SUPPLEMENTAL DIGITAL CONTENT

SDC, Methods

WGCNA algorithm

WGCNA approximates a network adjacency matrix by first computing the biweight midcorrelation matrix. WGCNA next alters the adjacency matrix by raising each element to a common exponent, loosely chosen as the smallest number that sufficiently maximizes a scale-free fit. The motivation for this lies with the assumption that real biological networks are approximately scale-free networks. A soft-threshold parameter of 4 was selected for this analysis. Finally, a Topological Overlap Matrix (TOM) is computed, which uses topological information to improve the reliability of the adjacency matrix. The adjacency matrix is then partitioned by hierarchical clustering, using biweight mid-correlation as a similarity measure, and a dynamic tree-cutting algorithm to optimize module assignment. Genes unassigned to a specific module were excluded from the analysis. Each module still consists of several hundred genes, and in order to reduce this dimensionality, WGCNA uses Principal Component Analysis (PCA) to compute a representative eigengene that summarizes the bulk expression of the entire module and uses the correlation between eigengenes to visualize the eigengene network. In order to relate the modules to the clinical phenotypes, we calculated the correlation following the ISHLT, the Unsupervised Class (UC) and clinical variables with each module's eigengene. The statistical significance of each correlation was corrected using the BH method.

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Figure S1. Analysis of network topology depicting multiple soft-thresholding powers. Mean connectivity (y-axis) as a function of the soft thresholding power (x-axis).

Figure S2. Heart tissue biopsy network dendrogram of genes (top) constructed using topological overlap matrix as a similarity measure to cluster into modules (bottom) to represent highly coexpressed genes and were labeled random color assignments for visualization. For each module, a color is assigned arbitrarily for reference.

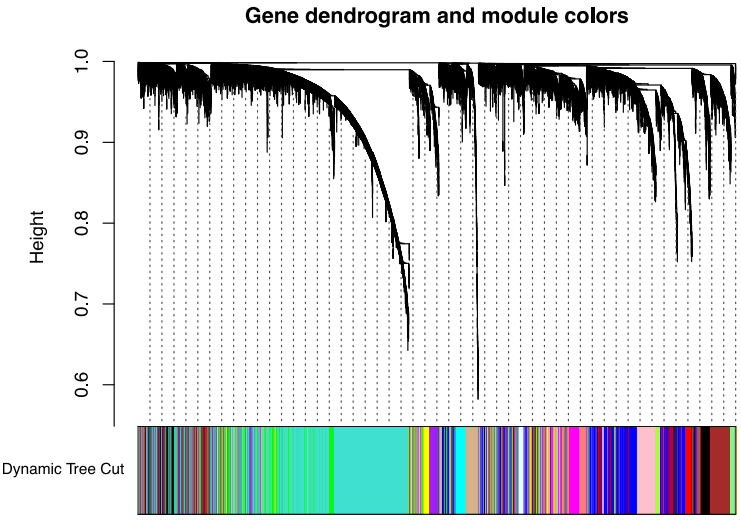

Figure S3. Heat map depicting the association of the eigengene module to clinical phenotype of ACR, the 3 unsupervised classes, hemodynamic variables, White Blood Cells (WBC), Brain Natriuretic Peptide (BNP), Cylex ImmuKnow, Allomap and Left Ventricular Ejection Fraction (LVEF) information. Each row corresponds to a module eigengene. The column represents a clinical trait. Within each cell, correlation value (top) and p-value (bottom) are depicted. Upon computing the gene coexpression network, a soft threshold power was applied inferring a network composed of 16 modules with size ranging from 86 to 3348 genes. Module trait relationship was evaluated for all samples using both the ISHLT graded biopsies. The gene modules with the highest module-trait correlation were blue (2077 genes) and turquoise (3348 genes). Further analysis revealed enrichment of processes and pathways related to immune function in the *turquoise* module and mitochondria function in the blue and midnightblue modules.

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