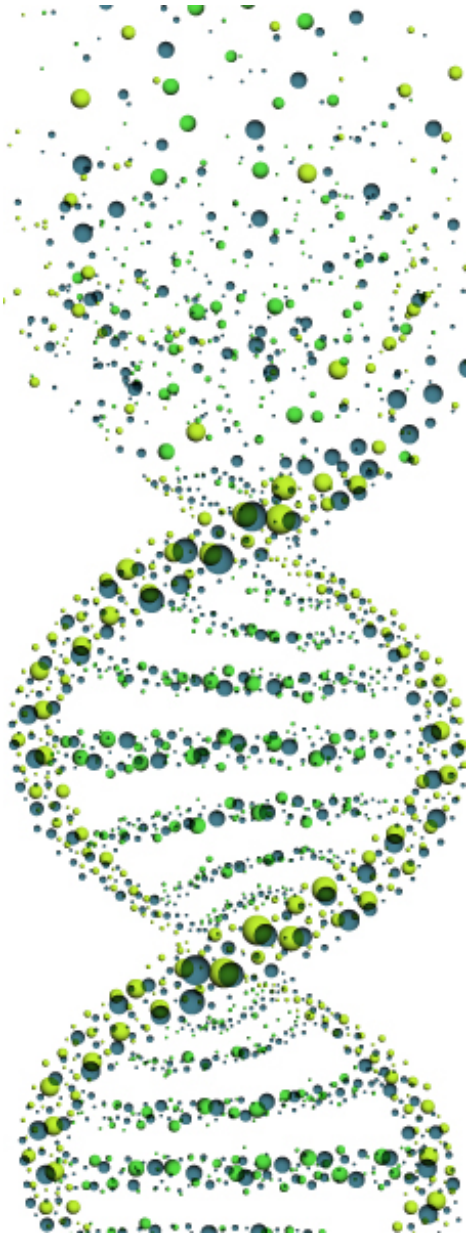
TargetCancer



# The TargetCancer Think Tank on Cholangiocarcinoma

*Organized by*

*Nabeel Bardeesy, PhD*
*and*
*Jay Bradner, M.D.*

November 16, 2012

7:30 a.m. – 1:30 p.m.

McGladrey
80 City Square, at the Charlestown Navy Yard
Boston, MA 02129

TargetCancer promotes the development of lifesaving treatment protocols for rare cancers. TargetCancer directly supports initiatives at the forefront of cancer treatment by funding innovative research, fostering collaborations, and raising awareness among scientists, clinicians, and patients.

# The TargetCancer Think Tank on Cholangiocarcinoma
# Agenda

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| 7:30 | **Breakfast** |
| 8:00 | **Introduction**<br>*Jim Palma, Executive Director*<br>*TargetCancer, Inc.* |
| 8:05 | **Think Tank Vision and Overview of Agenda**<br>*Jay Bradner, M.D.* |
| 8:15 | **Cholangiocarcinoma Genetics**<br>*Nabeel Bardeesy, PhD* |
| 8:30 | **Clinical Overview**<br>*David Ryan, M.D. and Andrew Zhu, M.D., PhD* |
| 9:00 | **Liver Development and Regeneration**<br>*Ben Stanger, M.D., PhD* |
| 9:30 | **Mouse Models**<br>*Aram Hezel, M.D.* |
| 10:00 | **Coffee break** |
| 10:20 | **IDH biology and drug development**<br>*Sam Agresta, M.D., MPH* |
| 10:50 | **Genomic Approaches to rare diseases**<br>*Adam Bass, M.D.* |
| 11:05 | **Clinical Trial Overview**<br>*Cristina Ferrone, M.D.* |
| 11:20 | **New systems and resources**<br>*Nabeel Bardeesy, PhD* |
| 11:45 | **Lunch and discussion of next steps** |
| 1:30 | **Meeting End** |

# The TargetCancer Think Tank on Cholangiocarcinoma
# Participant List

**Samuel Agresta, M.D., MPH,** Senior Director; Head, Clinical Development,
Agios Pharmaceuticals
*sam.agresta@agios.com*

**Nabeel Bardeesy, PhD,** Associate Professor, Harvard Medical School
Massachusetts General Hospital Cancer Center; Center for Regenerative Medicine
*Bardeesy.nabeel@mgh.harvard.edu*

Dr. Nabeel Bardeesy is an Associate Professor of Medicine at the Harvard Medical School and the Massachusetts General Hospital Cancer Center. He received his PhD from McGill University in Montreal where he studied the genetics of pediatric kidney cancers, and identified a genetic switch that converts normally curable tumors into a lethal subtype. He then moved to the Dana-Farber Cancer Institute for his postdoctoral fellowship where he worked on pancreatic cancer studies with Dr. Ron DePinho. During this time, Dr. Bardeesy used newly available genetic information and novel genetic engineering approaches to develop mouse models that precisely mimic human pancreatic cancer. These models have contributed to the significant growth of pancreatic cancer studies, and they are now widely used by the research community to investigate this cancer and test new therapeutics. Dr. Bardeesy has had his own laboratory at MGH Cancer Center since 2005, and in addition to his work on pancreatic cancer has developed a program in liver cancer; particularly biliary cancer. Among his findings, he showed that the size of the liver is precisely controlled by two proteins. When these proteins are inactivated, the liver undergoes uncontrolled growth, developing cancer. Dr. Bardeesy's approach to researching biliary cancer is concentrated on three primary areas: The development of mouse models that recreate the genetic building blocks of biliary cancer; defining the role of stem cells in the development of biliary cancer; and the development of targeted therapies tailored to a patient's individual genetic makeup.

**Adam Bass, M.D,** Assistant Professor, Harvard Medical School, Dana-Farber Cancer Institute;
Associate Member, Broad Institute
*adam_bass@dfci.harvard.edu*

Dr. Adam Bass is an Assistant Professor of Medicine at the Harvard Medical School and Dana-Farber Cancer Institute and also is an associate member of the Broad Institute. He completed clinical training in internal medicine at the Massachusetts General Hospital and medical oncology training at the Dana-Farber Cancer Institute. He subsequently pursued research training in cancer genomics and cancer biology at both the Dana-Farber Cancer Institute and Broad Institute. During that time he developed a research interest in studying the somatic-genomic alterations in gastrointestinal cancer using new emerging genomic technologies and also studying candidate genomic alterations in the laboratory using more traditional functional biology. Since 2010, Dr. Bass been an independent investigator at the Dana-Farber Cancer Institute ,where his laboratory continues to pursue the understanding of the genomic alterations in gastrointestinal cancers, with a special interest in esophageal and gastric cancers. In addition, Dr. Bass is co-chairing The Cancer Genome Atlas (TCGA) studies into gastric and esophageal cancer. Beyond genomic characterization, his laboratory continues to work to understand select

oncogenes and tumor suppressors in these tumors and build off the elucidation of genomic alterations to identify new therapeutic vulnerabilities for patients with these diseases.

**Jay Bradner, M.D,** Assistant Professor of Medicine, Harvard Medical School, Dana-Farber Cancer Institute
*James_bradner@dfci.harvard.edu*

Dr. Bradner is an Assistant Professor of Medicine at the Dana-Farber Cancer Institute and Harvard Medical School in Boston, MA. His clinical practice centers around the treatment of hematologic malignancies, specifically using allogeneic stem cell transplantation. Additionally, he leads a research laboratory focused on the discovery, optimization and clinical translation of new targeted cancer therapeutics. Dr. Bradner received an A.B. from Harvard University, a M.D. from the University of Chicago-Pritzker School of Medicine and a M.M.S. from Harvard Medical School. He completed postdoctoral research training with Prof. Stuart Schreiber in the Department of Chemistry and Chemical Biology at Harvard University and the Broad Institute of Harvard and MIT.

**Jeff Engleman, M.D., PhD**, Director, Center for Thoracic Cancers, Massachusetts General Hospital Cancer Center; Assistant Professor of Medicine, Harvard Medical School
*jengelman@partners.org*

**Cristina Ferrone, M.D.**, Massachusetts General Hospital Department of Surgery
*cferrone@partners.org*

Dr. Ferrone is an Assistant Professor of Surgery at Harvard Medical School and a physician in the Department of Surgery/Surgical Oncology at Massachusetts General Hospital. A magna cum laude graduate of University of Pennsylvania, Dr. Ferrone received her M.D. from Washington School of Medicine in St. Louis. Her areas of research and clinical activities focus on pancreas and hepatobiliary malignancies and disorders, specializing in translational research in pancreatic adenocarcinoma, pancreatic neuroendocrine tumors, and cholangiocarcinomas. Dr. Ferrone is also an Assistant Program Director of the general surgery residency at MGH.

**Sushma Gurumurthy, PhD,** Research Scientist- Target Discovery, Belfer Institute for Applied Cancer Science, Dana-Farber Cancer Institute
*sgurumurthy@partners.org*

**Aram Hezel, M.D.,** Assistant Professor - Department of Medicine, University of Rochester Medical Center
*aram_hezel@urmc.rochester.edu*

Aram F. Hezel, is an assistant professor of Medicine, and member of the Gastrointestinal Oncology Team at the Wilmot Cancer Center at the University of Rochester in Rochester NY. He specializes in the research and treatment of pancreatic and liver cancers. He has studied the genetics of pancreatic and biliary tract cancers and tested novel treatments in preclinical settings. His research, including clinical trials in pancreatic and hepatobiliary cancers, is published in oncology and science journals.

Hezel is originally from Buffalo NY and a graduate of Vassar College and the State University of New York at Buffalo School of Medicine. He completed residency in internal medicine at Beth Israel Deaconess Medical Center, Boston followed by a Fellowship in medical oncology at Dana-Farber Cancer Institute. He was on staff at Massachusetts General Hospital Cancer Center and an instructor at Harvard Medical School from 2006- 2009.

He has received funding from the National Cancer Institute and Howard Hughes Medical Institute. He is an active member of the American Society of Clinical Oncology and American Association for Cancer Research.

**Anthony Letai, M.D., PhD,** Associate Professor in Medicine, Harvard Medical School, Dana-Farber Cancer Institute
*Anthony_letai@dfci.harvard.edu*

Dr. Letai has been a faculty member in the Department of Medicine at Harvard Medical School and at the Dana-Farber Cancer Institute since 2004, where he is now an associate professor. Dr. Letai's clinical work continues in caring for patients with hematologic malignancies. His main research focus is on the mechanisms by which cancer cells escape cell death. Dr. Letai's laboratory has invented a technique called "BH3 profiling" which can be used to identify the type of block employed by a cancer cell to escape programmed cell death. More recently, his laboratory has found that BH3 profiling can predict response to conventional chemotherapy. His laboratory continues to explore new ways to kill cancer cells, and better methods for personalizing care for cancer patients.

Dr. Letai is a recipient of the Dunkin' Donuts Rising Star Award, Forbeck Foundation Scholar Award, Smith Family New Investigator Award, Kimmel Translational Science Award, and the V Scholar Award. He is a Leukemia and Lymphoma Society Scholar and a member of the American Society of Clinical Investigation.

Dr. Letai graduated from Princeton with a bachelor's degree in Physics. He attended University of Chicago where he obtained his MD, as well as a PhD under the mentorship of Elaine Fuchs. He performed his internship and residency in internal medicine at Brigham and Women's Hospital in Boston, followed by fellowship in Hematology and Oncology at Dana-Farber Cancer Institute. Dr. Letai was introduced to the field of cell death as a post-doctoral fellow in the laboratory of the late Stanley J. Korsmeyer, a world authority on programmed cell death and cancer.

**Jakob Lovén, PhD,** Whitehead Institute for Biomedical Research
*loven@wi.mit.edu*

Jakob is a postdoctoral fellow in Dr. Richard Young's lab investigating genome regulation and gene expression in cancer. Jakob completed his undergraduate degree at Cambridge University in 2003, and received his PhD in Medical Sciences from the Karolinska Institute in 2010, where his research focused on Myc proteins and microRNA (miRNA) regulation, expression, and function in a variety of cancers. During his training in Dr. Richard Young's lab, Jakob has applied powerful genomics methods to decipher cancer cell states and developed new genome-wide strategies to identify dependencies of specific cancer types on particular genes and pathways. Jakob's father, Hans Lovén, passed away from cholangiocarcinoma on September 15th, 2012.

**Andrea McClatchey, PhD**, Professor of Pathology, MGH Center for Cancer Research and Harvard Medical School
*mcclatch@helix.mgh.harvard.edu*

Andrea I. McClatchey received her Ph.D. in Genetics from Harvard Medical School, and carried out postdoctoral training in cancer biology at the Massachusetts Institute of Technology before establishing her own laboratory at MGH. Dr. McClatchey was one of the first five recipients of the prestigious Research Scholar Award and was named the Patricia and Scott Eston MGH Research Scholar. A Professor of Pathology at Harvard Medical School, Dr. McClatchey is the first woman faculty member to achieve the rank of Professor in the Center for Cancer Research. Her work has focused on the molecular basis of neurofibromatosis type 2 (NF2), a familial cancer syndrome caused by mutation of the NF2 tumor suppressor gene. These patients are genetically predisposed to developing tumors that grow within the cranial and spinal nerves. Dr. McClatchey's research uncovered fundamental rules by which cells organize

their outer cortex so as to appropriately interface with their environment during tissue morphogenesis. Her work also revealed that these rules are broken by many types of tumors. This may ultimately lead to new therapeutic approaches for individuals suffering from this disease and other human cancers, as well as a better appreciation of the link between normal development and cancer.

**Christine Parachoniak, PhD**, Postdoctoral Fellow, MGH Cancer Center/Harvard Medical School
*cparachoniak@partners.org*

Christine completed a Bachelor of Science honors degree in Biophysics at the University of British Columbia, in 2005 and a doctoral degree at McGill University in the department of Biochemistry in the summer of 2012. During her doctoral training in the laboratory of Dr. Morag Park, she worked on understanding molecular mechanisms of the Met receptor tyrosine kinase in cancer cell signaling and migration. Christine has recently joined the laboratory of Dr. Nabeel Bardeesy as a postdoctoral fellow to study metabolic reprogramming in the pathogenesis of cholangiocarcinoma.

**David Ryan, M.D.,** Chief of Hematology/Oncology at Massachusetts General Hospital
*dpryan@partners.org*

Dr. Ryan joined the MGH Cancer Center in 1998. He is an Assistant Professor of Medicine at Harvard Medical School and served as Clinical Director of the Tucker Gosnell Center for Gastrointestinal Cancers at MGH until his appointment to Chief of Oncology in October 2012. A graduate of Columbia College of Physicians and Surgeons, Dr. Ryan specializes in experimental therapies for gastrointestinal cancers.

**Supriya Saha, M.D., PhD,** Medical Oncology Fellow, Dana-Farber/Partners Cancer Care Program
*supriya_saha@dfci.harvard.edu*

Supriya is a 3rd year medical oncology fellow in the Dana-Farber/Partners Cancer Care Fellowship program. Supriya completed his undergraduate degree at Harvard University, concentrating on Biochemical Sciences in 2001 and graduated from the Medical Scientist Training Program at the David Geffen School of Medicine at UCLA in 2008, where he studied molecular immunology in the laboratory of Dr. Genhong Cheng. Supriya then returned to Boston and obtained his Internal Medicine training at the Brigham and Women's Hospital from 2008-2010. After an initial year of clinical medical oncology training in the DF/PCC fellowship program, he joined the laboratory of Dr. Nabeel Bardeesy where he has been working for the past year to develop mouse models of cholangiocarcinoma.

**Ben Stanger, M.D., PhD**, Assistant Professor of Medicine, University of Pennsylvania Perelman School of Medicine
*bstanger@exchange.upenn.edu*

Dr. Stanger graduated from the Massachusetts Institute of Technology in 1988 with an SB in Life Sciences. He then earned an MD and PhD at Harvard Medical School, where he worked on mechanisms of apoptosis. Dr. Stanger completed a residency in Internal Medicine at UCSF and a fellowship in Gastroenterology at the Massachusetts General Hospital, performing postdoctoral work on development of the gastrointestinal tract at Harvard College. Dr. Stanger held the position of Instructor at Harvard Medical School from 2003-2006. In 2006, he moved to the University of Pennsylvania, where he holds the position of Assistant Professor of Medicine and Cell and Developmental Biology. Dr. Stanger's research revolves around the formation of gastrointestinal organs – specifically the pancreas and liver – and how developmental programs are utilized during regeneration and carcinogenesis of these tissues.

**Lori Stetz, M.D., MPH,** Medical Director, Aetna International
*stetzl2@aetna.com*

Dr. Stetz is a physician trained in Family Medicine who has practiced primary and urgent care for the past nine years. She has recently transitioned to serve as the Medical Director for Aetna International, where she has clinical responsibilty for the company's international medical management strategy. She holds a B.A. in Comparative Literature from Haverford College, an M.P.H. in International Health from Boston University, and an M.D. from SUNY Downstate.

**Matthew Vander Heiden, M.D., PhD,** Howard S. and Linda B. Stern Assistant Professor, Koch Institute for Integrative Cancer Research and the Department of Biology at the Massachusetts Institute of Technology
*mvh@mit.edu*

Matthew Vander Heiden is the Howard S. and Linda B. Stern Assistant Professor in the Koch Institute for Integrative Cancer Research and the Department of Biology at the Massachusetts Institute of Technology. He is also an Instructor of Medicine at the Dana-Farber Cancer Institute and Harvard Medical School. Dr. Vander Heiden received his MD and PhD degree from the University of Chicago. He also completed clinical training in Internal Medicine and Medical Oncology at the Brigham and Women's Hospital / Dana-Farber Cancer Institute prior to completing a post-doctoral fellowship at Harvard Medical School.

**Fang Wang, PhD,** Principle Scientist, Department of Biology, Agios Pharmaceuticals
*fang.wang@agios.com*

**Kwok Wong, M.D., PhD,** Scientific Director, Belfer Institute for Applied Cancer Science, Associate Professor in Medicine, Harvard Medical School
*kwong1@partners.org*

**Andrew Zhu, M.D., PhD**, Director of Liver Cancer Research, MGH Cancer Center; Associate Professor of Medicine, Harvard Medical School
*azhu@partners.org*

Dr. Andrew X. Zhu is Director of Liver Cancer Research at Massachusetts General Hospital Cancer Center and an Associate Professor of Medicine at Harvard Medical School. He is also a Member of Dana-Farber Harvard Cancer Center. Dr. Zhu is board-certified in internal medicine and medical oncology.

The major focus of his research is to develop more effective therapies for hepatocellular carcinoma (HCC) and biliary tract cancers (BTCs) through phase I, II and III clinical trials. The second area of his research interests is highly complementary and is directed at the development of novel circulating and imaging biomarkers for targeted therapeutics that have prognostic and/or predictive significance. The third area of his research is to define and characterize known or novel genetic mutations in HCC and BTCs and assess their potential correlation with clinical outcomes and as therapeutic targets.

As a widely published author, Dr. Zhu has served as a principle investigator in many clinical trials in HCC, BTCs and other gastrointestinal cancers. An internationally recognized leader in HCC and BTCs, he has led early efforts of developing several molecularly targeted agents in hepatobiliary cancers and studying the predictive and surrogate circulating and imaging biomarkers. He is a founding board member of the International Liver Cancer Association, Vice President of CanLiv-The Hepatobiliary Cancers Foundation, Fellow of American College of Physicians, and a member of the American Society of Clinical Oncology (ASCO) and the American Association for Cancer Research. Dr. Zhu serves on the Hepatobiliary Cancer committee of the National Comprehensive Cancer Network , the Grants Selection Committee of ASCO, and the Hepatobiliary Cancer Task Force of The NCI Gastrointestinal Cancer Steering Committee (GISC).