

**2020 RECIPIENTS OF THE HILLCREST
COMMITTEE CANCER RESEARCH AWARD**





**KNIGHT
CANCER**
Institute

Hillcrest Committee

Cancer Research Award 2020

Project Description: Activation of immunogenicity cell death pathways in colorectal cancer using radiation-enhancing nanoparticles

Treatment with immune modulating/activating drugs has revolutionized cancer therapy over the past decade. We are now able to extend the lives of many patients with lung cancer, melanoma, and colorectal cancer far beyond what would have been achievable only a few years ago using drugs that increase anti-tumor immune activity. These drugs can be used alone or in combination with radiation and chemotherapy to achieve these improved results.

However, there are many tumor types which have not yet proven to be amenable to treatment with immune modulating drugs. Recently, there has been laboratory and early clinical data showing that if tumors are injected or infused with microscopic particles of metals such as gold or platinum prior to radiation therapy the radiotherapy is more effective at killing what would otherwise be treatment resistant tumors. The goal of this work is to understand how and why tumor cells die following combination treatment with nanoparticles and radiation so that we can combine these treatments with appropriate immune modulating agents in future clinical trials.



Josh Walker, M.D., Ph.D.

I am a physician scientist who practices radiation oncology and I have a basic science laboratory where we utilize mouse models of colorectal cancer to evaluate the interplay between radiation therapy and immune modulating treatments.

I have studied how the body is able to use the immune system to respond to viral infections and cancer for the last 20 years in many different roles as trainee, principal investigator, and clinician. My research group is currently exploring ways of engineering anti-tumor immune responses by combining nanoparticle therapy with high dose radiotherapy.

May 6, 2021



Josh Walker

Assistant Professor
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Dear Hillcrest Committee Members,

Thank you so much for your generous support of my research program studying the effects of gold nanoparticle treatment combined with radiation therapy in colorectal cancer models. Your generosity is enabling my research group to pursue a series of experiments which would not have otherwise been possible without your support.

I am a physician scientist at OHSU who practices radiation oncology and I have a basic science research laboratory where we explore the role that radiation therapy can play in augmenting anti-tumor immune responses in cancer. In my lab we utilize nanoparticles to deliver drugs, deliver gene therapy, or (in the case of the research you are supporting) deliver radiation sensitizing metals to the tumor.

The support you have provided is allowing my group to study how tumor cells die following combination treatment with gold nanoparticles and radiation. There is already evidence in preclinical models and from human trials that combining nanoparticle therapy with radiation results in increased tumor cell death and response to treatment. The goal of our current work is to utilize advanced microscopy techniques following these combination treatments to understand how and why the cancer cells are dying so that we can combine these treatments with immunotherapy. Our hypothesis is that combination therapy with gold nanoparticles and radiation will result in increased immune response to the tumor which can then be amplified by delivering immune modulating therapies to the animals in our experiments. The goal of this work is to understand which immunotherapies will work most effectively with radiation and nanoparticle therapy so that we can treat radiation resistant tumors (such as sarcoma) more effectively.

I had the opportunity to read through your website and I'm impressed by the extensive fundraising and philanthropic activity your group participates in each year. Your dedication in supporting cancer research, your support of pediatric and adult cancer patients, and the role you play in your community are all admirable. Your philanthropy is enabling me to dedicate personnel and resources to a research project which has the potential to inform future clinical trials and change the way we treat radiation resistant tumors. Please know you are investing in the ever-important and necessary basic research that catapults and sustains progress in cancer research well into the future. Your dedication to cancer research and therapy is appreciated and your impact will be felt by those we care for.

Sincerely,

A handwritten signature in black ink, appearing to be "Josh Walker", with a long, sweeping horizontal line extending to the right.

Josh Walker



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Cancer Research Award 2020

Project Description: Single cell characterization of PTEN;MYC triple-negative mouse tumors

Triple negative breast cancer (TNBC) represents between 15 to 20 percent of diagnosed breast cancers cases and though it kills faster than other types of breast cancer, it has few effective treatment options. The median survival for patients with metastatic TNBC, many of whom are women younger than 50 years old, is about one year. There is therefore an urgent need for more effective treatments for patients with this disease. A deeper understanding of the molecular basis of this disease would aid in development of effective therapeutic strategies. We have recently developed a mouse model of TNBC which has many of the same qualities as observed in patient samples. We propose here to study this mouse model to learn about the differences between different types of TNBC tumors. We will study individual cells from different mouse tumors and examine both the cancer cells and the cells surrounding the cancer cells that help the tumor to grow and resist therapy. This information will be used to identify therapies that could be used to treat patients with different types of TNBC tumors, and will also provide information about how different cells in a tumor contribute to disease.



Dr. Laura Heiser, Ph.D.

Dr. Heiser is Associate Professor and Vice Chair of the Department of Biomedical Engineering and co-Leader of the Knight Cancer Institute Quantitative Oncology Program. Her laboratory is focused on understanding the phenotypic and molecular responses of cancer and normal cells to diverse stimuli including small molecule inhibitors and growth factors. She has had leadership roles in the development of international DREAM challenges and was the sole leader of a multi-center LINCS “Common Project” designed to deeply profile the dynamic molecular and phenotypic responses of mammary epithelial cells to diverse microenvironmental factors.



Dr. Rosalie Sears, Ph.D.

Dr. Sears is a professor in the OHSU Department of Molecular and Medical Genetics and holds the Krista L. Lake Chair in Cancer Research. She is Co-Director of the OHSU Brenden-Colson Center for Pancreatic Care and a senior member in the Knight Cancer Institute. She received her Bachelor's degree in Biology from Reed College, her Ph.D. in Cell Biology from Vanderbilt University and conducted her post-doctoral studies at Duke University prior to coming to OHSU in 2001. Dr. Sears' research expertise is in cellular signaling pathways that control tumor cell phenotype and tumor stromal cross talk. She is working on novel therapeutic strategies that are being tested in innovative patient-derived models cancer.

May 6, 2021

Dear Committee Members,

Thank you for your generous support of our project on triple negative breast cancer (TNBC) entitled "Single cell characterization of PTEN;MYC triple-negative mouse tumors". Your funding enables us to continue work that is vital toward developing effective therapies for a disease that continues to be one of the most fatal forms of cancer.

Dr. Sears and I bring decades of experience in cancer biology to this exciting project. Dr. Sears is a cancer biologist with expertise in mouse models, tumor heterogeneity, and the tumor microenvironment, and I am a cancer systems biologist with expertise in data integration, single cell analyses of cancer, and studies of therapeutic response.

Your support allows us to tackle one of the biggest challenges in cancer biology – investigating why tumors resist therapy – and to therefore make vital progress toward developing treatments and saving lives. By understanding the molecular basis for TNBC, we hope to better understand why TNBC tumors don't respond to current standard treatments. We believe tumor heterogeneity – meaning differences both within one tumor and between tumors in the same body – is at the core of what we need to target to develop TNBC treatments. In this project, we will investigate tumor heterogeneity by using a novel mouse model we have developed that imitates multiple subtypes of TNBC and the different tumors the disease produces.

There are few effective treatment options for TNBC patients, and even when patients initially respond to therapy, resistance frequently arises. The research you are funding aims to make that reality a thing of the past. Your support will continue to make a powerful impact on our research for years to come as the preliminary data from this project will be used as the basis for another major federal funding application.

By supporting our research, you have made possible a project that could have far reaching impacts on the field of cancer biology and ultimately may help us to identify treatment strategies that can improve outcomes for patients with this devastating disease.

Thank you for your dedication to this cause.

Sincerely,



Laura Heiser, Ph.D.



Rosalie Sears, Ph.D.



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