



Our Funding at Work:

Indiana University // Paul Macklin, PhD

Over several years of collaboration across JKTGF-funded projects, the Macklin lab has developed a new analytic architecture to create “virtual laboratories” where teams can rapidly run simulated experiments to understand how cancer and immune cells interact to drive growth, metastasis, and response to therapies. The lab created a modeling language that allows scientists without bioinformatics or programming training to write intuitive, “human language” cell rules that are automatically translated into simulation models. This *open source* work enables broad use and continuous improvement by the scientific community. In 2027, this work will expand into a new center for cancer simulation modeling focusing on developing “digital twins” to forecast and improve patient-specific therapy responses ultimately accelerating discovery.

Johns Hopkins University // Andrew Ewald, PhD

Understanding and targeting reactive oxygen signaling during breast cancer metastasis. This project examined how reactive oxygen levels change within breast cancer cells as they spread through the body. We discovered that we could prevent metastasis by disrupting specific reactive oxygen control machinery in the cancer cells. This work led to two major NCI grants and a series of high-profile publications on the molecular regulation of breast cancer metastasis.

Johns Hopkins University // Daniele Gilkes, PhD

This project investigates why some breast cancer cells are able to survive and grow in the liver, where metastatic disease is especially difficult to treat. We hypothesize that low oxygen exposure in the primary tumor leaves a lasting “memory” that helps tumor cells adapt to the metabolic and oxidative stresses of the liver. The study may identify AKR1C-mediated detoxification as a key survival mechanism that enables already disseminated cancer cells

(Johns Hopkins University // Daniele Gilkes, Ph.D., continued)

to persist and expand in this liver. If successful, this work could reveal a new therapeutic vulnerability and support the development of more targeted treatment strategies for metastatic breast cancer. Ultimately, the goal is to move toward more effective, biology-driven therapies for patients whose disease has already spread.

Johns Hopkins University // Robert Ivkov, PhD

Through a series of JKTF-funded projects, this work explores the use of nanoparticles for the detection and treatment of breast cancer tumor(s). Nanoparticles attach to cells near tumors and, when exposed to a magnetic field, can either emit signals for detection or generate heat to kill cancer cells. Nanoparticles are often taken up by inflammatory immune cells associated with clusters of BC cancer cells. We believe that may enable identification of metastatic sites and are researching further. In addition to detection and therapy, the particles can be used to deliver chemotherapy directly to tumors. Early findings also suggest nanoparticles can simulate the immune system, shifting toward an anti-tumor response. Research is ongoing here as well with the goal of optimizing therapeutic impact.

M. D. Anderson Cancer Center // Hekio Enderling, PhD

This work applies mathematical modeling to better understand and treat cancer across three areas. First, the team is developing models to predict patient-specific responses to intermittent hormone therapy in prostate cancer, helping guide when to pause and resume treatment. Second, this work is identifying tumor growth patterns that define both primary and metastatic tumors, using differential equation and calibrated model parameters. Using model selection metrics, we identified that Gompertz growth with a shared carrying capacity parsimoniously described the pan-cancer experimental data. The third project tackles a major problem in oncology: lack of sufficient biomarkers to predict how an individual patient will respond to different treatment options. Using routine biopsy tissue, the team extracts additional insights on tumor growth and invasion creating the first opportunity to calibrate mathematical models of cancer therapy and predict how a patient will respond to available treatment options.

Oregon Health and Science University // Laura Heiser, PhD

This project aims to build a “virtual tumor” for triple negative breast cancer that captures both cancer cells and their surrounding environment. By simulating how these components interact, the model can predict how tumors will respond to single drugs or combination therapies. Importantly, the work recognizes that treatments can reshape the tumor’s environment, influencing long-term outcomes. This approach enables efficient identification of effective treatment strategies, prioritizing the most promising options for real-world testing and accelerating development of improved treatments for patients with aggressive breast cancer.

University of North Carolina-Chapel Hill School of Medicine // Charles Perou, PhD

This work focuses on triple negative breast cancer, which has a high risk of metastasis, particularly to the lungs and liver. We are focused on developing computational models to predict metastatic potential for individual patients and using these insights to guide new therapies that target metastasis drivers. Early models predict lung/liver metastasis risk and are being validated across additional datasets. The work also implicates the RAF-RAF-MEK pathway as a driver of metastasis with ongoing studies evaluating targeted inhibition. This research will inform treatment decisions and improve progression-free survival for patients.