A METHOD FOR THE CHARACTERIZATION OF CARDIAC SPECIFIC MICROVESICLES

CHALLENGE
Development of a simple, accurate and powerful tool for characterizing, sorting and quantifying circulating tissue-derived MVs, focusing on cardiac-derived MVs (C-MVs), for disease staging, prognosis and assessment of treatment responsiveness.

THE TECHNOLOGY
Our method is based on a “sequential stepwise gating strategy”, using multicolour flow cytometry (FACS) to directly assess MVs in plasma of cardiovascular disorders (CVD) patients. Using antibodies with high specificity and with a cross reaction <10%, we can identify and quantify C-MVs in plasma samples. By employing an antibody recognizing a molecule present on human cardiomyocytes that has not yet been described for the sorting of C-MVs, we proved that the absolute count of circulating C-MVs significantly changes in several CVDs, namely hypertrophic cardiomyopathy, coronary artery disease and aortic stenosis. In patients with these types CVD, C-MVs were selectively increased as compared to (heart disease) HDs, demonstrating that ischemic, but not necrotic, myocardium releases C-MVs.

We have data on about 300 patients demonstrating the uniqueness of C-MVs compared to other circulating biomarkers: patients with aortic stenosis undergoing transcatheter aortic valve replacement (TAVR) surgery present with a dramatic drop in circulating C-MVs one year after the procedure. We were also able to classify patients according to the level of circulating C-MVs before the procedure: those with a higher level of C-MVs had a better prognosis at early stage of one year and at long term at three years compared to those with a lower level.

APPLICABILITY
It is conceivable that circulating C-MVs will be included in the class conventional CVD biomarkers, which includes cardiac troponin T (cTnT), a biomarker of myocardial injury, and brain natriuretic peptide (BNP and NT-proBNP), biomarkers of heart failure. cTnT and BNP or NT-proBNP are the main biomarkers used in cardiovascular clinical practice. Specifically, they help assess myocardial necrosis (cTnT) or myocardial stress (BNP), and thus help guide therapeutic choices. However, they have a limited value in many clinical settings. In particular, they do not help discriminate which patients need specific invasive procedures. For this reason, we envision the application of C-MVs for staging patients with CVDs affecting myocardial function.

Thus, C-MVs could be used for diagnosis and the assessment of risk, treatment efficacy and prognosis of CVDs, a large category of pathologies that includes hypertrophic cardiomyopathy, myocardial hypertrophy, heart failure associated with valve diseases and myocardial ischemia. Further studies will define whether other disease conditions could be included, for instance chemotherapy-induced cardiotoxicity.

COMMERCIAL OPPORTUNITY
Following the increasing applicability of MVs and the wide range of CVDs they can assess, is possible to envison the generation of user-friendly technology for detecting and quantifying the level of circulating C-MVs, through commercial magnetic beads coated with antibodies, customized dried antibody cocktails for multicolour analysis or columns with sized filter cartridges. We therefore seek a commercial partner interested in developing our promising program, under a license, co-development agreement or creation of a spin-off company.

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