Spit tests may soon replace many blood tests

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One day soon patients may spit in a cup, instead of bracing for a needle prick, when being tested for cancer, heart disease or diabetes. A major step in that direction is the cataloguing of the “complete” salivary proteome, a set of proteins in human ductal saliva, identified by a consortium of three research teams, according to an article published today in the Journal of Proteome Research. Replacing blood draws with saliva tests promises to make disease diagnosis, as well as the tracking of treatment efficacy, less invasive and costly.

Saliva proteomics and diagnostics is part of a nationwide effort to create the first map of every human protein and every protein interaction, as they contribute to health and disease and as they act as markers for disease states. Following instructions encoded by genes, protein “machines” make up the body’s organs and regulate its cellular processes. Defining exact protein pathways on a comprehensive scale enables the development of early diagnostic testing and precise drug design. In the current study, researchers sought to determine the “complete” set of proteins secreted by the major salivary glands (parotid, submandibular (SM) and sublingual (SL)). Recent, parallel efforts that mapped the blood (plasma) and tear proteomes allows for useful comparisons of how proteins and potential disease markers are common or unique to different body fluids.

“Past studies established that salivary proteins heal the mouth, amplify the voice, develop the taste buds and kill bacteria and viruses,” said James E. Melvin, D.D.S., Ph.D., director of the Center for Oral Biology at the University of Rochester Medical Center, and an author on the

paper. “Our work, and the work of our partners, has shown that salivary proteins may represent new tools for tracking disease throughout the body—tools that are potentially easier to monitor in saliva than in blood,” said Melvin, who conducts his research at the Eastman Dental Center, in collaboration with the research labs of Mark Sullivan, Ph.D., and Fred K. Hagen, Ph.D.

The National Institute of Dental and Craniofacial Research (NIDCR), part of the National Institutes of Health, funded the current study. The saliva proteome study represents a consortium effort with research teams at The Scripps Research Institute (John R. Yates III), University of Rochester, University of Southern California (Paul Denny), The University of California at San Francisco (Susan J. Fisher) and UC Los Angeles (David T. Wong, Joseph A. Loo).

Not Your Parent’s Saliva

To describe the results of the current study, it is important to note that the definition of saliva is evolving. Saliva once referred to everything in oral fluid, including: bacterial waste products, dead cells that had shed from mucous membranes and substances oozing from gum crevices. Among researchers today, however, the term saliva is increasingly reserved for just the salivary gland secretions (ductal saliva). The new definition is significant because of the emerging theory that the mix of proteins in ductal saliva tracks closely with that of blood, making saliva a potential diagnostic stand-in for blood.

To construct a credible protein list for saliva, the teams used competing techniques both to capture the greatest number of protein candidates for the list and to lend extra credibility to those found using different methodologies. Each team subjected saliva collected from patients to some form of mass spectrometry, which determines the identity of proteins based on measurements of their mass and charge. Saliva was

collected from 23 adults of several races and both sexes. Although small, the set of study subjects was large enough to serve as a baseline list for near-future comparisons between healthy people and individuals with major diseases, researchers said.

Using mass spectrometry techniques, three teams at five institutions identified 1,166 proteins in parotid and submandibular/sublingual saliva. The results indicated that more than a third of saliva proteins were found in the blood proteome, as well. Comparison of these proteins against known protein pathways and other proteomes provided a first glimpse of the function of the core proteins. In addition, a number of the salivary proteins were found to match proteins with known roles in Alzheimer's, Huntington's and Parkinson's diseases; breast, colorectal and pancreatic cancer; and type I and II diabetes. Specifically, a majority of the proteins were found to be part of signaling pathways, which is central to the body's response to (and thus diagnosic of) system-wide diseases, researchers said.

Determining the salivary proteome is only the first step toward salivary-based diagnosis and treatment. These findings provide crucial protein information that is already being incorporated into microarray technology, a high-speed test that can determine the levels of multiple proteins, during disease progression. Related work is underway under within the NIH-funded Bioengineering Nanotechnology Initiative to design biochips, nano-scale computer chips packed with salivary protein chains. Protein probes on the chip react with proteins in a saliva sample, say from the mouth of someone with oral cancer, and inform a computer about which proteins are present.

"We believe these projects will dramatically accelerate diagnosis and improve prognosis by treating diseases at the earliest stages," said Mireya González Begné, D.D.S., Ph.D., research assistant professor of Dentistry in the Center for Oral Biology at the Medical Center.

“Researchers have already shown that saliva proteins can be used to detect oral cancer and HIV infection. We think this list will soon expand to include leading causes of death like cancer and heart disease, which, if caught early, are much more likely to be successfully treated.”

Source: University of Rochester