



THE DEGREGORIO FAMILY FOUNDATION:
**A Unique Paradigm for
Donors and Researchers Alike**

The DeGregorio Family Foundation (DFF) is uniquely positioned to identify and fund promising research focused on curing upper gastroesophageal malignancies – including cancers of the stomach, esophagus and gastroesophageal junction (GEJ).

Our Scientific Advisory Board consists of the world's leading minds in gastroesophageal cancer research and our grant review process uses the same methodology as the NIH.

In 14 years, we have funded 19 grants for a total of \$3.45 million.

Our funding serves as the seed money that allows for the research to mature and ultimately attract institutional funding.

Those 19 grants have received almost \$30 million in follow-on funding, the majority of it from the NIH, where only approximately 5% of applicants for gastroesophageal cancer research receive funding.

On average at DFF, every dollar allocated to a grant has attracted more than \$10 in follow-on funding – a unique paradigm for donors and research scientists alike.

We have made meaningful progress towards a cure thanks to the support of many of you.

The narratives below from a selection of our distinguished grant winners illustrate just how far we have come.



David Frank, MD, PhD

Dana-Farber Cancer Institute
Harvard Medical School

“The funding received from the DeGregorio Family Foundation was essential to our work in developing new targeted treatments for stomach and esophageal cancer. It came at an early and critical time in our research, making possible additional grants from other sources.

It is known that chronic irritation of the lining of the stomach and esophagus are major causes of these forms of cancers. We had found that irritation alters the way genes are expressed in esophagus and stomach cells, through proteins called STAT3 and NF-kB, ultimately leading to the unrestrained growth and invasion characteristic of these aggressive cancers.

Through the funding received from the Foundation, we have been able to identify drugs that block these proteins that cause this abnormal gene expression. These drugs are safe in people and are now being introduced into clinical trials for cancer patients. Furthermore, since these proteins often drive the malignant behavior of other types of cancers, we are hopeful that the funding provided by the DeGregorio Foundation will not only benefit patients with esophagus and stomach cancer, but those with other forms of cancer as well.



Adam Snook, PhD

Sidney Kimmel Cancer Center /
Medical College at Jefferson

“Funding from the DeGregorio Family Foundation has been instrumental in our starting a new research program to develop therapies for patients with stomach and esophageal cancer. We had an idea for a new and powerful treatment for these cancers, but little data to support it. Funding from the DeGregorio Family Foundation allowed us to generate the “proof-of-concept” data confirming that this idea has promise.

With that data, we were able to secure significant federal funding to move the therapeutic idea from concept to a clinical product that could be tested in patients. With continued work, funding and luck, we will be able to start testing this therapy in patients with stomach and esophageal cancer who desperately need innovative new treatments. Without the DeGregorio Family Foundation, this idea may have never gotten off the ground.



William Grady, MD

Fred Hutchinson Cancer
Research Center

“Funding from the DeGregorio Family Foundation allowed my laboratory to pursue an innovative hypothesis about a class of molecular alterations in esophageal cancer called “methylated genes,” and their use to make molecular marker tests for detecting and preventing esophageal cancer. This support came at a critical time when our results were considered too novel to be fundable by organizations like the National Cancer Institute. The DeGregorio award led to our studies that showed molecular markers based on abnormal DNA methylation (i.e., methylated genes) can be used to detect a precancerous condition of the esophagus called Barrett’s esophagus, and an early stage of esophageal cancer that is treatable using endoscopic, non-surgical therapy.

We have now obtained additional funding from the National Cancer Institute and other foundations to carry out clinical trials that will determine whether our molecular marker tests can be used in a convenient, doctor’s office-based test that will be an FDA-approved screening test for detecting people with Barrett’s esophagus, which is a silent condition of the esophagus. We have also developed promising tests for monitoring people with Barrett’s esophagus with another class of molecular markers that would indicate when they should be treated with endoscopic therapies.

These molecular marker tests are showing great promise and have the potential to prevent many cases of esophageal cancer.



Dechen Lin, PhD

Cedars-Sinai
Department of Medicine

“The DeGregorio Foundation award has provided an important jump-start for my research. With this support, I was able to complete some of the key experiments, to apply for more funding and to create a positive and healthy circle of research-funding-more research. This allows me to have more capacity and effort to focus on my basic research on how to reduce the risk of developing esophageal cancer.



Ellen Beswick, PhD

University of Utah
School of Medicine

“Funds from the DeGregorio Family Foundation allowed my lab to continue our pursuit of research in gastric cancer. Gastric cancer is a particularly difficult type of cancer to study due to the lack of relevant clinical models. However, funds we received have helped us to develop a much-needed pre-clinical model and begin studies on a novel drug target for improved treatment of gastric cancer. Since most clinical trials for new drugs in patients are conducted in cases where metastasis is present, the ability to study gastric cancer metastasis is critical to developing new treatments. Thus, we have recently been able to work with another group to develop a model of metastasis.

Furthermore, specific funding we received from the DeGregorio Foundation allowed us to begin researching a new drug target. Studying this target in pre-clinical models has provided us with more of an understanding of both gastric tumors and the poor immune response to tumors. Our work is to gain knowledge about how to activate the immune system to fight tumors using this novel drug to turn on anti-tumor immune responses. Our long-term goal is to see our work with this drug move from the lab to patients to improve their outcomes for gastric cancer.



Sam Yoon, MD

Memorial Sloan Kettering
Cancer Center in association with
Sandra Ryeom, PhD,
Univ. of Pennsylvania

“In our labs, we are first trying to understand how stomach cancers spread from the stomach to other parts of the body, and, second, trying to find new therapies that can prevent or eradicate metastatic disease. These goals may sound overly ambitious, but we’ve made significant progress in the past two years with the help of funding from the DeGregorio Family Foundation.

We think one of the keys to stopping gastric cancers from spreading or metastasizing is to target gastric cancer stem cells. Gastric cancer stem cells are a small subset of cancer cells in a stomach tumor that are a likely a source of both metastasis and chemotherapy resistance. With the funding, we have been studying these cells and identified two new classes of drugs that may specifically be used to destroy them. We are currently testing these new drugs to see if they can prevent the spread of gastric cancer in a mouse model and reverse chemotherapy resistance.

This funding supported our studies in the mouse model of gastric cancer that was instrumental in obtaining a \$3 million

Stand Up to Cancer Grant in 2020 for the early detection and interception of gastric cancer. Dr. Ryeom is the Co-leader on this award working with the Team leader Dr. Andrew Chan at Mass General Hospital to coordinate a team of investigators including myself as a team.



Adam Bass, MD

Dana-Farber Cancer Institute
Harvard Medical School



Timothy Wang, MD

Columbia University
Medical Center

“Our research program has benefited greatly over the past decade from working with the DeGregorio Family Foundation, twice receiving critical seed funding from them that enabled us to move forward with our research into the basic biology and genomics of gastric and esophageal cancer. Foundations such as the DeGregorio Foundation play a critical role in biomedical research, providing the spark funding to catalyze new projects and to enable new lines of inquiry that otherwise would never happen.

Our first grant enabled us to do early work in categorizing the underlying genome of esophageal/gastric cancer. This funding then provided early data and justification that allowed us to compete for well over \$1 million in follow-on funding and enabled huge projects that have been foundational for the field and have impacted research many times over.

More recently and indeed in follow up of our work in mapping the genome enabled by the DeGregorio Foundation, we made several pivotal findings, including the discovery of an entirely new class of highly recurrent mutations in a subclass of gastric cancer called “diffuse gastric cancer.” In order to understand the function of these new mutations, we were able to get seed funding again from the DeGregorio Foundation to build a new research team spanning investigators at the Dana-Farber Cancer Institute in Boston and New York’s Columbia University. Through the seed funding we were able to establish a new mouse model of this type of cancer and to pursue the basic functions of these mutations.

This funding from the DeGregorio Foundation enabled us to successfully compete for a 5-year grant from the National Institutes of Health to continue this work and also enabled some key discoveries of the function of this new gene, discoveries that are pointing to a clear, therapeutic approach to be evaluated in these patients. We are currently working with pharmaceutical companies to build new clinical trials to follow up on this work.

Overall, it is important to say how instrumental and critical foundations such as the DeGregorio are for sparking new scientific investigation, especially in diseases like gastric and esophageal cancer where there is such sparse funding.



Manish Shah, MD

Weill Cornell Medical College /
New York-Presbyterian Hospital

“Although *Helicobacter pylori* infection is the most prevalent cause of gastric cancer worldwide, the molecular mechanisms leading to the development of malignancy as a consequence of infection remain unknown. The prevailing theory is that *H. pylori* infection results in a chronic inflammatory condition within the gastric mucosa that leads to dysplastic mucosal changes over time, and that ultimately promotes malignant transformation. More recently, it is the realization that a gastric microbiome may also play an important role in chronic gastric inflammation and gastric cancer carcinogenesis. We set out to identify the gastric microbiome using next-generation sequencing techniques that also allow us to interrogate the immune microenvironment of the gastric mucosa.

We have established that there are other bacteria besides *H. pylori* that reside in the stomach and the different bacterial clusters seem to have unique local immune signatures. We have also identified a new cluster of bacteria that is present in the context of some gastric cancers. These data demonstrate that the microbiome, i.e., the bacteria that live within the stomach, interact with the lining of the stomach, influencing the local immune response and reacting to disturbances in the lining, such as from cancer.



Anisia Shaker, MD

Keck School of Medicine of USC

“For an exploration of the connection between gastroesophageal reflux disease (GERD) and esophageal cancer, I needed to gather critically validating data to secure funding from the National Institutes of Health (NIH). The DeGregorio Family Foundation provided the important starter funding to accumulate the necessary data. Had it not been for the Foundation, I may have been forced to abandon my research. Its support led to my \$1.25 million NIH grant, which planted the seeds for an Esophageal Cancer Research Program at USC.

In addition, the Foundation’s Scientific Advisory Board comprises the world’s leading minds in gastroesophageal cancer research. I was emotionally buoyed knowing that my research was peer-reviewed by these individuals.



Tony Godfrey, PhD

Boston University
School of Medicine

“For me, the DeGregorio Family Foundation funding came at a challenging time when I had recently moved to Boston and NIH funding rates were very low. I had what I thought was a good idea for early detection of esophageal cancer but did not have the funding to pursue it.

I still remember getting that personal phone call from Lynn DeGregorio while driving home one evening! That call, and the resulting DeGregorio Family Foundation funding, served as a catalyst that led to major funding from the NIH, and development of international collaborative studies with colleagues in Canada and India.

While our initial concept for early detection of esophageal cancer ran into some scientific challenges, the resources generated, and connections made as a result of the DeGregorio Family Foundation funding still form the foundation of major research efforts that are ongoing eight years later. While the technical details of our approach have changed, we are still optimistic that our continuing studies will be successful in developing a test for early detection of esophageal cancer, and that this will lead to improved survival for patients with this deadly disease.



Phillip Smith, MD

University of Alabama
at Birmingham

Support from the DeGregorio Family Foundation provided the financial resource for the following projects focusing on the role of H. pylori, the major risk factor for gastric cancer, in altering the gastric microbiota and inducing tumor gene expression in the gastric epithelium:

First, DeGregorio support allowed us to complete an important research project in which we showed that H. pylori infection of the stomach alters the normal gastric bacterial composition (called the microbiota) in Venezuelan children and then showed that therapeutic clearance of the H. pylori caused the altered microbiota composition to return to that of the uninfected condition.

Second, DeGregorio funding also enabled us to learn how to isolate gastric epithelial stem cells and establish stem cell organoids from which we derive normal and gastric cancer epithelial cell monolayers. Using these primary human epithelia, we showed that H. pylori induces an enzyme in cancer epithelium that blocks normal cell turnover, thereby inducing a stem cell phenotype and prolonging epithelial cell survival, key features of cancer cells.

Third, the above two DeGregorio-funded projects allowed us to initiate a very large collaboration with investigators in Chile, where H. pylori is endemic and where gastric cancer is the second leading cause of cancer-related mortality. This project characterizes the gastric microbiota and epithelial cell tumor gene expression at each stage of the gastric premalignancy cascade leading to, and including, gastric cancer. In preliminary findings, we have shown a striking difference in the gastric microbiota at each premalignancy stage and a progressive increase in tumor gene expression. These findings are being evaluated as biomarkers for predicting the likelihood of people with H. pylori-induced gastric pathology to progress to gastric cancer.

Fourth, the above projects have formed the basis for an NIH grant submission entitled “Identifying a Biomarker of Irreversibility in the Premalignancy Cascade Leading to Gastric Cancer” (R01: CA256620-01). We are awaiting review of the grant.

These projects and grant submission would not have been possible without the DeGregorio Foundation.