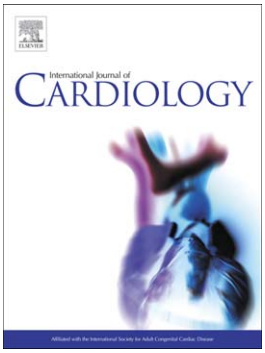

Biomarkers of vascular inflammation. Cell stress offers new clues

Enrico Tombetti, Norma Maugeri, Patrizia Rovere-Querini, Angelo A. Manfredi

PII: S0167-5273(17)33190-X
DOI: doi:10.1016/j.ijcard.2017.05.115
Reference: IJCA 25073

To appear in: *International Journal of Cardiology*

Received date: 26 May 2017
Accepted date: 31 May 2017

Please cite this article as: Tombetti Enrico, Maugeri Norma, Rovere-Querini Patrizia, Manfredi Angelo A., Biomarkers of vascular inflammation. Cell stress offers new clues, *International Journal of Cardiology* (2017), doi:10.1016/j.ijcard.2017.05.115

Biomarkers of vascular inflammation. Cell stress offers new clues.

Enrico Tombetti, Norma Maugeri, Patrizia Rovere-Querini & Angelo A. Manfredi

Vita-Salute San Raffaele University, School of Medicine, and San Raffaele Scientific Institute, via Olgettina 58, 20132 Milano, Italy. E-mail: manfredi.angelo@hsr.it

Biomarkers are important for the diagnosis and management of vascular diseases. Acute coronary syndrome (ACS) are an example (**Figure 1**). In these settings proteins uniquely expressed within viable myocardiocytes, such as cardiac troponins, are released in the bloodstream upon disruption of the plasma membrane. Accordingly, rather sharp elevations of such signals followed by prolonged release are used to identify myocardial necrosis with the highest sensitivity and specificity and represent the current gold standard for the non–invasive diagnosis of this condition. However patients with unstable angina are supposed not to undergo myocardial necrosis and there is a risk of misdiagnosis, also depending on the analytical assay used [1]. Conversely troponin raises in other acute and chronic conditions, including heart failure, renal failure, myopericarditis, pulmonary embolism, or stable coronary artery disease and chronic kidney disease or heart failure [2]. The interpretation of necrosis markers in the blood is rarely univocal. It requires the evaluation of the kinetics of the markers and the various other clinical information, thus hampering early and accurate diagnosis. A second group of biomarkers are useful in cardiovascular medicine, revealing haemodynamic impairment/heart failure. This group comprises natriuretic peptides, cardiac troponin itself and a rather vast array of molecularly heterogeneous signals [3]. Varying concentration in the blood provides information valuable for the clinical severity and the prognosis. As such it might possibly in the future guide therapeutic decisions [3].

A third group of signals focuses, directly or indirectly, on the extent and the characteristics of ongoing inflammation. Inflammation is a key player in ACS and in various other cardiovascular diseases, including heart failure. Lipid-driven chronic inflammation fuels systemic and coronary artery atherosclerosis and fosters thrombotic complications. Various signals generated in response to the cross talk of immune cells and during acute phase responses are solid biomarkers, pentraxins in particular[4]. The integration of biochemical, cellular, genetic and molecular imaging tools will prove critical for the relative risk assessment of patients with cardiovascular disease [5-8]. Identifying novel cardiovascular biomarkers thus represents a crucial medical need to progress toward pathophysiologic patient stratification and precision medicine

In this issue of the *International Journal of Cardiology* novel cogent results indicate that myocardial stress might provide additional information in the setting of ACS. The authors have used an elegant and unbiased approach to identify new candidates. They have retrieved the antibodies that appear in ACS patients' blood and identified the cognate auto-antigens. Thus they have used the powerful recognition and discrimination abilities of the patients' immune system to identify molecules that become immunogenic in ACS, because they are over-expressed or expressed in a still poorly characterised inflammatory contest. Among them nardilysin (N-arginine dibasic convertase) appeared as a promising target. Nardilysin is a secreted metalloproteinase that regulates the shedding of multiple transmembrane proteins, including TNF-α. V*ia* active extracellular proteolysis of various substrates, it influences the amount and the pattern of cytokines and growth factors present in the microenvironment, thus eventually regulating the outcome of autoimmune responses [9].