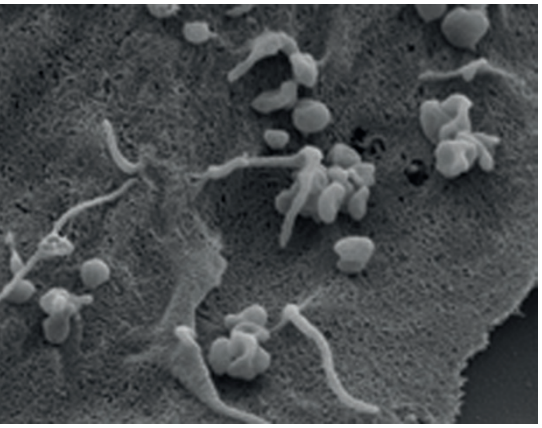
Nature Reviews Clinical Oncology **10**, 4 (2013); published online 27 November 2012; doi:10.1038/nrclinonc.2012.210

BIOMARKERS

Nanotechnology opens up new realm of detection in GBM

New research has shown that the microvesicles (exosomes, see image) glioblastoma multiforme (GBM) cells shed can be detected and used to assess treatment response in real time. The work brings together protein typing, antibody recognition, nanotechnology and lab-on-a-chip diagnostics, resulting in a point-of-care assay that is more sensitive than ELISA and western blotting for protein detection.



Courtesy of H. Shao, R. Weissleder and H. Lee

"Unlike in peripheral cancers, patients with GBM seldom have circulating tumour cells due to a preserved blood–brain barrier," investigator Hakho Lee explains. The barrier essentially limits the traditional cell-based assay for detecting and monitoring the disease. However, a large number of microvesicles exist in the blood of these patients, and the protein profiles of these exosomes reflect those of their parent cells. This feature was leveraged by the researchers to label exosomes with magnetic nanoparticles (MNPs) that are specific to these proteins. In the case of GBM, these targeted proteins are EGFR, EGFR*vIII*, podoplanin and cytosolic isocitrate dehydrogenase.

MNPs enhance the nuclear magnetic resonance (NMR) signal, therefore, the MNP–exosome conjugates can be detected using NMR relaxometry. Also, the method detects in bulk—that is, the signals can be detected from blood samples without excessive processing. Indeed, the team developed an on-chip device that mixes the MNPs with blood samples, filters the specimen and performs the NMR measurement.

The researchers assessed their detection device to monitor treatment effects *in vivo*. Using a mouse model with xenografted human GBM, in animals treated with temozolomide, the efficacy index (a measure of tumour progression) rose rapidly compared with untreated animals. This change preceded tumour shrinkage (detected by MRI) by several days. Similar predictions were also made in patients.

"We envision that disease-specific exosomes will become an important class of biomarker for early disease detection and therapy monitoring," concludes Lee. The Harvard-based team next plan on expanding their device to other tumour types.

Mina Razzak

Original article Shao, H. *et al.* Protein typing of circulating microvesicles allows real-time monitoring of glioblastoma therapy. *Nat. Med.* doi:10.1038/nm.2994