Unique Gene Expression Patterns in a Rat Model for Cardiorenal Syndrome

Entin-Meer, Michal[1]; Ben Shoshan, Jeremy[1]; Pasmanik-Chor, Metsada[2]; Shomron, Noam[2]; Maysel-Auslender, Sofia[1]; Goryainov, Pavel[1]; Karni, Varda[2]; Keren, Gad[1]

[1]Tel Aviv Sourasky Medical Center, Tel Aviv, Israel; [2]Tel Aviv University, Tel Aviv, Israel

Background: Using rat model for concomitant cardiac and renal dysfunction- cardiorenal syndrome (CRS), we sought to identify genes whose expression in the heart is modified upon nephrectomy, MI or CRS.

Methods: Lewis rats underwent 5/6 nephrectomy, 3 weeks prior to induction of acute MI by LAD ligation, in order to allow animals to develop chronic renal failure (CRF) prior to the cardiac event. Five days post MI, animals were terminated, the cardiac tissue composed of the right+left ventricles was collected and RNA was isolated from the following four arms: sham, nephrectomy, MI and nephrectomy+MI (4 animals/group). We chose time point of 5 days post MI in order to monitor genes within the acute-inflammatory phase which takes place after AMI. The RNA was amplified and loaded onto affymerix rat gene chip arrays which interrogate 27,342 genes across 722,254 distinct probes. Differentially expressed genes were obtained using cutoff of $p<0.05$ and fold-change cutoff >+2 or <-2 .

Results: We first found up to 100 genes whose expression profoundly changed following MI. These included multiple genes related to cell function and survival. Subsequently, we identified two genes, involved in cardiac remodeling and neovascularization, whose expression is synergistically modified upon CRS compared to AMI or RF alone. In addition, we revealed two different genes, known to play a role in maintenance of cell membrane integrity and apoptotic cell removal that are strongly downregulated during CRF, but not in the presence of AMI insult.

Conclusions: We report the identification of specific cardiac genes potentially involved in CRS development in CRF patients. Further investigation based on these findings might shed light on the markedly worsened post-MI prognosis observed in CRF patients and point out to new possible therapeutic targets for treatment of CRS patients.