



Dear Friends, Board Members, and Supporters of the Harold E. Eisenberg Foundation:

For nearly 25 years, the Harold E. Eisenberg Foundation has been a remarkable partner to the Robert H. Lurie Comprehensive Cancer Center of Northwestern University. We remain truly grateful for the Harold E. Eisenberg Foundation's commitment to fund breakthrough research to fight gastrointestinal (GI) cancers and increase survivorship, while honoring the memory of Harold Eisenberg.

Fueled by life-changing research, our Cancer Program at Northwestern Memorial Hospital is again ranked among the nation's top 10 by *U.S. News & World Report* in 2022-2023 and continues to be the top Cancer program in Chicago and Illinois.

We are pleased to share this report with highlights on our Gastrointestinal Oncology Program and Harold E. Eisenberg Foundation GI Cancer OncoSET Program, as well as updates on the research of past recipients who received Harold E. Eisenberg Research Scholar Awards.

As we move forward in our campaign to raise \$100 million in philanthropic dollars, we recognize and value the support and commitment from our community of wonderful donors, advocates, and friends. Thank you for all you have done and continue to do to raise awareness and funds to advance life-saving cancer medicine.

With gratitude,

Leonidas C. Platanias, MD, PhD

Jesse, Sara, Andrew, Abigail, Benjamin, and Elizabeth
Lurie Professor of Oncology
Director, Lurie Cancer Center

Al B. Benson III, MD, FACP, FASCO

Professor of Medicine (Hematology and Oncology)
Associate Director, Cooperative Groups, Lurie Cancer Center



Harold E. Eisenberg Foundation GI Cancer OncoSET Program

OncoSET

OncoSET harnesses the power of precision medicine to identify tailored therapies for patients based on the abnormal genes specific to their tumor. Following three vital steps—Sequence, Evaluate, and Treat—this breakthrough program targets tumors from any type of cancer that is not responsive to standard forms of treatment. The Harold E. Eisenberg Foundation GI Cancer OncoSET Registry continues to enroll patients with GI malignancies. A total of 487 patients have enrolled who have cancers of the esophagus, pancreas, stomach, liver, small intestine, colon, rectum, anus, and other digestive organs. Over the past year, we have worked to implement some changes that will enhance the study. This includes amendments that will allow patients to enroll electronically, and when from away from clinic, rather than having to wait for their next appointment. We also have added a different type of blood collection that will capture plasma in a way that allows evaluation for minimal residual disease (MRD). Detection of MRD is a new forefront in the management of GI malignancies. Together these changes will make the study significantly more impactful.



Clinical Trials Update

In the past year, there have been 171 GI patients accrued to correlative, diagnostic, supportive care, and treatment trials at Lurie Cancer Center. The majority of these patients have been enrolled to interventional trials that include Phase I, II, III, and pilot studies. A total of 69 trials have been open to accrual for this population in the last year. Also, we have added our Northwestern Medicine Northwest and South Regions (McHenry, Huntley, Grayslake, Glenview, Orland Park, and Palos Park Hospitals)

as network sites for our National Cancer Institute trials so that patients can have access to novel therapies closer to home. This is in addition to already having Lake Forest and West Region (Central DuPage, Warrenville, Proton Center, and Kishwaukee) sites open to accrual for National Cancer Institute trials as well as some investigator-initiated trials.

Spotlight on GI Oncology Research Nurses

Heidi Ray, RN, BSN, OCN, works at the Lurie Cancer Center as the clinical operations coordinator in the Infusion Suite. Heidi assists with the daily clinical needs of staff and patients. Heidi has worked in oncology since becoming a nurse in 1981. Recently, Heidi became the clinical contact for the Eisenberg Foundation care packages. The care packages are hand delivered to new patients with GI cancers who are beginning therapy. Heidi shares: “New patients are extremely anxious about beginning therapy, but after I introduce myself and deliver these fabulous care packages, they seem to take a deep breath.”

Focus on Precision Medicine

Over the past few years, Lurie Cancer Center has partnered with technology companies in the area of GI cancers, specifically colon cancer. Using the Harold E. Eisenberg GI Cancer Tissue Bank, these partners have helped complete next-generation sequencing of 500+ of our colon cancer cases. With these results, our physicians and scientists will have both pathology and genomic characterizations of 500+ colon cancer samples. The data are compiled by our Cancer Informatics team and our Quantitative Data Science Core Facility and then used by investigators to help guide new research questions.

In addition to the next-generation sequencing, Lurie Cancer Center has collaborated to create organoids from gastrointestinal cancer over the past few of years. Organoids provide a detailed view of how organs form and grow, which can also provide new insights on human development, disease, and treatment options. Drug interaction with these “mini-organs,” can potentially revolutionize the field of drug discovery and open new approaches to personalized medicine.

Over the past year, we have continued creation of Tissue Microarrays (TMA) of colon cancer cases with next generation sequencing data, various clinical data, and outcomes. Tissue MicroArrays contain small representative tissue samples from potentially 700+ cases within the

Bringing Breakthroughs to Patients

same paraffin tissue block that allows high throughput analysis of multiple patient tissue samples at the same time. MicroArrays have various uses, including analysis of diagnostic, prognostic, and new treatment predictive biomarkers. Additional efforts over the past year involve digital pathology, which is the process of digitizing the tissue bank's glass slides using a whole slide scanner, enabling quantitative analysis of histological tissue images. These collaborative efforts would not have been possible without the Harold E. Eisenberg Foundation Tissue Bank, which provided many of the tumor samples for these forward-thinking partnerships.

26,949

specimens
in tissue bank

1,507

patients
contributed

Past Research Scholar Updates

Through the prestigious Harold E. Eisenberg Research Scholar Award, our dedicated scientists can continue to explore new ideas aimed at discovering cures for GI cancers.

Arthur Prindle, PhD

2022 Scholar

Area of focus: Inflammatory bowel disease therapy



Integration of synthetic biology into clinical practice promises to be a transformative approach to modernizing disease diagnosis and monitoring. In particular, inflammatory bowel disease (IBD) is a spectrum of chronic inflammatory gastrointestinal diseases that is difficult to monitor due to the relapsing and remitting nature of disease flares that often result in downstream complications. We have successfully demonstrated proof-of-principle for our probiotic IBD diagnostic using animal models and human patient samples. This work is currently in revision at *Proceedings of the National Academy of Sciences* after receiving positive reviews. We are planning to submit a patent application and continue developing this probiotic diagnostic to improve noninvasive readout, integrate temporal recording of IBD biomarkers, and potentially add therapeutic capabilities with nanobody

production. Identifying active IBD and intervening to control the disease is an important effort to reduce the risk of colon cancer in IBD patients. In addition, we have received other pilot funding for related work from the American Society for Gastrointestinal Endoscopy and are currently preparing an National Institutes of Health (NIH) R01 application based on this Eisenberg-supported pilot study.

Jonathan Xia, MD, PhD, is a Physician-Scientist Training Program fellow in Dr. Prindle's group who led this work. Dr. Xia has presented at Digestive Disease Week 2022, secured a 2022 American Society for Gastrointestinal Endoscopy research award, and will be moving on to the next stage of his career in the next year.

Devalingam Mahalingam, MBBChBAO

2021 Scholar

Area of focus: Metastatic colorectal cancer therapy



B-Raf mutated colon cancer constitutes eight to ten percent of all colon cancer patients. Patients with B-Raf mutated advanced colon cancer have worse overall survival. The Food and Drug Administration has approved the doublet therapy of encorafenib (B-Raf inhibitor) and cetuximab (anti-EGFR therapy) combination (EC) in BRAF V600E-mutated metastatic colorectal cancer, although the efficacy remains modest. Based on previous work in B-Raf inhibitors in melanoma, acquired resistance to therapy results in disease progression. Autophagy induction may lead to resistance to this therapy. Our group has worked extensively on autophagy modulation to overcome resistance to novel cancer therapeutics, using the autophagy inhibitor hydroxychloroquine (HCQ), through National Institutes of Health/Cancer Prevention and Research Institute of Texas-funded clinical studies. HCQ is a cost effective anti-malarial and anti-lupus drug. Based on some clinical efficacy of addition of HCQ to B-Raf inhibitors, observed in B-Raf mutated melanoma patients we wanted to evaluate this in colon cancer.

The goal is to show that the addition of HCQ may results in better tumor responses and duration of therapy with B-Raf inhibitors in colon cancer.

The study opened at the end of 2022 and has enrolled two patients. Given this rare mutation, we anticipate one patient enrolled every two months. To date, both patients are tolerating therapy and remain on study.

Investing in Top Scientists

Research Scholar Update *continued*

Beatriz Sosa-Pineda, PhD

2020-2021 Scholar

Area of focus: Immunotherapy for pancreatic cancer



Pancreatic ductal adenocarcinoma (PDAC) has one of the worst cancer survival rates worldwide. Tumor heterogeneity, lack of early detection, and limited therapeutic options are major challenges to overcome. Dr. Sosa-Pineda seeks to understand how the unique biological repertoire of distinct PDAC subtypes impacts tumor development, tumor metastasis, and therapeutic responsiveness. She is interested in dissecting the role of the transcription factor ONECUT2 in PDAC. ONECUT2 controls malignancy in many cancers and is highly expressed in metastatic PDAC of the “classical” subtype. Her goal is to fully disclose how ONECUT2 function contributes to PDAC growth and malignancy.

With support of this award, Dr. Sosa-Pineda was able to perform experiments of ONECUT2 functional inactivation and generated preliminary data that will be used for an RO3 grant proposal to be submitted in June 2023.

Hidayatullah G. Munshi, MD

2020-2021 Scholar

Area of focus: Immunotherapy for pancreatic cancer



Unlike other cancers, pancreatic cancer remains refractory to immunotherapy. Given the very poor prognosis of pancreatic cancer, there is interest in enhancing response to immunotherapy. We have found that targeting regulators of protein expression can enhance the efficacy of immune response in mouse models. These regulators of protein expression allow immune cells to enter the tumor, but the tumor microenvironment blocks their killing of the cancer cells. But when we combine our inhibitors with anti-PD-1 antibodies, we could then activate the immune cells and kill the tumors. We are now in the process of identifying additional combination therapies, using protein expression inhibitors that are already approved for other indications.

Dr. Munshi and his group recently received an R01 grant from the National Institutes of Health/National

Cancer Institute. Additionally, their research resulted in a publication in *JCI Insight*.

Zhuoli Zhang, MD, PhD

2019-2020 Scholar

Area of Focus: Pancreatic cancer therapy



Dr. Zhang is currently a faculty member at the University of California, Irvine, and serves as director of the Translational Imaging Lab. While at Northwestern and with support of the Harold E. Eisenberg Foundation’s award, Dr. Zhang worked to optimize clinically translatable MRI approaches to amplify immune responses of combination therapy of dendritic cell vaccine and irreversible electroporation treatment. He received research grants from the Society of Interventional Radiology and National Institutes of Health. Dr. Zhang published articles in prestigious journals such as the *American Journal of Cancer Research*, *Cancer Imaging*, *Cytotherapy*, and others.

Sui Huang, MD, PhD

2018-2019 Scholar

Area of Focus: Using a molecule created in her lab to treat liver cancer



Dr. Huang is investigating a molecule her lab created, called MEAN. Dr. Huang hypothesizes that MEAN, which stands for 6-methoxyethylaminonumonaide, may be an effective way to treat liver cancer. Dr. Huang accomplished the project and is submitting grants to seek additional funding to build upon the results from this research. Additionally, Dr. Huang has now developed a second-generation compound and is in the process of evaluating *in vitro* and *vivo* efficacy.



Investing in Top Scientists

Ronen Sumagin, PhD

2017-2018 Scholar

Area of Focus: Investigating the connection between inflammation and cancer



In this study, Dr. Sumagin and his colleagues demonstrate that neutrophils migrating into developing colon tumors can shape the way cancer cells repair broken DNA. By doing so, neutrophils affect progression of colorectal cancer and its response to commonly used treatments known as DNA-repair targeted therapy. The project was completed, and the results were published in *Gastroenterology*, a very high-impact and prestigious journal. Dr. Sumagin's initial findings garnered an American Cancer Society grant of approximately \$800,000. He also received a senior research award from the Crohn's and Colitis Foundation.

Guang-Yu Yang, MD, PhD

2016-2017 Scholar

Area of Focus: Gene mutation profiling of colorectal cancer



Through a large patient cohort study, Dr. Yang and his colleagues identified the unique profile of genetic alteration in young colorectal cancer patients. Specifically, the Braf mutation and Lynch syndrome are among the common genetic alterations in this group of patients. Dr. Yang's group published their work last year in the journal *Human Pathology*. Dr. Yang also worked with Shannon M. Lauberth, PhD, associate professor of Biochemistry and Molecular Genetics, on a National Institutes of Health program grant proposal focusing on colorectal cancer, and with Bin Zhang, MD, PhD, professor of Medicine (Hematology and Oncology) and Microbiology-Immunology on a proposal on immunity and colon cancer (focusing on Braf mutation/Lynch syndrome and h-mutant burden colon cancer).

Thank You for Your Generosity

The Harold E. Eisenberg Foundation is an invaluable partner in helping us to propel our GI oncology program and our efforts to provide patients with personalized medicine. Northwestern University Feinberg School of Medicine and the Robert H. Lurie Comprehensive Cancer Center of Northwestern University remain grateful for your philanthropic support, which enables our physicians and scientists to push boundaries, break down barriers, and transform the future of cancer care.

If you would like more information regarding this report or Lurie Cancer Center, please contact:

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