News

Research Highlights

New delivery option for anticancer drugs demonstrated in a clinical trial

First human trial shows 'minicells' are safe, well tolerated and can induce stable disease in cancer patients.

Research results of a Phase I clinical trial, recently presented at the 24th European Organization for Research and Treatment of Cancer–National Cancer Institute–American Association for Cancer Research Symposium on Molecular Targets and Cancer Therapeutics (Dublin, Ireland), have shown 'minicells' can be safely given to patients with advanced, incurable cancers. In total, 28 patients were treated with the minicells at four centers in Australia. Ten patients had stable disease at 6 weeks and thus received more than one cycle of minicells.

The minicells, designed to deliver anticancer drugs directly to tumor cells, were developed by Himanshu Brahmbhatt and Jennifer MacDiarmid, founders of EnGeneIC (Sydney, Australia). The targeted delivery method aims to reduce toxicity side effects, which are currently seen in the systemic delivery of chemotherapy and advance personalized treatment, specific to the genetic make-up of the tumor. Created from small bubbles of cell membrane pinched off the surface of mutant bacteria, the minicells measure 400 nm in diameter, can be loaded with anticancer drugs and further coated with tumor-seeking antibodies that target surface receptors. Consequently, following delivery, cancer cells recognize the minicell, which is internalized, exposing the anticancer drug to the cancer cell nucleus.

Benjamin Solomon, principal investigator and consultant medical oncologist at the Peter MaCallum Cancer Centre (Melbourne, Australia) explained the benefits of the larger minicells over the synthetic particles currently being developed, "This larger size means that the minicells preferentially fall out of the leaky blood vessels around the tumor and do not end up in the liver, gut and skin where they could cause nasty side-effects like smaller particles do."

Solomon went on to describe the study protocol, "We loaded the cells with a cytotoxic chemotherapy drug (paclitaxel) and coated the minicells with an antibody targeting the loaded minicells to tumors expressing the EGF receptor – a protein that is found on the surface of many cancer cells. The study was then conducted in the way standard Phase I studies are conducted to determine the safety and toxicity of minicells by treating small groups of patients with progressively higher doses of minicells and closely monitoring their safety and toxicity."

Noting that the key finding of the study was that minicells can be safely delivered to patients with advanced cancer forms, Solomon added, "Additionally, we showed that we could give multiple doses and one patient received 45 doses over 15 months. The major toxicity we observed was a mild self-limiting fever seen on the day of the infusion with little or no side-effects seen in the remainder of the following week. At higher doses we found that there were additional side effects, in particular changes in liver function tests, which, although asymptomatic, prevented us from raising the doses of the treatment higher."

Phase II trials of the minicells are now being planned, including a trial in patients with glioblastoma using minicells loaded with doxorubicin. Furthermore, the scientists are looking to develop imaging methods to track the minicells in patients.

– Written by James Potticary

Source: European Cancer Organisation press release: www.ecco-org.eu/Global/News/ENA-2012-PR/2012/11/9_11-First-trial-in-humans-of-minicells.aspx

Future Medicine part of fsg

Novel technique for detecting tumor microvesicles

A new diagnostic platform, developed by combining a nuclear magnetic resonance device and nanotechnology, has proven to be a quick and effective way of detecting and profiling small cell particles, shed by brain cancer cells, known as tumor microvesicles. This miniature platform is much faster and simpler compared with current gold standard techniques for tumor detection, potentially allowing a test to be able to be carried out for glioblastoma multiforme (GBM) in a doctor's office from just a small blood sample.

Hakho Lee, co-senior author of the study and part of the investigative team at Massachusetts General Hospital Center for Systems Biology (MA, USA) responsible for developing the platform, explained "About 30 or 40 years ago, people noticed something in the bloodstream that they initially thought was some kind of debris or 'cell dust'. But it has recently become apparent that these vesicles shed by cells actually harbor the same biomarkers as their parent cells."

These tumor microvesicles are much more abundant in the bloodstream than those released by normal cells. The detection of these by this new system could be a reliable way of diagnosing cancer. Tumor microvesicles are also smaller than circulating tumor cells, another potential key target for cancer diagnosis, and have the added benefit of being able to cross the blood–brain barrier.

The most common and aggressive type of brain cancer in humans is GBM and long-term monitoring of this cancer can be invasive and difficult. Patients usually have 15 months to live following diagnosis; however, it is hoped that earlier and more reliable diagnosis methods than biopsies and imaging tests could extend this life expectancy.

This new technology has been successfully trialed in humans. Using nanotechnology, the researchers were able to magnetically label GBM tumor microvesicles, which were then detected by a hand-held nuclear magnetic resonance device. The research team is now hoping to develop the platform to detect other cancers and diseases.

– Written by Sophie Breeze

Source: Shao H, Chung J, Balaj L et al. *Protein typing of circulating microvesicles allows real-time monitoring of glioblastoma therapy.* Nat. Med. *doi:10.1038/nm.2994 (2012) (Epub ahead of print); Massachusetts General Hospital press release: www.massgeneral.org/about/pressrelease.aspx?id=1519*

First clinical trial of gold nanoshells for treating lung cancer to be carried out in the USA

Cancer Treatment Centers of America and Nanospectra Biosciences (TX, USA) have announced that they plan to conduct the first clinical trial of a gold nanoshell-based therapy for lung cancer. Patients receiving the nanoparticle-based system, known as AuroLase® therapy (Nanospectra Biosciences), will be infused with a single dose of the nanoshells into the bloodstream. After 12–24 h, the patient will be exposed to the near-infrared energy of a laser, which the nanoshells convert into heat to thermally destroy the tumor.

The trial will be led by Mark Lund, director of the Advanced Center for Lung and Thoracic Oncology at Cancer Treatment Centers of America. According to Lund, the selectivity of the nanoshell technology is an advantage over other methods, "… this technology holds the promise of offering new and exciting treatment options for tumor destruction with minimal collateral damage to adjacent tissues and structures."

> "It's extremely gratifying to see this technology progress from the lab into the clinic."

The nanoshells were originally pioneered by Naomi Halas, Stanley C Moore Chair of Electrical and Computer Engineering at Rice University (TX, USA) and Jennifer West, Isabel C Cameron Professor of Bioengineering at Rice University.

Commenting on the prospect of the trial, Halas remarked, "It's extremely gratifying to see this technology progress from the lab into the clinic."

The AuroLase therapy system is also being tested in ongoing clinical trials for prostate cancer and metastatic head-and-neck tumors.

– Written by Hannah Stanwix

Source: Rice University Press Release. Early tests find nanoshell therapy effective against brain cancer: http://news.rice.edu/2012/11/02/nanoshell-therapy-to-be-tested-in-lung-cancer-clinical-trial

About the News

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Ultrasensitive and cheap ELISA developed for virus and cancer diagnosis

The plasmonic ELISA is ten-times more sensitive and ten-times cheaper than the gold standard.

Roberto de la Rica and Molly Stevens of Imperial College (London, UK) have developed a plasmonic ELISA for ultrasensitive disease detection. The technology employed by this ELISA allows naked eye diagnosis of early stage disease and the analyte can be detected at ultralow concentrations in this low-cost assay. This research was published recently in *Nature Nanotechnology* and has promise as a future diagnostic tool for use in resource-constrained countries.

> "These results are potentially significant for the early detection of some cancers and for the diagnosis of diseases in resource-constrained countries, where sophisticated detection equipment may not be available."

Stevens' group have shown that this assay is ten-times more sensitive than the current gold standard; the group have detected the HIV-1 capsid antigen p24 and prostate-specific antigen in whole serum at the ultralow concentration of 1×10^{-18} g/ml^{-1}.

Stevens explained to *Future Medicine*, "We have demonstrated the detection of protein biomarkers at ultralow levels. Furthermore, the detection can be performed with the naked eye in the absence of external equipment. These results are potentially significant for the early detection of some cancers and for the diagnosis of diseases in resource-constrained countries, where sophisticated detection equipment may not be available."

"It is vital that patients get periodically tested in order to assess the success of retroviral therapies and check for new cases of infection. Unfortunately, the existing gold standard detection methods can be too expensive to be implemented in parts of the world where resources are scarce. Our approach affords for improved sensitivity, does not require sophisticated instrumentation and it is ten-times cheaper, which could allow more tests to be performed for better screening of many diseases," added Stevens.

The group's ELISA differs from the traditional assay in that the enzyme label controls the agglutination of gold nanoparticles, which causes a distinct color change in the presence of the target antigen. If the analyte is at a high concentration, the gold nanoparticles will form irregular clumps, leading to a blue color signal; if the analyte is at a normal concentration, the nanoparticles separate into little balls and the assay turns red. Stevens told *Future Medicine* that the future therapeutic implications of this novel ELISA, "may allow physicians to detect ultralow levels of disease biomarkers with the naked eye, thereby adding a new tool to the existent repertoire of tests for clinical diagnosis."

The team hopes to be funded by not-for-profit global health organizations in the future as their aim is for resource-constrained countries to have access to this easy-to-use, cheap and sensitive diagnostic tool. Stevens told *Future Medicine*, "We are planning on adapting the method for its utilization by nonexperts and in decentralized settings."

– Written by Claire Raison

Source: de la Rica R, Stevens MM. Plasmonic ELISA for the ultrasensitive detection of disease biomarkers with the naked eye. Nat. Nanotechnol. *doi:10.1038/nnano.2012.186 (2012) (Epub ahead of print).*