these and similar activities in that it provides for creative energy and innovative thinking at a time when our most pressing need is for new ideas. We thank you and all of your colleagues for allowing us to make progress toward the ultimate elimination of cancer from all of our lives.

Sincerely,

Larry Norton, M.D.
Deputy Physician-in-Chief, for Breast Cancer Programs
Medical Director, Evelyn H. Lauder Breast Center
Norna S. Sarofim Chair of Clinical Oncology
Professor of Medicine, Weill Medical College of Cornell University

Elizabeth Comen, MD
Assistant Attending, Breast Medicine Service