



Timeline of Achievements The Swim Across America Lab at Johns Hopkins

2011 – With funds raised in the inaugural Swim Across America Baltimore, the Swim Across America Laboratory was established at the Hopkins Kimmel Cancer Center, dedicated to understanding human cancers and formulating effective patient care. The primary objective of the lab is to translate laboratory science “from the bench to the bedside” and bring the science closer to the patient. Support from Swim across America is invaluable to projects that involve cancer re-search and patient care. Appointed to direct the lab is Luis Diaz, M.D.

2012 – Swim Across America Baltimore funded, among numerous projects, an important therapeutic trial for patients suffering with pancreatic cancer. Also, genomic sequencing was accomplished on pediatric brain tumors. A colon cancer survivorship clinic was established that helps patients through their journey with cancer. Additionally, the first couples retreat for patients with metastatic cancer took place that allowed couples to connect and share with each other and learn from Johns Hopkins experts.

2013 – Swim Across America funded groundbreaking research in endometrial and ovarian cancers that garnered world-wide attention. The Papgene Test study was a significant advance that promises early detection of these two deadly cancers. It is based on the Pap test, routinely performed since the 1950’s in gynecologists’ offices across the country to de-tect and prevent cervical cancer. The PapGene test captures DNA that is shed from cancer cells that have been deter-mined to lead to endometrial and ovarian cancers, according to Dr. Diaz and his colleagues. There are currently no screening tests for these cancers, and the new test could one day make it possible to test for three female cancers at a woman’s wellness exam.

2014 – Swim Across America Lab Director Luis Diaz, M.D. was a senior author on an international study that provides strong evidence that that circulating tumor DNA (ctDNA) can be used as a "personalized biomarker" test and cancer screening tool. It is an extrapolation of the PapGene Test study which was made possible in part through funding from Swim Across America last year. According to results of the study, certain fragments of DNA shed by tumors into the bloodstream can potentially be used to non-invasively screen for early-stage cancers, monitor responses to treatment and help explain why some cancers are resistant to therapies. The study "provides a wealth of information on the potential utility and limitations of ctDNA measurements to assess patients with various cancers," according to Diaz.

2015, 2016 and 2017 - Monies from SAA Baltimore funded groundbreaking research in immunotherapy. In a report of a proof-of-principle study of patients with colon and other cancers for whom standard therapies failed, researchers at the Johns Hopkins Kimmel Cancer Center saw that mistakes in so-called mismatch repair genes, first identified by Johns Hopkins and other scientists two decades ago, may accurately predict who will respond to certain immunotherapy drugs known as PD-1 inhibitors. Results of the trial with pembrolizumab, marketed as Keytruda, was published by the New England Journal of Medicine on June 25, 2015. On May 23, 2017 the U.S. Food and Drug Administration granted accelerated approval to a treatment for patients whose cancers have a specific genetic feature (biomarker). This is the first time the agency has approved a cancer treatment based on a common biomarker rather than the location in the body where the tumor originated.

We have also continued our patient outreach and survivorship program for patients with colorectal cancers. This clinic is run by our nurse coordinator and has been visited by dozens of patients through their journey with cancer. Lastly, we are supporting an internship program to work with the Swim Across America Lab research team. They are integral in the daily activities of the SAA laboratory. We hope to continue this important program that introduces young people to science and medicine with the support of SAA.

2018 – A number of exciting projects were launched in neuroendocrine, pancreatic, prostate and lung cancers, and leukemia.

Dr. Katie Bever is studying a rare type of aggressive cancer known as high grade neuroendocrine carcinoma or small cell carcinoma. She is specifically interested in studying the host immune response to these cancers and plans to perform analyses of banked tissue samples, with the ultimate goal of identifying targets for novel therapies to serve as a basis for future clinical trials in these patients.

Dr. Jonathan Webster knows that targeted therapies have become a major component of treatment in many different cancers and have led to significantly improved survival in a number of poor-risk leukemias. However, when treated with targeted agents, these leukemias disproportionately relapse in the central nervous system (CNS). In Dr. Webster's study he seeks to better understand how well these targeted therapies enter the central nervous system and how effective they are in hitting their target when they get there.

Dr. Dung Le is continuing her multi-agent chemotherapy clinical trial for pancreatic cancer. She has found that multi-agent chemotherapy regimens such as FOLFIRINOX and gemcitabine/nab-paclitaxel have demonstrated a survival benefit over single-agent chemotherapy in metastatic pancreatic cancer, and it is likely that multiple agents are necessary to delay the emergence of resistant populations and disease progression. Dr. Le's study is testing the safety and activity of,

and determining the maximum tolerated dose of, the combination gemcitabine, nab-paclitaxel, capecitabine, cisplatin and irinotecan in treatment of previously untreated metastatic pancreatic cancer.

Dr. Valsamo “Elsa” Anagnostou’s SAA funded study is using non-invasive dynamic genomic analyses of circulating tumor DNA (ctDNA) to develop a liquid biopsy assay predictive of response and resistance to combination epigenetic therapy and checkpoint blockade in non-small cell lung cancer (NSCLC) patients. This study will provide an innovative combination of genomic and immune analyses and the basis for novel molecular approaches for identifying patients that would respond or develop resistance to immune checkpoint blockade. If successful, this study will lead to the development of a predictive immunogenomic assay capable of assessing dynamic responses to cancer immunotherapy and expedite clinical translation through tailored cancer immunotherapy strategies and novel approaches to clinical trial design that could be immediately implemented in health care decisions within the next 5 years.

Dr. Woonyoung Choi is studying biological mechanisms in prostate cancer in hopes of distinguishing lethal intermediate-risk tumors from the ones that will never pose a significant threat to the patient. This research will seek to determine whether intrinsic molecular subtypes exist in human prostate cancers. If so, their discovery will help to define candidate biological mechanisms driving molecular heterogeneity in prostate cancer, improve prognostication, and identify novel targets for therapeutic intervention.

2019 – Two new research projects were launched at the Kimmel Cancer Center focusing on colon cancer, and the immune system’s role in lung cancer.

Franck Housseau, Ph.D., associate professor of oncology at the Johns Hopkins Kimmel Cancer Center and the Bloomberg~Kimmel Institute for Cancer Immunotherapy, is focusing on whether adding a third checkpoint inhibitor drug (IL-17) to a combination of two others might prove to be effective in activating a patient’s immune system to fight colorectal cancer.

A subset of colon tumors have markers that suggest they are evading the immune system by locally suppressing it, triggering intense interest in using a new class of immunotherapeutic drug known as checkpoint inhibitors to fight it. However, these drugs haven’t been effective on their own.

To boost their efficacy, researchers have tested adding in a second drug known as an IDO1 inhibitor, which might inactivate the cancer cells’ immunosuppressive activity. Though promising in early clinical trials, this approach recently failed in a larger phase III trial. His work adding a third checkpoint inhibitor drug to the mix will examine the immune and metabolic activity in samples of human colorectal cancer and test IL-17 inhibition in an animal

model. This work could eventually lead to a new approach to effectively treat some types of colorectal cancer.

Kellie Smith, Ph.D., assistant professor of oncology at the Johns Hopkins Kimmel Cancer Center and the Bloomberg~Kimmel Institute for Cancer Immunotherapy, and her team developed a lab test, called MANAFEST, that identifies which cancer-specific proteins can be recognized by immune cells called T cells. However, this approach doesn't show which genes are active in these cells, which could offer further insight on their activity.

Her new study will integrate these two methods, linking tumor-specific proteins with the genetic activity of the T cells that respond to them. Using this combined approach, she and her colleagues will test the blood of patients with non-small cell lung cancer whose tumors were surgically removed to better understand how their T cells fight tumors. They'll also develop full gene expression profiles of the T cells that respond to cancer-specific proteins to better understand the genetic program that activates the immune response. The abundance of data that this approach provides could eventually help researchers develop better ways to harness and boost the cancer-fighting capabilities of the immune system.

2020 – Three new projects have been launched this year thanks to SAA Baltimore grants.

Patrick A. Brown, M.D., is Associate Professor of Oncology and Pediatrics, and Director of the Pediatric Leukemia Program at the Johns Hopkins Kimmel Cancer Center. Dr. Brown and his team will perform state of the art immunoassays to address the basis of response and resistance to blinatumomab. This study will evaluate the bone marrow and peripheral blood prior to and during exposure to blinatumomab in a large number of pediatric B-ALL patients. They hypothesize that patient-specific innate and adaptive immune cell subsets determine response to blinatumomab, and that characterization of these components will allow for the development of a biological model to accurately predict response to blinatumomab and define mechanisms of resistance, leading to a rational combinational approach to improve response rates.

Rajarsi Mandal, M.D., Assistant Professor of Otolaryngology-Head and Neck Surgery at the Johns Hopkins Kimmel Cancer Center will undertake an in depth analysis of HNSCC human tumors and patient-derived organoids (PDO's) in pre/post anti-PD-1 neoadjuvant immunotherapy. They hypothesize that the interrogation of both the HNSCC tumor samples and their corresponding organoids at the genomic, epigenomic, transcriptome, and protein levels will help elucidate the poorly understood mechanisms of immunogenicity and immune escape in these tumors. The rationale is that an understanding of the mechanistic basis of variable adaptive resistance to checkpoint blockade will aid in patient selection for immune-based therapies not only in HNSCC but across a number of cancers, and will also facilitate developing rational combination therapies/clinical trials targeting these specific mechanisms of resistance.

Brian Ladle, M.D., Ph.D., is Assistant Professor of Oncology and Pediatrics at the Johns Hopkins Kimmel Cancer Center. The SAA grant provides an opportunity for Dr. Ladle and his team to investigate the immunology and translational applications of cryotherapy and intratumoral STING agonist therapy in canine osteosarcoma – which many consider an optimal pre-clinical model for pediatric osteosarcoma. The study will compare the impact of MRI-guided cryoablation of canine OSA tumors alone, CT-guided intratumoral STING agonist injection alone, and the combination therapy of both, which will couple the immune activating capabilities of both modalities. Rigorous immune analysis and clinical outcome measures will direct the next steps toward a human clinical trial.



Work also continues this year by three Kimmel Cancer Center physician scientists on grants funded by the 2018 Swim Across America. **Dung Le**, whose seminal research has earned worldwide attention, has designed additional innovative studies in pancreatic cancer for 2020, thanks to SAA funding since 2014. **Kellie Smith** and **Franck Housseau** are continuing their immunotherapy research in lung cancer and colon cancer, respectively, in 2020. Kellie and Franck are in the second year of two-year funding grants.