

DEBBIE'S DREAM FOUNDATION-AACR PARTNERSHIP 2014-2024 Overview



This partnership has provided
\$1,850,000
in research funding since 2014

Grantees are sharing their science and impacting the field...

>30
Presentations



19 Grantees



32 Project-generated Publications
with **>700** Citations



19 Collaborations



...publishing their work in leading journals



Heterogeneity and Dynamics of Active Kras-induced Dysplastic Lineages From Mouse Corpus Stomach

Jimin Min^{1,2}, Paige N Vega^{2,3}, Amy C Engevik^{1,2}, Janice A Williams⁴, Qing Yang^{1,2,5}, Loraine M Patterson⁶, Alan J Simmons^{2,3}, R Jarrett Bliton⁷, Joshua W Betts², Ken S Lau^{2,3}, Scott T Magness^{6,7,8,9}, James R Goldenring^{1,2,3,10}, Eunyoung Choi^{11,12}
Nat Commun, 10 (1), 5549 2019 Dec 5

CANCER DISCOVERY

Genomic Heterogeneity as a Barrier to Precision Medicine in Gastroesophageal Adenocarcinoma

Pectasides E, Stachler MD, Derks S, et al.
Cancer Discov, 8 (1), 37-48 Jan 2018

RESEARCH ARTICLE | SEPTEMBER 05 2023

Single-cell Profiling Uncovers a *Muc4*-Expressing Metaplastic Gastric Cell Type Sustained by *Helicobacter pylori*-driven Inflammation

Valerie P. O'Brien, Yuqi Kang, Meera K. Shenoy, Greg Finak, William C. Young, Julien Dubrulle, Lisa Koch, Armando E. Rodriguez Martinez, Jeffery Williams, Elizabeth Donato, Surinder K. Batra, Cecilia C.S. Yeung, William M. Grady, Meghan A. Koch, Raphael Gottardo, Nina R. Salama

Check for updates

Author & Article Information

Cancer Research Communications (2023) 3 (9): 1756–1769.

<https://doi.org/10.1158/2767-9764.CRC-23-0142> Article history

PNAS

Striking heterogeneity of somatic L1 retrotransposition in single normal and cancerous gastrointestinal cells

Katsumi Yamaguchi, Alisha O. Soares, Loyal A. Goff, and Haig H. Kazazian Jr

December 4, 2020 | 117 (51) 32215-32222

CANCER DISCOVERY

Gain-of-Function *RHOA* Mutations Promote Focal Adhesion Kinase Activation and Dependency in Diffuse Gastric Cancer

Haisheng Zhang, Antje Schaefer, Yichen Wang, Richard G. Hodge, Devon R. Blake, J. Nathaniel Diehl, Alex G. Papageorge, Matthew D. Stachler, Jennifer Liao, Jin Zhou, Zhong Wu, Fahire G. Akarca, Leonie K. de Klerk, Sarah Derks, Mariarelena Pierobon, Katherine A. Hoadley, Timothy C. Wang, George Church, Kwok-Kin Wong, Emanuel F. Petricoin, Adrienne D. Cox, Douglas R. Lowy, Channing J. Der, Adam J. Bass

Cancer Discov (2020) 10 (2): 288–305.

New Results

Follow this preprint

Mutant TP53 switches therapeutic vulnerability during gastric cancer progression within Interleukin-6 family cytokines

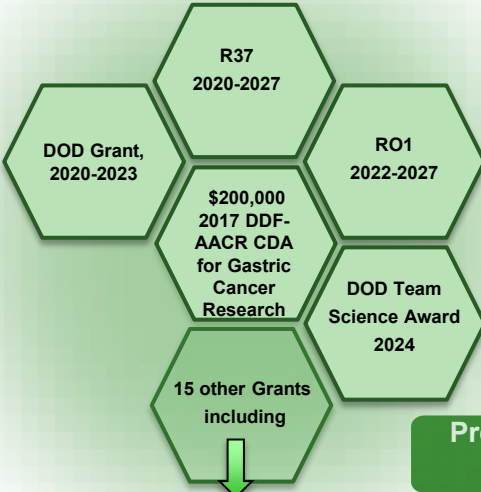
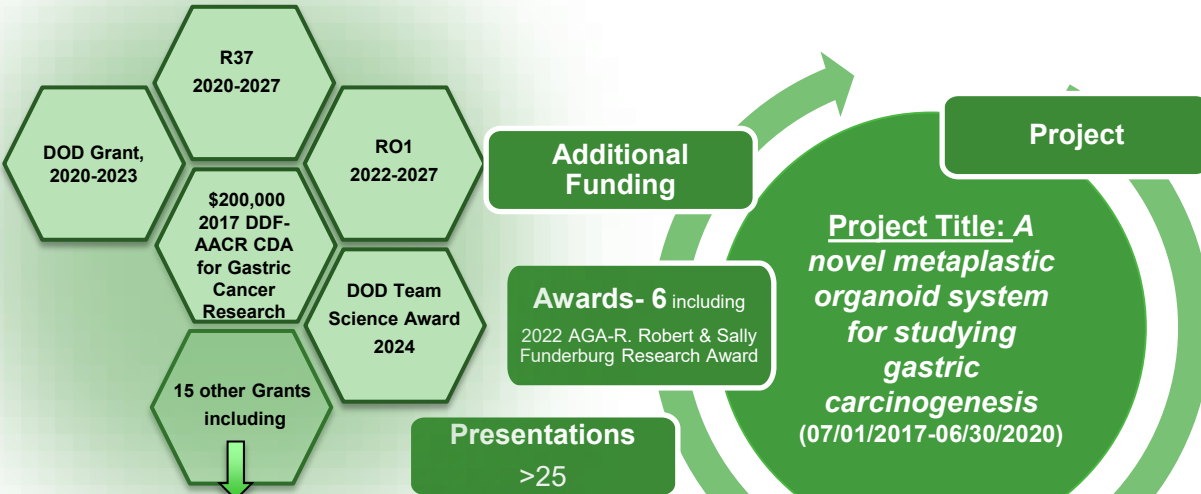
Anne Huber, Amr H. Allam, Christine Dijkstra, Stefan Thiem, Jennifer Huynh, Ashleigh R. Poh, Joshua Konecnik, Saumya P. Jacob, Rita Busuttill, Yang Liao, David Chisanga, Wei Shi, Mariah G. Alorro, Stephen Forrow, Daniele V.F. Tauriello, Eduard Batlle, Alex Boussioutas, David S. Williams, Michael Buchert, Matthias Ernst, Moritz F. Eissmann

doi: <https://doi.org/10.1101/2024.04.22.590499>

...and presenting their research findings worldwide.



DDF-AACR continuous grant support empowers grantees to embark on pioneering research...



2023 AACR-DDF Innovation and Discovery Grant

Goal: Investigate changes in metabolism during the transition of pre-cancerous cells into cancer-initiating cells. This will be accomplished using a novel technology that allows for spatial and quantitative profiling of metabolites found in the stomachs of human patients with pre-cancerous lesions



Gastrointestinal cancer typically progresses through a carcinogenic cascade beginning with pre-cancerous stages, advancing to dysplasia, and ultimately, leading to adenocarcinoma. Dysplastic cells, considered the initiators of cancer, mark a critical time point for gastric cancer prevention and early intervention.

Dr Choi's team established the first gastric pre-cancer organoid system.

Using this platform, they identified a drug that may potentially reverse high-risk, pre-cancerous lesions and allow repopulation of the stomach with cells of normal lineages, thereby abrogating increased cancer risk.

Publications
6 (> 60 citations)

nature COMMUNICATIONS
Decrease in MiR-148a Expression During Initiation of Chief Cell Transdifferentiation

Gastroenterology
Heterogeneity and Dynamics of Active Kras-induced Dysplastic Lineages From Mouse Corpus Stomach

THE JOURNAL OF Pathology
Trop2 is upregulated in the transition to dysplasia in the metaplastic gastric mucosa

cmgh
Active Kras Expression in Gastric Isthmus Cells Induces Foveolar Hyperplasia but Metaplasia

cmgh
Cystine/Glutamate Antiporter (xCT) Is Required for Chief Cell Plasticity After Gastric Injury

MEK Inhibitor Reverses Metaplasia and Allows Re-emergence of Normal Lineages in Helicobacter pylori-Infected Gerbils

Valerie Phoebe O'Brien, PhD

2018 Debbie's Dream Foundation-
AACR Gastric Cancer Research
Fellowship, in Memory of Sally
Mandel



Assistant Professor
Purdue University

Funded Project: Assessing *Helicobacter pylori* contributions to stomach cancer progression

One well known risk factor for gastric cancer is *Helicobacter pylori* (Hp) infection, a bacterium that drives gastric inflammation and is found in 50% of the world's population (2). However, the exact mechanisms of Hp-driven gastric cancer are not well defined.

With support of the Debbie's Dream Foundation-AACR Gastric Cancer Research Fellowship, Dr. O'Brien demonstrated that Hp infection is not only involved in initiating gastric cancer but also in altering the disease trajectory by inducing expansion of precancerous gastric epithelial cells.

Additional Funding:

Irvington Postdoctoral Fellowship (Cancer Research Institute)
NIH/NCI K99/R00 Pathway to Independence Award

Post-Award:

Dr. O'Brien was a postdoctoral fellow at the Fred Hutchinson Cancer Center in Seattle, Washington, when she was awarded this grant. She is now an assistant professor and runs an independent laboratory at Purdue University's College of Pharmacy, where her research group continues to explore mechanisms of Hp-driven gastric cancer and develop therapeutics to combat this disease.

In Dr. O'Brien's words:

"I am so grateful to the AACR for their support. I am proud to be an AACR member and will continue publishing my best work in AACR journals."

... to ultimately improve gastric cancer patient outcomes.

Moritz Eissmann, PhD

**2022 AACR-Debbie's Dream
Foundation Career Development
Award in Gastric Cancer Research**



Head,
Olivia Newton-John
Cancer Research Institute

Funded Project: Identification of therapeutic vulnerabilities that promote clonal fitness and metastatic spread of gastric cancer cells in vivo

Close to half (48%) and 15% of metastatic gastric cancer patients have lesions in their liver and lung, respectively. Inflammatory processes involving a protein called Stat3 may contribute to the development and growth of stomach tumors and might also be involved in the metastasis of the cancer.

With ongoing support of the Debbie's Dream Foundation-AACR Gastric Cancer Research Career Development Award, Dr. Eissmann has:

- established a novel murine gastric cancer organoid model to study liver metastasis
- demonstrated that deficiency in IL6/ IL6-trans and IL11 signaling restricts growth of liver metastases.

Post-Award:

Dr. Eissmann was recently appointed as Head of the newly formed Cytokine and Cancer Signaling Group at the Olivia Newton-John Cancer Research Institute. His work focuses on understanding cytokine signaling that drives the crosstalk between the cancer cells and the tumor microenvironment in gastric and colorectal cancers.

In Dr. Eissmann's words:

"This funding helped establish new powerful gastric cancer models; establish my independent research group; gaining recognition for my work and motivation to continue to pursue ambitious goals to improve gastric cancer patient outcomes."

The 2023 DDF-AACR grant recipients are poised to make an impact.

Heather McGee, MD, PhD

2023 AACR-Debbie's Dream
Foundation Career Development
Award for Gastric Cancer Research



Assistant Professor,
City of Hope

Funded Project: Radiation-Induced inflammasome Activation and Alarmins in Gastric Cancer

With support of the Debbie's Dream Foundation-AACR Gastric Cancer Research Career Development Award, the McGee lab will investigate if radiation induces inflammasome-mediated pyroptosis in gastric cancer and determine if radiation-induced IL-18 activates immune cells in the gastric tumor microenvironment.

Potential Project Impact: This project will help to understand how to enhance radiation's ability to activate anti-tumor immune responses in gastric cancer to enhance treatment options for patients with this devastating disease.

Reviewer's Comment on Project:

"The proposed studies, if successful, will fill an unmet need for the treatment of gastric cancer. Specifically, this work will explore whether the pharmacologic activation of the NLRP3-caspase1-IL18 pathway in combination with radiation will lead to better results in the treatment of patients with gastric cancer.

Successfully applying immunotherapy techniques to the treatment of gastric cancer is highly significant and likely to have an important impact."

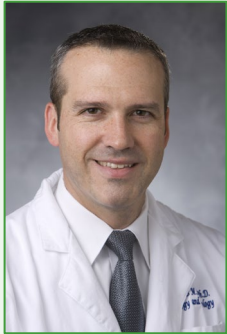
Grantee Acknowledgment of Support:

"I am very grateful to receive the AACR-Debbie's Dream Foundation Award. This grant allows me to expand my lab's research in a new direction to investigate the role of radiation-induced immune cell activation in gastric cancer. I am honored to partner with the AACR to study this rare gastrointestinal malignancy."

The 2023 DDF-AACR grant recipients are poised to make an impact.

Brent Allen Hanks, MD, PhD

2023 AACR-Debbie's Dream Foundation Innovation and Discovery Grant



Associate Professor,
Duke University

Funded Project: The NLRP3-HSP70 axis and immunotherapy resistance in gastric cancer

Despite the recent availability of checkpoint inhibitor immunotherapies, the majority of gastric cancer patients do not benefit from this treatment modality. The Hanks Lab has identified the tumor-intrinsic NLRP3 inflammasome-HSP70 signaling axis as a driver of checkpoint inhibitor resistance in melanoma. Dr. Hanks team will examine the ability of pharmacologic inhibitors of both NLRP3 and HSP70 to overcome resistance to anti-PD-1 immunotherapy and determine whether NLRP3 genetic amplification may serve as a marker of response to this treatment strategy.

Potential Project Impact: This work aims to support a phase I clinical trial testing NLRP3 inhibitors in combination with anti-PD-1 immunotherapy in advanced gastric cancer patients.

Reviewer's Comment on Project :

“Novel drug combination and nice pivot taking the data that was first acquired to a more sensitive to IO tumor type (melanoma) and now taking it to GE cancers. Rationale for doing so is strong and the potential for translation is high. Significance: Could lead to potentiation of current IO therapies in gastroesophageal cancers.”

Grantee Acknowledgment of Support:

“It is truly an honor to be selected as a recipient of the 2023 AACR-Debbie's Dream Foundation Innovation and Discovery Grant. This award provides critical support as we transition our cancer immunotherapy resistance and toxicity research program into the field of gastrointestinal oncology.”

The 2023 DDF-AACR grant recipients are poised to make an impact.

Ryan H. Moy, MD, PhD

2023 AACR-Debbie's Dream
Foundation Innovation and
Discovery Grant



Assistant Professor,
Columbia University

Funded Project: Targeting CCNE1 amplification in gastric cancer

Cyclin E1 (CCNE1) amplifications are found in approximately 10% of stomach cancers and are associated with DNA replication stress, chromosomal instability, therapeutic resistance, and immune cell exclusion. Recent studies found that CCNE1-amplified tumors are selectively vulnerable to loss of Protein Kinase, Membrane Associated Tyrosine/Threonine 1 (PKMYT1).

Dr. Moy and colleagues will leverage CCNE1-amplified gastric cancer patient-derived organoids and syngeneic mouse models to investigate the activity and mechanism of combined PKMYT1 inhibition and immune checkpoint blockade.

Potential Project Impact: These studies have the potential to lead to clinical trials and new biomarker-driven immunotherapy approaches with rapid translatability as PKMYT1 inhibitors are already in the clinic.

Reviewer's Comment on Project :

"The project is highly innovative and feasible given the existing preliminary data and resources."

Grantee Acknowledgment of Support:

"I am extremely honored to be a recipient of the 2023 AACR Debbie's Dream Foundation Innovation and Discovery Grant. This award will allow my group to investigate a novel combination of targeted therapy and immunotherapy for gastric cancer, which we hope will eventually lead to new therapeutic options for patients."

The AACR looks forward to our continued collaboration to support the next generation of gastric cancer researchers.

AACR

