Blood Test for Early Detection of Pancreatic Cancer Headed to Clinic

A newly identified biomarker panel could pave the way to earlier detection and better treatment for pancreatic cancer, according to new research from the Perelman School of Medicine at University of Pennsylvania. Currently over 53,000 people in the United States are diagnosed with pancreatic cancer -- the fourth leading cause of cancer death -- every year. The blood biomarkers, detailed last week in Science Translational Medicine, correctly detected pancreatic cancer in blood samples from patients at different stages of their disease.

The majority of pancreatic cancer patients are not diagnosed until an advanced stage, beyond the point at which their tumors can be surgically removed.

A team led by Ken Zaret, PhD, director of the Penn Institute for Regenerative Medicine and the Joseph Leidy Professor of Cell and Developmental Biology, and Gloria Petersen, PhD, from the Mayo Clinic, identified a pair of biomarkers that physicians could soon use to discover the disease earlier.

“Starting with our cell model that mimics human pancreatic cancer progression, we identified released proteins, then tested and validated a subset of these proteins as potential plasma biomarkers of this cancer,” Zaret said. The authors anticipate that health care providers will use the early-detection biomarkers to test for their presence and levels in blood from pancreatic cancer patients and blood drawn from individuals with a high risk of developing pancreatic cancer, including those who have a first-degree relative with pancreatic cancer, are genetically predisposed to the disease, or who had a sudden onset of diabetes after the age of 50.

“Early detection of cancer has had a critical influence on lessening the impact of many types of cancer, including breast, colon, and cervical cancer. A long standing concern has been that patients with pancreatic cancer are often not diagnosed until it is too late for the best chance at effective treatment,” said Robert Vonderheide, MD, DPhil, director of the Abramson Cancer Center (ACC) at the University of Pennsylvania. “Having a biomarker test for this disease could dramatically alter the outlook for these patients.”

The biomarker panel, enabled by discovery work of first author Jungsun Kim, PhD, a postdoctoral fellow in Zaret’s lab, builds on a first-of-its-kind human-cell model of pancreatic cancer progression the lab described in 2013. They used stem-cell technology to create a cell line from a patient with advanced pancreatic ductal adenocarcinoma. Genetically reprogramming late-stage human cancer cells to a stem-cell state enabled them to force the reprogrammed cells to progress to an early cancerous state, revealing secreted blood biomarkers of early-stage disease along the way.

The best candidate biomarker, plasma thrombospondin-2 (THBS2), was screened against 746 cancer and control plasma samples using an inexpensive, commercially available protein-detection assay. The team found that blood levels of THBS2, combined with levels of a known later-stage biomarker called CA19-9, was reliable at detecting the presence of pancreatic cancer in patients.

The team refined the assay with independent investigations of plasma samples from patients with different stages of cancer, from individuals with benign pancreatic disease, and from healthy controls, all obtained from Petersen, who directs the biospecimen resource program for pancreas research at the Mayo Clinic.

“Positive results for THBS2 or CA19-9 concentrations in the blood consistently and correctly identified all stages of the cancer,” Zaret said. “Notably, THBS2 concentrations combined with CA19-9 identified early stages better than any other known method.” The combination panel also improved the ability to distinguish cases of cancer from pancreatitis. The panel will next be validated in a set of samples from pancreatic cancer patients who provided a research blood sample prior to their diagnosis.

Source: Penn Medicine Communications
Karen Kreeger, karen.kreeger@uphs.upenn.edu
Penn Pathologist Honored for Excellence in Ovarian Cancer Research

Ronny Drapkin, MD, PhD, director of the Penn Ovarian Cancer Research Center in the Perelman School of Medicine at the University of Pennsylvania, has been named the recipient of this year’s Rosalind Franklin Prize for Excellence in Ovarian Cancer Research. The prestigious award is from the Ovarian Cancer Research Fund Alliance in recognition of an individual’s contributions to basic science, translational, or clinical research in ovarian cancer.

Drapkin, who is also an associate professor of Pathology in Obstetrics & Gynecology and the director of Gynecologic Cancer Research for the Basser Center for BRCA in the Abramson Cancer Center of the University of Pennsylvania, directs a team of researchers focused on developing a comprehensive understanding of the genetic, molecular and physiological factors that drive the development of cancer, with a special focus on gynecologic malignancies. Recent work from his group has implicated the fallopian tube as the likely point-of-origin for a majority of advanced ovarian cancers – a finding that has created a paradigm shift in the field, refocusing the efforts of experts who long believed the deadly cancers originated in the ovaries.

Since the discovery, the Drapkin lab has been at the forefront in developing novel experimental platforms that address the role of the fallopian tube and its susceptibility to neoplastic transformation. These platforms include genetically engineered mouse models, fallopian tube-derived cell lines, and patient-derived tumor xenografts. These model systems have been shared with investigators around the world and have been a catalyst for numerous international collaborations. The lab is currently focused on using these models to understand how genetic and epigenetic alterations influence lineage dependencies, genomic instability, DNA repair, replicative stress, and metabolism. The goal is to define selective vulnerabilities that can guide novel therapeutic approaches and biomarker development.

The Rosalind Franklin Prize is named for the molecular biologist Dr. Rosalind Franklin, who played a vital role in discovering the structure of DNA. Her life was cut short in 1958 when she died of ovarian cancer at age 37. Throughout her life, she was a committed researcher.

Given in her honor, recipients of the award have a track record of high achievement in the field of ovarian cancer research, as demonstrated by significant contributions to the care of women with gynecologic cancer and to the literature in the field, as well as having obtained significant extramural research funding. The prize rewards past achievement and provides further incentive for an outstanding working scientist to continue to do exceptional research into the causes, prevention, and treatment of ovarian cancer.

Source: Penn Medicine Communications
Katie Delach, katie.delach@uphs.upenn.edu

Common Insurance Plans Put Care at NCI Cancer Centers Out of Reach

Cancer patients in the United States may be unable to access care at the nation’s top hospitals due to narrow insurance plan coverage – leaving patients to choose between lower premiums or access to higher-quality cancer care. A new study from the Perelman School of Medicine at the University of Pennsylvania shows common, so-called “narrow network” insurance plans – lower-premium plans with reduced access to certain providers – are more likely to exclude doctors associated with National Cancer Institute (NCI)-Designated Cancer Centers. Researchers published their findings this week in the Journal of Clinical Oncology and call for greater access for patients and more transparency from insurers.

“Because cancer care and monitoring is costly, there are strong incentives for insurers to be selective when it comes to oncologists, excluding those who are most likely to attract the most complex and expensive cases,” said the study’s lead author Laura Yasaitis, PhD, a postdoctoral researcher at Penn’s Leonard Davis Institute of Health Economics.

“Consumers may benefit financially from the fact that these narrow networks generally have lower premiums, but they may face reduced access to the higher-quality providers in their market,” added Daniel Polsky, PhD, the executive director of the Leonard Davis Institute of Health Economics and the study’s co-senior author.

The study authors examined cancer provider networks offered on the 2014 individual health insurance exchanges and then determined which oncologists were affiliated with NCI-Designated Cancer Centers or National Comprehensive Cancer Network (NCCN) Cancer Centers. These cancer hospitals are recognized for their scientific and research leadership, quality and safety initiatives, and access to expert physicians and clinical trials. NCCN Member Institutions

(Continued on page 3)
Burroughs Wellcome Awards $1.9M in Grants to 3 Penn Researchers

The Burroughs Wellcome Fund has named Penn Medicine dermatology expert Elizabeth A. Grice, PhD, as a recipient of the 2017 Investigators in the Pathogenesis of Infection Disease Award. Grice was selected for the five-year, $500,000 award for her research proposal on skin microbiome functions in colonization resistance to pathogens. She is one of just 12 researchers to receive the award this year. In addition, the Fund has awarded 2017 Career Awards for Medical Scientists (CAMS) to two additional Penn researchers, Vijay Bhoj, MD, PhD and Kara Maxwell, MD, PhD. They are among 12 physicians who will each receive a five-year, $700,000 grant.

Grice is an assistant professor of Dermatology in the Perelman School of Medicine at the University of Pennsylvania. Her lab uses an interdisciplinary approach to understand how microbial communities coexist and interact with the skin of their host in health and disease. She will use the award to further investigate how microbial communities colonizing healthy skin are protective against colonization and/or infection by pathogenic microorganisms such as Staphylococcus aureus.

The Investigators in the Pathogenesis of Infections Disease Award provides opportunities for accomplished researchers still early in their careers to bring multidisciplinary approaches to the study of human infectious diseases. The goal of the program is to provide opportunities to study what happens at the points where the systems of humans and potentially infectious agents connect. The program supports research that sheds light on the fundamentals that affect the outcomes of these encounters, specifically how colonization, infection, and other relationships play out. For a complete list of the 2017 honorees, visit the Burroughs Wellcome Fund website.

Bhoj is a Blood Bank/Transfusion Clinical Fellow at Penn. The grant will fund his research on the development of CAR T-cell immunotherapy for the prevention and eradication of FVIII inhibitors in Hemophilia A.

Maxwell is an instructor in the division of Hematology-Oncology who focuses on care and research for patients with hereditary cancers. The grant will fund her study of tumors from patients with inherited mutations in DNA repair genes, with a specific focus on the genetic makeup of those tumors and how those genes may affect response to targeted therapies.

The goal of the CAMS grant is to help physicians transition into a full-time career as a biomedical research scientist and tenured faculty member. The full list of winners is published online.

Source: Penn Medicine Communications
John Infanti, john.infanti@uphs.upenn.edu

Narrow-Network Insurance Plans

(Continued from page 2) are particularly recognized for higher-quality care, and treatment at NCI-Designated Cancer Centers is associated with lower mortality than other hospitals, particularly among more severely ill patients and those with more advanced disease. Narrower networks were less likely to include physicians associated with NCI-Designated and NCCN Member Institutions.

“To see such a robust result was surprising,” Yasaitis said. “The finding that narrower networks were more likely to exclude NCI and NCCN oncologists was consistent no matter how we looked at it. This is not just a few networks. It’s a clear trend.”

Researchers said the results point to two major problems: Transparency and access.

“Patients should be able to easily figure out whether the physicians they might need will be covered under a given plan,” said the study’s co-

senior author Justin E. Bekelman, MD, an associate professor of Radiation Oncology and Medical Ethics and Health Policy, and a senior fellow in the Leonard Davis Institute for Health Economics. The authors suggest that insurers report doctor’s affiliations with NCI and NCCN Cancer Centers so that consumers can make more informed choices.

The authors also suggest that insurers offer mechanisms that would allow patients to seek care out of network without incurring penalties in exceptional circumstances. “If patients have narrow network plans and absolutely need the kind of complex cancer care that they can only receive from one of these providers, there should be a standard exception process to allow patients to access the care they need,” Bekelman said.

Source: Penn Medicine Communications
John Infanti, john.infanti@uphs.upenn.edu
Funding Opportunities

PA-17-325/PA-17-323 Ethical, Legal, and Social Implications (ELSI) of Genomics Research Grant Programs (R01/R21)

Application Deadline: Standard dates apply

These FOAs invite applications that propose to study the ethical, legal and social implications (ELSI) of human genome research.

R01 applications may propose studies using either single or mixed methods. Proposed approaches may include but are not limited to data-generating qualitative and quantitative approaches, legal, economic and normative analyses, and other types of analytical and conceptual research methodologies, such as those involving the direct engagement of stakeholders.

R21 applications should propose single or mixed methods studies that break new ground, extend previous discoveries in new directions or develop preliminary data in preparation for larger studies. Of particular interest are studies that explore the implications of new or emerging genomic technologies or novel uses of genomic information.

R01: https://grants.nih.gov/grants/guide/pa-files/PA-17-325.html


RFA-HL-18-021 Consortium Linking Oncology with Thrombosis (CLOT) (U01)

LOI Due: 30 days before application deadline

Application Deadline: October 23, 2017

The purpose of this FOA is to establish a program which will provide support for the collaborative efforts of oncologists and coagulovascular experts to identify, further develop, and implement advances in thrombosis and hemostasis research into practice for cancer patients.


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