Stanford Lab Explores Fundamental Nature of Cancer Using Mass Spectrometry

NEW YORK, March 17, 2015 /PRNewswire-USNewswire/ -- Stanford University Chemistry Department's Zarelab is pioneering an innovative and multidisciplinary approach to understanding more deeply the biochemical processes related to how cancer begins and progresses. By combining sophisticated analysis at the molecular level using transgenic animal models and cell samples, desorption electrospray ionization mass spectrometry imaging, and statistical modeling, it is producing new insights about the relationship between metabolic patterns and oncogene expression.

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In a research paper recently published in the *Proceedings of the National Academy of Sciences*, it was reported that in mouse lymphoma there were marked differences in the lipid profiles of the cancer cells when the oncogene MYC or the oncogene RAS was overexpressed. Interestingly, similar patterns were observed in human lymphomas that had MYC overexpression. This work also reported the presence of lipids with more double bonds in tissue samples with MYC overexpression; the enzyme in the cell that adds double bonds to the lipids is regulated by MYC.

"This work is giving us deep insight into how different types of cancer are making themselves apparent through the resulting distribution of lipid molecules," states lab director Richard N. Zare, the Marguerite Blake Wilbur Professor in Natural Science, and a board member of the

Camille & Henry Dreyfus Foundation. "This information also suggests possible new targets for cancer treatment."

How it works

A chemical map is made by bombarding tissue samples with droplets that dissolve fat molecules called lipids and other cell metabolites. The resulting splash of smaller droplets enters a mass spectrometer where the mass of each dissolved compound can be determined. Hundreds of different molecules are identified and a sophistical statistical analysis is used to find which molecules are different in tumors versus normal tissue. Cancers usually arise from a small number of mutations in small segments of DNA, which are called oncogenes. This study uses genetically engineered animals in which different oncogenes can be turned on and off. As a consequence it is possible to identify which lipids are associated with which types of oncogenes.

The mass spectrometry technique used is the brainchild of *R. Graham Cooks*, the Henry Bohn Hass Distinguished Professor of Chemistry at Purdue University, and the winner of the 2013 Dreyfus Prize from the Camille & Henry Dreyfus Foundation. Cooks, a pioneer in the field of mass spectrometry in which contents of a sample are identified by turning its molecules into ions and measuring their mass, developed the ambient ionization technique allowing samples to be tested in the air or directly on a surface, and created opportunities for new applications, eliminating the need for mass spectrometry samples to be chemically manipulated.

Primary researcher Livia S. Eberlin, a postdoctoral scholar in chemistry, conducted the research under Zare's direction. The interdisciplinary team for the study included oncologist Professor Dean Felsher of the Stanford School of Medicine who developed the animal models and statistician Professor Rob Tibshirani of the Stanford School of Humanities and Science who developed the algorithms for data analysis.

Eberlin, who joined Cooks' research team in 2008 at Purdue as a graduate student, led the design and testing of a tool that used this technique in the operating room to characterize the type and grade of brain cancer and detect boundaries between healthy and cancerous brain tissue. When finishing as a graduate student, Eberlin and Cooks won the American Chemical Society's Nobel Laureate Signature Award for Graduate Education in Chemistry. She was recently selected as one of five scientists to receive the 2014 L'Oreal USA for Women in Science Fellowship and also has been named as one of the top 30 researchers under age 30 by *Forbes* magazine.

The Zarelab is now investigating how various metabolic patterns are found in different tumors, specifically in skin, lung, prostate, pancreatic and kidney cancers. "By using mass spectrometry to directly analyze samples and detect molecular signatures that are characteristic of a cancer type and oncogene expression from biological samples," says Zare, "we expect one day to rapidly give a diagnosis and predict best treatment options for an individual."

The Camille and Henry Dreyfus Foundation (www.dreyfus.org), based in New York, is a leading non-profit organization devoted to the advancement of the chemical sciences. It was established in 1946 by chemist, inventor, and businessman Camille Dreyfus, who directed that the Foundation's purpose be "to advance the science of chemistry, chemical engineering, and related sciences as a means of improving human relations and circumstances around the world."

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