THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center
Making Cancer History®

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Elizabeth Ann Weathers Breast Cancer Research Fund
Community Foundation for Greater Chattanooga
1270 Market Street
Chattanooga, TN 37402

Re: Progress update and 2023 Grant

Dear David Tenenbaum - Fund Advisor,

I would like to personally thank The Elizabeth Ann Weathers Breast Cancer Research Fund for its generous support of our research focused on using single cell sequencing technologies to understand the progression of breast cancer and how to overcome resistance to therapy during treatment. Unlike our limited funding support from NIH which supports low-risk projects, the funding Ann Weathers has provided allows us to focus more on high-risk/high-reward projects that are more likely to make an impact on both patient care and scientific knowledge of breast cancer in a more rapid timeframe. The last year has been incredibly productive in our lab, and we have made huge progress on two breast cancer projects.

Our first project has focused on understanding the progression of the most common form of early breast cancer (Ductal Carcinoma In Situ) that is routinely detected during annual mammography,and its progression to invasive breast cancer. Understanding which DCIS patients progress to invasive breast cancer is very important, since only about 10-30% will ever progress during their lifetime, and currently all women are being treated aggressively, including many women who do not need treatment with radiotherapy, chemotherapy or hormonal therapy. Using single cell DNA-seq methods we have profiled 10 women that had DCIS breast cancer and an invasive recurrence that occurred 2-10 years later and identified genomic biomarkers that are associated with disease progression and recurrence. Our future work in expanded studies in more women will allow us to develop better diagnostics to predict which women are likely to progress to invasive disease, and therefore require aggressive treatment, while other women can elect 'watchful waiting' or active surveillance without treatment after their surgery.

Our second project has focused on understanding chemotherapy resistance in Triple-negative breast cancer (TNBC). By leveraging clinical biopsy samples from a large trial (360 women) in collaboration with the Breast Medical Oncology (BMO) department called ARTEMIS we have used single cell RNA sequencing methods to study the differences between patients that have complete response to therapy and good overall survival, compared to patients that are non-responders. Our data from 101 patients, has identified many gene expression changes in both the cancer cells and their surrounding cell types that can be used to predict which patients are likely to respond to chemotherapy and which patients should seek alternative treatment strategies. We are in the processof writing up a major scientific publication based on this work.

Finally, in new news I recently became the chair of a new department (Systems Biology). In this new leadership position, I will continue to lead our efforts to study breast cancer and develop newtechnologies for cancer research and clinical translation. We plan to recruit new faculty and lab personnel to expand these efforts, now at a larger scale of a whole department. I am very grateful foryour generous support of our research in breast cancer, and truly enjoyed meeting you over zoom about a year ago. I would love to invite you to visit our lab and new department if you ever plan to bein the Houston area.

Warm regards,

Nicholas Navin
Professor & Chair
Department of Systems Biology