U.S. Department of Health and Human Services
NIH News
National Institutes of Health

National Institute of Dental and Craniofacial Research

For Immediate Release
Wednesday, August 8, 2007

Contact:
Bob Kuska
301-594-7560

Lab on a Chip for Oral Cancer Shows Promise

Finding out whether that unusual sore in your mouth is cancerous should become a lot faster and easier in the years ahead. Scientists supported by the National Institute of Dental and Craniofacial Research (NIDCR), part of the National Institutes of Health, have engineered the first fully automated, all-in-one test, or lab on a chip, that can be programmed to probe cells brushed from the mouth for a common sign of oral cancer.

About half the size of a toaster, the portable device yields results in just under 10 minutes, or well within the duration of a routine visit to a dentist or doctor. Currently, patients must undergo an often painful tissue biopsy and usually wait three days to a week for the lab results. "What's exciting is the speed and efficiency that this test will bring to the diagnostic process," said John McDevitt, Ph.D., a scientist at the University of Texas at Austin and the senior author on the paper, published in the August issue of the journal Lab on a Chip. "No longer will patients need to endure referrals, long waits for test results, and scheduling follow up consultations. Patients will get immediate results and feedback from their dentist or doctor on how best to proceed."

McDevitt said his group's proof of principle study showed that their test could accurately measure levels of epidermal growth factor receptor, or EGFR, on three distinct types of oral cancer cells. This protein, which is normally displayed on the surface of our cells, tends to be overproduced in oral tumor cells and serves as a measurable marker of oral cancer.

His group's next step is to program the device to read not just EGFR levels but those of other proteins and genes that, when altered, are indicative of a developing oral tumor. This work already is well under way, and the group anticipates evaluating their test in the clinic with patients in the foreseeable future. "It could take several months to more than a year before we make the transition," said McDevitt. "But the diagnostic platform has been built, and it's just a matter of fine tuning the components that already are in place."

According to McDevitt, the lab on a chip evolved from a conversation that he had a few years ago with Dr. Spencer Redding of the University of Texas Health Sciences Center in San

Antonio about the difficulties of diagnosing oral cancer. Redding explained that dentists routinely face the dilemma of whether or not to refer patients to an oral surgeon for biopsies of suspicious sores, particularly possible recurrences of a previously diagnosed oral cancer. On the one hand, early detection is a key to fighting cancer and saving lives and, on the other, if the pathology report comes back negative, dentists risk upsetting their patients.

McDevitt was uniquely qualified to consider the problem. He studied in his laboratory functional molecular assemblies, or manipulating individual molecules to assemble miniaturized electronic or sensor components. This area of research has contributed greatly toward developing nano scale devices and popularizing the new discipline of nanotechnology.

The McDevitt laboratory already had an excellent track record of assembling novel, easy-to-use sensing devices that involve microfluidics, the science of precisely controlling micro or nano volumes of fluid. Among their accomplishments were a novel, miniaturized sensor to detect anthrax spores for the Nation's biodefense efforts and thereafter a test for HIV infection and immune function in resource poor African nations. The laboratory also was working in the mouth, having received an NIDCR research grant to develop similar tests that use saliva, rather than blood, as a diagnostic fluid.

Combining these areas of research expertise, the McDevitt laboratory developed a test for oral cancer that begins with brushing cells from a suspicious lesion, suspending them in fluid, and loading roughly a drop of the mixture into their device. When activated, the device conveys the fluid down a tiny, microfluidic channel to a chamber with a porous membrane. "The cells stick to the membrane floor like starfish in a net," said Shannon Weigum, a member of the McDevitt laboratory and lead author on the paper. "The floor has little exit holes that drain the fluid out of the chamber and allow us to pump in a cocktail of, in this case, antibodies that are tagged with a fluorescent dye and that are programmed to seek out and attach to the EGFR displayed on the cells."

"The chamber creates a nice, miniaturized platform with a digital camera interface to display the fluorescent tags for analysis on a computer screen," she continued. "We can then read the level of fluorescence and determine how much EGFR is present on the cell surface. It automates a process that is done now by a pathologist. Think of the test as pathology on a chip."

In their initial experiments, the all-in-one test detected significantly higher levels of EGFR in three known oral cancer cell lines compared to normal cells, which would have been expected. This indicated that the lab on a chip had excellent specificity for its protein target. The scientists also found that their results correlated well with those using flow cytometry, the current gold-standard analytical technique to quantify protein expression.

The scientists reported that their lab-on-a-chip protocol took about nine minutes to complete, from sample collection to digital display. For flow cytometry, the protocol took two hours and five minutes. "We are doing our immune function test in eight minutes, and that includes the software manipulation and collecting the sample," said McDevitt. "I feel comfortable saying

that, with further manipulations, the oral cancer test ultimately will be completed somewhere between five and ten minutes. We have developed tests that can be performed in thirty seconds, but there is some loss in accuracy when you do things in an ultra fast manner."

The Food and Drug Administration approved the EGFR-targeted monoclonal antibody called cetuximab in March 2006 to treat oral squamous cell carcinoma, the most common type of oral cancer. This marked the first new drug approved for this cancer in 45 years. But challenges remain to identify patients who might benefit from this therapy. With further development and clinical validation, the oral cancer lab on a chip could one day fill this diagnostic niche.

The National Institute of Dental and Craniofacial Research (NIDCR) is the Nation's leading funder of research on oral, dental, and craniofacial health.

The National Institutes of Health (NIH) — *The Nation's Medical Research Agency* — includes 27 Institutes and Centers and is a component of the U.S. Department of Health and Human Services. It is the primary federal agency for conducting and supporting basic, clinical and translational medical research, and it investigates the causes, treatments, and cures for both common and rare diseases. For more information about NIH and its programs, visit www.nih.gov.

Home > News & Events E-mail this page Subscribe to receive future NIH news releases.