TECHNOLOGY OFFER

METHOD AND SYSTEM FOR RAMAN-BASED CHARACTERIZATION OF SINGLE EXTRACELLULAR VESICLES

BIOMARKED, a consortium of research laboratories of Ghent University, member of the Cancer Research Institute Ghent (CRIG), is seeking partners interested in licensing.

Introduction

Extracellular vesicles (EV), are membrane enclosed vesicles released by all cells.
Extracellular vesicles released in bodily fluids (e.g. blood, urine, saliva) receive a lot of attention as possible biomarkers for disease detection and progression, e.g. tumor growth and metastasis. Substantial efforts go into developing techniques suitable for EV identification. Identifying the origin of EVs is typically done using biomolecular characterization techniques to determine the protein, nucleic acid and lipid content.
Currently, most EV based diagnostic approaches focus on one specific molecular component as a biomarker for the presence of diseased cells by elaborate genomic, proteomic, metabolomic or lipidomic studies.
. Despite the fact that these techniques provide detailed molecular information, they require complicated and time-consuming protocols. Additionally, these analyses are performed on the overall EV population level which makes it less likely to find low abundant subpopulations. Considering that most cells secrete EVs as part of their normal function, it is to be expected that the amount of EV derived from diseased cells is comparatively low. Accordingly, the detection of altered levels of low abundant components in a bulk analysis is quite challenging. Furthermore, it is becoming apparent that one cell type may release multiple subtypes of EVs due to which bulk analysis is prone to missing specific subtypes or subtype ratios of EV.
One interesting alternative approach is the use of Raman spectroscopy as the Raman fingerpring of EVs represents their composition – and therefore their origin – in a label free manner.

Technology

Researchers at Ghent University have developed a surfaced enhanced Raman spectroscopy (SERS) based method for characterizing single EVs in the context of disease detection and progression and allowing non-invasive diagnosis in plasma and urine.
The method characterizes EVs at an individual level and is performed by functionalizing EVs with plasmonic material, irradiating the functionalized individual EVs with a laser beam and detecting a SERS signal from said individual EV. Afterwards the obtained Raman spectra are analyzed using dedicated statistical models to allocate each EV to its respective cellular origin based on a spectra library.

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Applications

In combination with a method for isolating (centrifugation based or lab-on-chip based), this technology:

+ can be used for non-invasive cancer diagnosis in plasma and urine
+ enables individual EV fingerprinting
+ allows to identify rare types in polydisperse EV samples.
+ allows quantification of the single 'rare' EVs
+ enables discriminating EVs from different cellular origins
+ allows to build libraries of SERS signals of EV types identified in EV containing samples

Advantages

In combination with method for isolating EVs and in combination with a platform for automated Raman spectra collection, this technology offers significant advantages:

+ enables characterization of EV at an individual level. The latter may be advantageous since it is expected that the amount of 'diseased' cell-derived EVs is low. By being capable of determining at a particle by particle base, the detectability of pathologies based on characterization of EVs can be drastically improved.
+ enables characterization of rare types or low abundant types in polydisperse EV samples.
+ enables discrimination of cancer EVs versus 'non cancer' EVs isolated from plasma.
+ EVs can be identified in a label free manner.

Status of development

The method has been validated for a mixture containing EVs from melanoma cells spiked in EVs from healthy red blood cells. The method has been validated for EVs obtained from tumor conditioned medium from breast cancer patients and SERS fingerprinting was obtained in comparing with plasma EVs from healthy subjets. A discriminating statistical analysis method is in place. Functionalization of the the EVs to obtain a SERS signal has been optimized for discriminating cancer EVs from healthy EVs .

Partnership

Ghent University is seeking a licensing partner or a collaboration with a lab-on chip partner to further validate the combination technology.

Intellectual property

An International Patent application WO2017/103245 "Method And System For Characterizing Extracellular Vesicles" has been filed with priority date December 18th 2015 (publication date: 22/06/2017).

The inventors

Braeckmans Kevin, Stremersch Stephan, Skirtach André, De Smedt Stefaan, Raemdonck Koen, Demeester Joseph, Fraire Juan

References

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Stremersch S. et al., *Small*, 2016

Keywords

Exosomes, Extracellular vesicles, cancer diagnosis, liquid biopsies, single EV characterization, Raman spectroscopy

Contact

Dr. Daisy Flamez – Business Developer
Biomarked Consortium, Ghent University
Cancer Research Institute Ghent (CRIG)
Coupure Links 653, Blok A room 032, B-9000 Ghent, BELGIUM
+32 9 264 99 12 - Daisy.Flamez@UGent.be