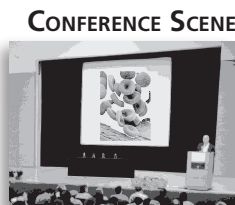


Nanomedicine



A potential nano-bio-chip for rapid detection of oral cancer is developed

Researchers have developed a minimally invasive, novel nano-bio-chip that would be able to differentiate between malignancies, premalignancies and nonmalignant lesions within 15 min

Swift detection of oral malignant and pre-malignant lesions has been made possible by the development of a nano-bio-chip able to detect oral cancer via an immediate, noninvasive technique. Importantly, preliminary studies by the researchers using the diagnostic chip have demonstrated comparable success rates to traditional techniques, such as biopsies, highlighting the new technique as a suitable alternative to the commonly utilized method.

.....
“Eventually, dentists may be the first line of defense against oral cancers, with the ability to catch early signs of the disease right there in the chair.”

The promising data are a result of collaborative work between Rice University, TX, USA, the University of Texas Health Science Centers at Houston and San Antonio, TX, USA, and the University of Texas MD Anderson Cancer Center, TX, USA. John McDevitt, the Brown-Wiess Professor of Chemistry and Bioengineering at Rice University, where the chip technology was developed, was inspired to develop this tool owing to the lack of successful diagnostic methods currently available. “This area of diagnostics and testing has been terribly challenging for the scientific and clinical community,” he stated. “Part of the problem is that there are no good tools currently available that work in a reliable way.”

Key to the success of the method is the noninvasive nature of the analysis. The new device, similar in size and shape to a toothbrush, is merely brushed onto the lesion on the cheek or tongue, in order to gain sufficient material for analysis. Compared with the invasive, painful biopsy method,

which normally takes several days for the results to be available, the new method is able to analyze the data in a swift 15 min.

Oral cancer afflicts more than 300,000 people a year, and whilst the 5-year survival rate is 60%, if the cancer is detected early, this rate can rise to 90%. “You want to catch it early on, as it is transforming from precancer to the earliest stages of cancer, and get it in stage one. Then, the 5-year survival rate is very high,” McDevitt explained. “Currently, most of the time, it is captured in stage three, when the survivability is very low.”

The published study was performed on 52 patients who had visible oral lesions and thus had been referred for surgical biopsies or complete removal of the lesions. The results of traditional diagnostic tests were compared with those obtained from the nano-bio-chips, with the novel technology found to be 97% sensitive and 93% specific in detecting malignant or pre-malignant lesions. “One of the key discoveries in this paper is to show that the miniaturized, noninvasive approach produces about the same result as the pathologists do,” McDevitt enthused.

The device is now close to being entered for an extensive trial involving 500 patients from both the USA and the UK, with the potential for US FDA approval a possibility in less than 4 years’ time. “Eventually,” McDevitt encouragingly commented, “dentists may be the first line of defense against oral cancers, with the ability to catch early signs of the disease right there in the chair.”

.....
 Sources: Rice University, Texas, USA: www.media.rice.edu/media/NewsBot.asp?MODE=VIEW&ID=14030; Weigum SE, Floriano PN, Redding SW et al.: Nano-bio-chip sensor platform for examination of oral exfoliative cytology. *Cancer Prev. Res.* 3(4), 518–528 (2010).



Zinc-stapled insulin molecule could reduce the risk of diabetes-associated cancer

A recent study demonstrates that careful protein engineering is able to reduce binding of an insulin analog to a cancer-related receptor

A team based at the School of Medicine at the Case Western Reserve University, OH, USA, have developed a ‘smart’ insulin protein molecule that not only self-assembles under the skin to provide a slow-release form of insulin, but also binds considerably less to receptors known to be associated with cancer.

The research was led by Dr Michael Weiss, Cowan-Blum Professor of Cancer Research and Chair of the Department of Biochemistry at the university. “It is quite a novel mechanism. Our team has applied the perspective of biomedical engineering to the biochemistry of a therapeutic protein. We regard the injected insulin solution as forming a new biomaterial that can be engineered to optimize its nano-scale properties,” said Weiss.

In the results published in the study,

the novel insulin analog exhibited reduced binding to the IGF receptor, a receptor associated with cell growth. Furthermore, through the application of supramolecular chemistry principles to nanobiotechnology, the teams were able to combine this enhanced selectivity with improved pharmacokinetic properties of the hormone via the inclusion of zinc ions. Upon subcutaneous injection, the analog self-assembles under the skin by ‘stapling’ itself using the bridging zinc ions, resulting in slow-release delivery of the therapeutic molecule.

Diabetes affects millions of people worldwide and the growing concern of associated risks of cancer from excess insulin has led to extensive research into improving the selectivity of the molecule. “We have sought to accomplish improved drug selectivity with our engineering a new and ‘smarter’ insulin

molecule, as the hormone’s primary job is to bind to the key receptors that regulate blood glucose concentration (designated the insulin receptor), not cancer-related receptors,” explained Weiss.

While the efficacy of the ‘smart’ molecule was only tested here in diabetic rats, the goal of investigating its use in human clinical trials is underway with approval by the NIH. As Weiss hypothesizes, “The notion of engineered zinc staples may find application to improve diverse injectable protein drugs to address a variety of conditions from cancer to immune deficiency.”

Sources: School of Medicine, Case Western Reserve University, OH, USA: <http://case.edu/medicine/breakingnews/diabetescare.html>; Phillips NB, Wan ZL, Whittaker L et al.: Supramolecular protein engineering: design of zinc-stapled insulin hexamers as a long acting depot. *J. Biol. Chem.* 285(16), 11755–11759 (2010).

Experimental acne drug-delivery system utilizes gold nanoparticles

California researchers have developed a smart nanoparticle system capable of direct delivery of liposomes to the skin-dwelling bacteria that cause common acne

The development of a ‘smart’ delivery system capable of delivering lauric acid-filled nanoscale bombs directly to skin-dwelling bacteria (*Propionibacterium acnes*) has been recently reported by a group at UC San Diego Jacobs, CA, USA. Dissaya Pornpattananangkul, a bioengineering graduate student from the School of Engineering at the university, developed the system that is able to deliver liposomes containing the natural product lauric acid.

Acne affects millions of people worldwide and whilst current treatments can be effective, side effects are often associated, including redness and burning. Professor Liangfang Zhang, who leads the team of researchers involved in the study, claims that the lauric acid-based smart delivery

system could avoid these side effects. “Precisely controlled nanoscale delivery of drugs that are applied topically to the skin could significantly improve the treatment of skin bacterial infections, boosting antimicrobial efficacy and minimize off-target adverse effects,” explains Zhang.

The new smart delivery system consists of lauric acid-containing liposomes or ‘nanobombs’ with gold nanoparticles attached to their surface. The nanoparticles stop the liposomes from fusing together whilst at a neutral pH value. However, in acidic environments where the pH is less than 5 (i.e., where the acne-causing bacteria is present on the skin), the gold particle stabilizers detach and the liposomes are thus free to fuse

with bacterial membranes and kill the *Propionibacterium acnes* bacteria via delivery of lauric acid.

Lauric acid is a natural product found in both coconut oil and human breast milk, hence its feasibility as a possible new acne treatment in humans appears quite realistic. As Zhang enthuses, “All building blocks of the nanobombs are either natural products or have been approved for clinical use, which means these nanobombs are likely to be tested on humans in the near future.”

Sources: School of Engineering, UC San Diego Jacobs, CA, USA: www.jacobsschool.ucsd.edu/news/news_releases/release.sfe?id=932; Pornpattananangkul D, Olson S, Aryal S et al.: Stimuli-responsive liposome fusion mediated by gold nanoparticles. *ACS Nano.* 4(4), 1935–1942 (2010).