

Strategies for Fostering Unique Biomarkers and Prospective Applications in Cardiovascular Proteomics

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ABOUT THE STUDY

Heart disease is the main cause of death and morbidity around the world. As a result, biomarkers are needed for AMI and chronic disease heart failure diagnosis, prognosis, treatment monitoring, and risk stratification. The biomarker development process includes the identification, validation, and translation into clinical practice of a panel of candidate proteins to monitor heart disease risk. There are two categories of biomarkers that can be used: Heart-specific markers and markers that monitor the circulatory and pulmonary systems. A decade ago, Australian researchers invented the term "proteomics" to characterise all of the proteins expressed by the DNA that defines an organism. Proteomics is the study of the complement of proteins in an organism's large-scale expression, function, and interaction in health and illness.

Recent improvements in proteomic technology have made it possible to assess systematic changes in protein expression in response to internal or extrinsic disturbances of the biologic system, such as those seen in cardiovascular disease. Large-scale protein profiling of a proteome or subcellular proteome, such as mitochondrial or nuclear proteins, is used in mechanistic proteomic studies with the goal of identifying changes in protein abundance or post-translational modification that may be involved in pathogenesis, either causally or consequentially. In this fashion, Cardiovascular Diseases (CVD) have been extensively studied, including what may be the two principal causes of CVD-related morbidity and mortality: Ischemic Heart Disease (IHD) and Heart Failure (HF).

It has recently been used to examine myofilament-associated and cytosolic proteomes in rat hearts, revealing alterations in the amount of, and/or modifications to, metabolic, structural, and contractile proteins. The significant degree of heterogeneity found in the vascular tissue, which is the site of the lesion, as well as the heterogeneity of the lesion itself, make proteomic investigations of atherosclerosis difficult. Despite this, the proteome of stable plaques has been mapped. Hsp27, B-crystallin, cathepsins, tumor necrosis factor receptor, peroxiredoxins, and many other putative mechanistic proteins

that are altered in damaged vasculature highlight the complexity of atherosclerosis disease. With systems biology techniques, the new proteomic tools have the potential to reveal higher complexity in previously unknown signaling networks, leading to increased biological understanding and evaluation as potential novel biomarkers. The proteomic profile of tissue after reversible injury has been extensively investigated in an attempt to identify specific proteins responsible for the phenotype of contractile loss (eg., sarcomeric or cytoskeletal proteins) as well as the signaling networks that underpin the disease phenotype, such as protein kinase cascades. Proteomic investigations of HF after cardiomyopathies have identified alterations to proteins in a variety of functional groups and have been thoroughly examined. For a long time, 2-DE has been the method of choice for investigating protein changes linked to cardiomyopathies and heart failure.

Biomarkers are proteins or peptides linked with specific diseases or stages of disease that can be discovered and utilized to identify a given clinical condition using proteomic techniques. Other biological variables and substances, such as cholesterol, blood pressure, and others, can be employed as markers of cardiovascular conditions in the broad sense of being "risk predictors." Protein markers have an advantage over traditional physiological variables in that they improve illness detection and monitoring specificity and sensitivity while also increasing the amount of information available to clinicians.

Proteomics has made a contribution to clinical cardiovascular science, both in terms of understanding disease mechanisms and in terms of allowing those same processes to be detected and treated more effectively. Although the protein networks involved in IHD and HF are far from fully understood, proteomics offers the potential to identify proteins linked to pathophysiology. With a better understanding of how information flows in pathogenic circumstances, there will be more opportunities for interventions to reduce disease's impact, and proteomics holds huge potential in this field. In addition to the mechanistic contributions of proteomic science, continued advancements in technical abilities (for example, in the field of mass

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discipline. In addition to the mechanistic contributions of proteomic science, continued improvements in technical ability (for example, in the field of mass spectrometry) will lead to more effective biomarker discovery and application; in particular, we are hopeful that these developments, in combination with proteomic research into early-stage ischemic heart disease, will

allow identification of ischemia at a point in time when the myocardium can be largely salvaged prior to cell death. This will, in turn, lead to increased diagnosis and/or treatment monitoring efficiency, perhaps enhancing the clinician's capacity to detect cardiovascular disease states at a very early stage and lowering morbidity.