G13 An Innovative Proteomic Approach for the Identification of Novel Plasma Biomarkers in Patients With Brugada Syndrome

Domenica Scumaci, PhD, Magna Græcia University of Catanzaro, Laboratory of Proteomics and Mass Spectrometry, Department of Experimental and Clinical Medicine, Salvatore Venuta University Campus, viale "S. Ve, Catanzaro, 88100, ITALY; Simona Grasso, Antonio Curcio, PhD, and Marco Gaspari, PhD, Magna Græcia University of Catanzaro, Salvatore Venuta University Campus, Viale Europa, Catanzaro, AL 88100, ITALY; Silvia Priori, PhD, Molecular Cardiology Laboratory, IRCCS, Via Ferrata 8, Pavia, AL 27100, ITALY; Ciro Di Nunzio, Institute of Legal Medicine, School of Medicine, Magna Graecia University, Viale Europa Germaneto, Catanzaro, 88100, ITALY; Antonio Oliva, PhD, and Francesco Ausania, MD, Institute of Forensic Medicine, Catholic University, School of Medicine, Largo Francesco Vito 1, Rome, 88100, ITALY; Ciro Indolfi, PhD, Magna Graecia University, Viale S Venuta, Catanzaro, AL 88100, ITALY; Pietrantonio Ricci, PhD, Università degli Studi Magna Grecia Catanzaro, Viale Europa - Località Germaneto, Catanzaro, 88100, ITALY; and Giovanni Cuda, PhD, Magna Graecia University of Catanzaro, Viale S. Venuta, Catanzaro, AL 88100, ITALY*

After attending this presentation, attendees will understand how plasma potentially carries important information whose knowledge could help to improve early disease detection and prognosis in Brugada syndrome.

This presentation will impact the forensic science community by providing potential new tools for the correct diagnosis of "at risk" individuals with Brugada syndrome carrying specific gene mutations. The molecular signature obtained by the study of plasma proteome will complement genomic information therefore increasing the chance of disease detection in these individuals who are exposed to a dramatic risk of sudden cardiac death.

Brugada syndrome (BS) is a polygenic inherited cardiac disease characterized by life threatening arrhythmias and high incidence of sudden death. In the family enrolled in the present study, the disorder is caused by Q1118X-mutation in the SCN5A gene, encoding the cardiac sodium channel. 2D-PAGE was used to investigate specific changes in the plasma proteome of BS affected patients and family members sharing the same gene mutation, compared to healthy controls, with the goal to identify potentially specific disease biomarkers.

In order to reduce plasma sample complexity, the combinatorial hexapeptide ligand libraries were used.[1] The use of the beads prior 2D- PAGE enabled detection of many new protein spots and increased resolution and intensity of low abundance proteins.

Approximately 900 protein spots were detected in each gel. Proteins, whose expression was significantly different among the two groups, were excised, trypsin-digested and analyzed by LC-MS/MS.

Data showed that the levels of several proteins were significantly altered in BS patients compared with controls. In particular, Apolipoprotein E, Prothrombin, Vitronectin, Complement-factor H, Vitamin-D-binding protein, Voltage-dependent anion-selective channel protein 3, and Clusterin were considerably increased in plasma sample of BS patients, whereas Alpha-1-antitrypsin, Fibrinogen, and Angiotensinogen were considerably decreased; moreover, post- translational modification of Antithrombin-III was detected in all affected individuals.

In the light of these results, it is hypothesized that these proteins might be considered as potential markers for the identification of disease status in BS. Further analysis is being conducted in our laboratory in order to validate these findings in a larger number of cases and to elucidate the pathogenetic role of these proteins in this specific cardiac disease.

Reference:

1. Boschetti E, Righetti PG. The ProteoMiner in the proteomic arena: anon-depleting tool for discovering low-abundance species. J Proteomics. 2008 Aug 21;71(3):255-64. Epub 2008 Jun 20. Review

Brugada Syndrome, Plasma Biomarkers, Proteomics

 ** Presenting Author*