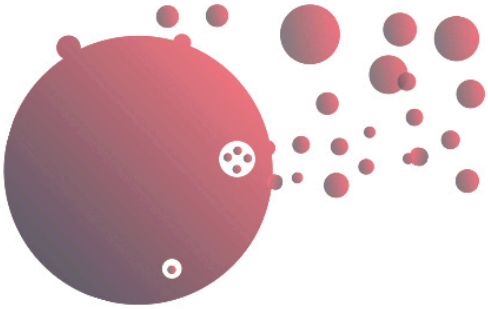
Detection of extracellular vesicles on a magnetoresistive sensor platform

Cherré, Solène; Fernandes, E.; Oliveira, M.; Dias, T.; Cardoso, S.; Rozlosnik, Noemi; Freitas, P.

Publication date:
2015

Document Version
Peer reviewed version



FIRST IBERIAN MEETING
ON EXTRACELLULAR VESICLES
30 SEPTEMBER 2015 | PORTO | PORTUGAL

ABSTRACT TEMPLATE: ***(Please follow the format below as an e.g.)***

SELECT ONE OF THE THEMATIC AREAS WITH AN (X):

_____ Applications in pathology: Infection

_____ Applications in pathology: Cancer

__X___ Other applications of Extracellular Vesicles

A magnetoresistive sensor for the detection of extracellular vesicles derived from HUVEC cells

S. Cherré [1*], E. Fernandes [2] , M. Oliveira [2], T. Dias [3], S. Cardoso [3], N. Rozlosnik [1], P. Freitas [2]

[1] Department of Micro- and Nanotechnology, Technical University of Denmark, Kgs. Lyngby, Denmark,

[2] INL - International Iberian Nanotechnology Laboratory, Braga, Portugal

[3] INESC–MN—Instituto de Engenharia de Sistemas e Computadores–Microsistemas e Nanotecnologias and IN—Institute of Nanoscience and Nanotechnology, Lisbon, Portugal

* solch@nanotech.dtu.dk

Abstract Body *(max. 3000 characters with spaces for text plus references, size-10 font)*

Extracellular vesicles (EV) have gained a wide interest in the biomedical field[1]. Even though they are presented as new type of diagnostic biomarkers for various diseases, the lack of adequate technologies for their characterization and detection remains an obstacle to their further use. Here, we present a proof-of-concept study for the sensing of EV using a magnetoresistive (MR) biochip platform. This MR platform was proven to be highly specific for the detection of DNA hybridization[2] and for *Salmonella* sensing[3] exhibiting detection limits lower than commercial devices and displaying results within less than one hour. The MR platform comprises 30

[1] Burger D, et al(2013) Microparticles: biomarkers and beyond. Clin Sci (Lond) 124:423–41.
[2] Martins VC, et al (2009) Femtomolar limit of detection with a magnetoresistive biochip. Biosens Bioelectron 24:2690–5.
[3] Fernandes E, et al(2014) A bacteriophage detection tool for viability assessment of Salmonella cells. Biosens Bioelectron 52:239–46.

spin valves sensors together with a microfluidic system for sample handling and an electronic setup for the acquisition of the data. The detection scheme was based on an immuno sandwich assay, where the EV were labeled with magnetic nanoparticles (MNP). The MNP were previously coated with an EV specific marker. A second EV specific antibody previously immobilized on the surface of the biosensor captured the MNP labeled EV. An electrical field of 1 mA was applied at the sensors and a magnetic field was used to magnetize the MNP. The binding of the EV on the sensor brought the MNP close to the surface of the sensors which led to a measurable voltage change. The difference of voltage before and after the bio-recognition event indicated the amount of EV in the sample [3]. In this study we used a model of endothelial EV shed by HUVEC cells undergoing apoptosis. As EV specific markers, we immobilized on the surface of the sensors anti-CD31 antibodies, which recognizes CD31 present on endothelial cells. We functionalized the MNP with annexin V, which binds to phosphatidylserine widely present on extracellular vesicles[4]. Within 50 minutes we detected $1x10^8$ EV/ml, i.e. within the dynamic concentration range of EV in blood serum. Experiments were also conducted using an unspecific probe. The unspecific binding was less than 1% of the specific signal.

Future work involves the evaluation of the dynamic detection range of the sensor as well as its lower detection limit for this particular application. This detection strategy allows the enrichment of the EV from complex samples such as serum. Multiplexing for the simultaneous detection of EV from different cells is also possible. With this work we expect to advance knowledge on the exciting field of EV by providing a robust and highly sensitive detection technology.

[4] Arraud N, et al.(2015) A simple flow cytometry method improves the detection of phosphatidylserine-exposing extracellular vesicles. J Thromb Haemost 13:237–47.