

Supplementary Figures Legends

Suppl. Figure 1: Protein expression profiles evaluation by using data clustering approach of proteins during RAM paradigm. **A.** Hierarchic cluster analysis of log₂ ratios of protein expression intensity of all tested groups in all three biological replicates separately. Amalgamation curve was calculated using Euclidean distance metrics and Wards linkage method. **B.** Validation of hierarchic clustering number using root mean square standard deviation, Davis-Bouldin's index pseudo F, Dunn's index, Pseudo T-square. **C.** Expression profiles of individual proteins enriched in a specific hierarchic cluster shown in A. **D.** Probability distribution functions of clusters of a selected variable 3/0 used as an example for k-mean clustering applied to the groups as in A. **E.** Per variable cluster averages profile calculated from k-mean cluster analysis applied to the groups as in A. **F.** Probability distribution functions of clusters of a selected variable 5/0 used as an example to demonstrate data separation by expectation maximization algorithm. **G.** Per variable cluster averages profile calculated from expectation maximization cluster analysis applied to the groups as in A.

Suppl. Figure 2: Validation of factor analysis outcome by regression support vector machine (SVM) algorithm type 1, training constant was set to 6, $\epsilon=0.1$, linear kernel type, v-fold cross validation v=10, seed 10000, grid search was set to from 1 to 10 with +1 increment for capacity and from 0.1 to 0.5, with increment of +0.1. Maximum number of iterations was set to 10,000, stop error was set at 0.001. Factor scores were used as independent, while corresponding protein measurement datapoint variable was used dependent. **A-C.** Correlation between protein datasets of a specific variable with predicted data based on the factor scores before (left panels) and after (right panels) factor analysis. In each cases variable, which exhibited maximal correlation with a specific factor was chosen, as in A. 5/0 for factor 1; **B.** 3/0 for factor 2, **C.** 1/0 for factor 3.

Suppl. Figure 3: Multivariate and functional analysis of the expression profiles of proteins correlating with factor 1. **A.** Hierarchic clustering of proteins correlating with factor 1. Agglomeration curve was

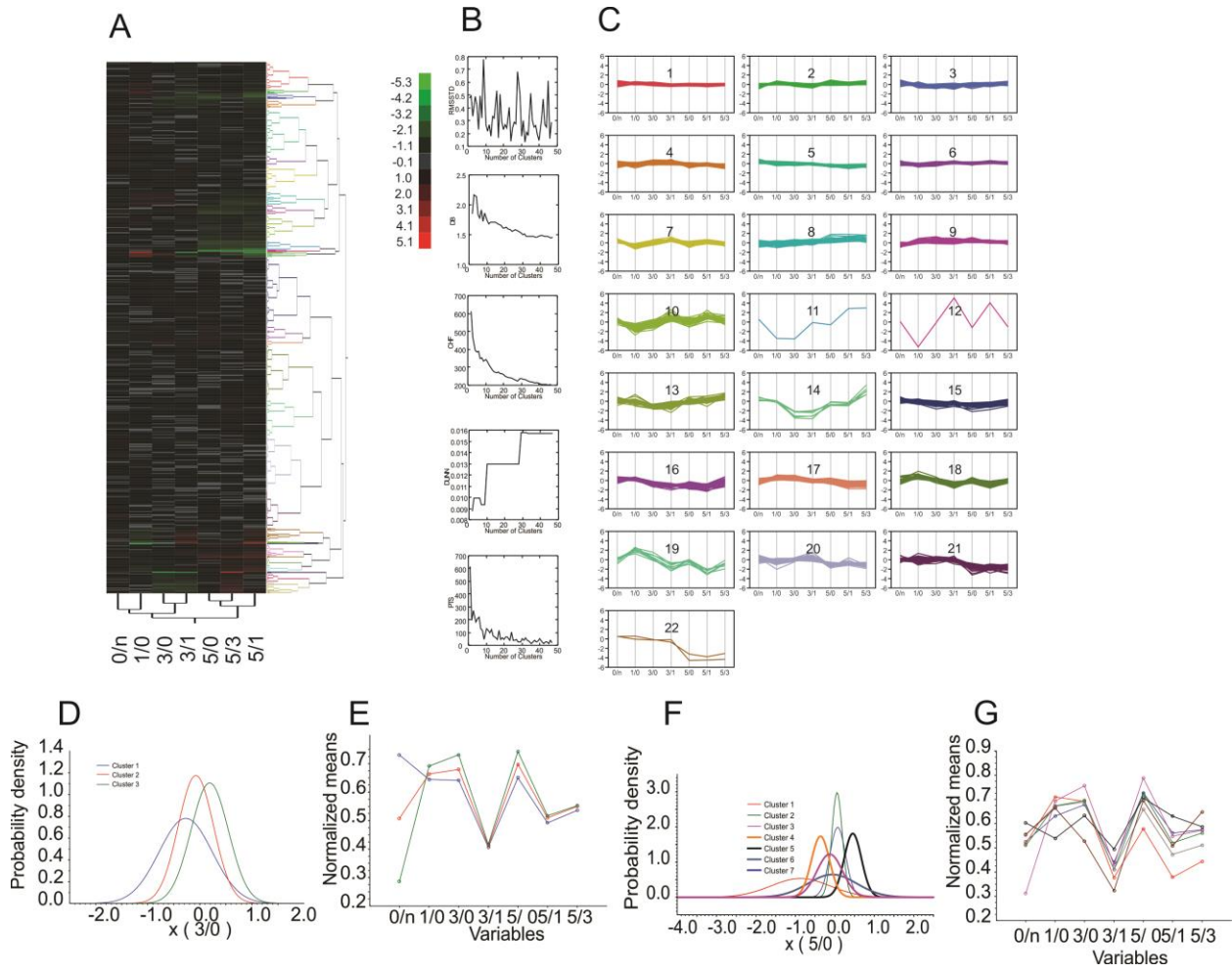
calculated using Euclidean metrics and Wards linkage. **B.** Expression landscape corresponding to variables 5/0, 5/1, 5/3 representing protein level changes days 5 vs 0, 1 and 3, respectively, for the group correlating with factor 1. **C.** Scatter plot of node characterization based on Guimerà-Amaral cartography network hub enrichment (see Methods) for networks of cluster 9. The networks were clustered using spectral clustering algorithm. Number of clusters were derived from FAG-EC (fast agglomeration algorithm based on edge clustering coefficient) algorithm implemented in ClusterViz plug-in of Cytoscape (This algorithm showed best fit with functional modularity of the networks). Partition coefficient describes how tend of a node to connect with nodes other than its module. Within-module z-score is a standard z-score, which evaluates connection distribution inside the module vs. the total connections. Hub and non-hub modules are defined by ranges of z and P. For any hub modules, $z > 2.5$, which correspond with three regions R5-7. Non-hub modules correspond with four regions (R1-4) depending on centrality of the node. Region boundaries are defined by value of partition coefficient. Inset: Graphic presentation of network assembled base on protein-protein interaction of proteins in cluster 9. **D.** Protein-protein interaction network assembled based on network analysis of proteins with more than 1.5-fold expression increase belonging to clusters 9-13. Network was generated STRING10 database. Yellow color code highlights proteins belonging to clusters 9-13. Green nodes were generated based on protein-protein interaction database analysis.

Suppl. Figure 4: Multivariate and functional analysis of the expression profiles of proteins correlating with factor 2. **A.** As in Suppl. Fig. 3A. **B.** Scatter plot of node characterization based on Guimerà-Amaral cartography network hub enrichment (see Methods) for networks of clusters 1 and 2.

Suppl. Figure 5: Multivariate and functional analysis of the expression profiles of proteins correlating with factor 3. **A.** As in Suppl. Fig. 3A. **B.** Protein-protein interaction network assembled based on network analysis of proteins with more than 1.5-fold expression increase belonging to clusters 3-6. Network was generated STRING10 database. Yellow nodes highlight proteins belonging to clusters 3-6. Green nodes were generated based on protein-protein interaction database analysis. Red note corresponds to AKT1 hub

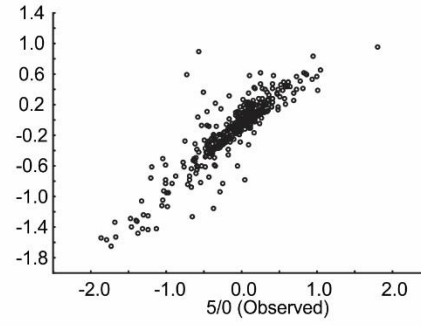
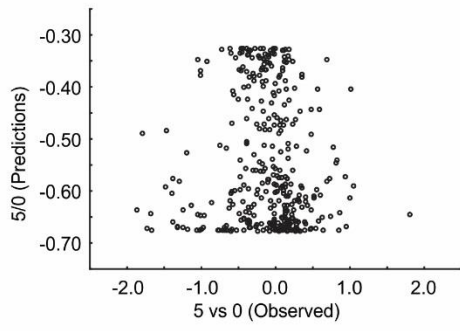
protein. Red and gray edges correspond to protein-protein interactions of yellow and non-yellow nodes, respectively.

Suppl. Figure 1:

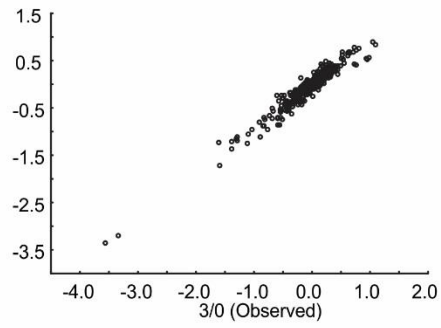
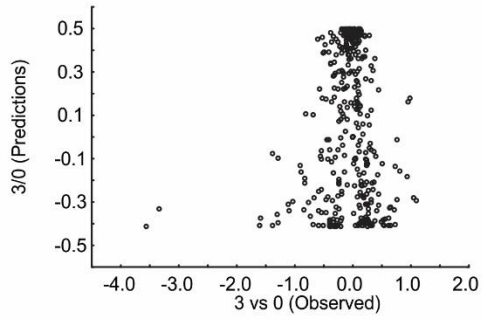


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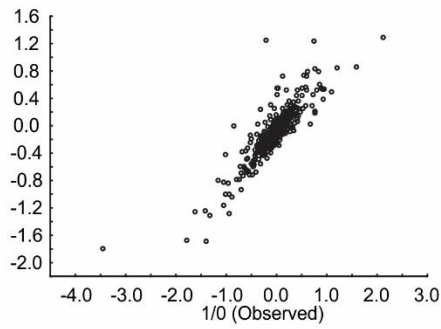
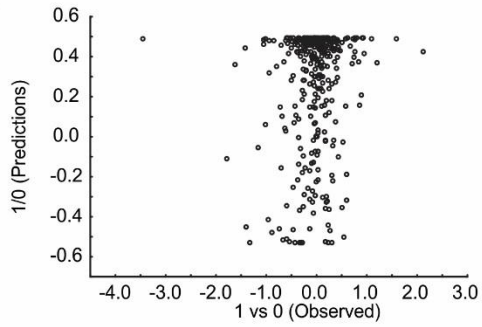
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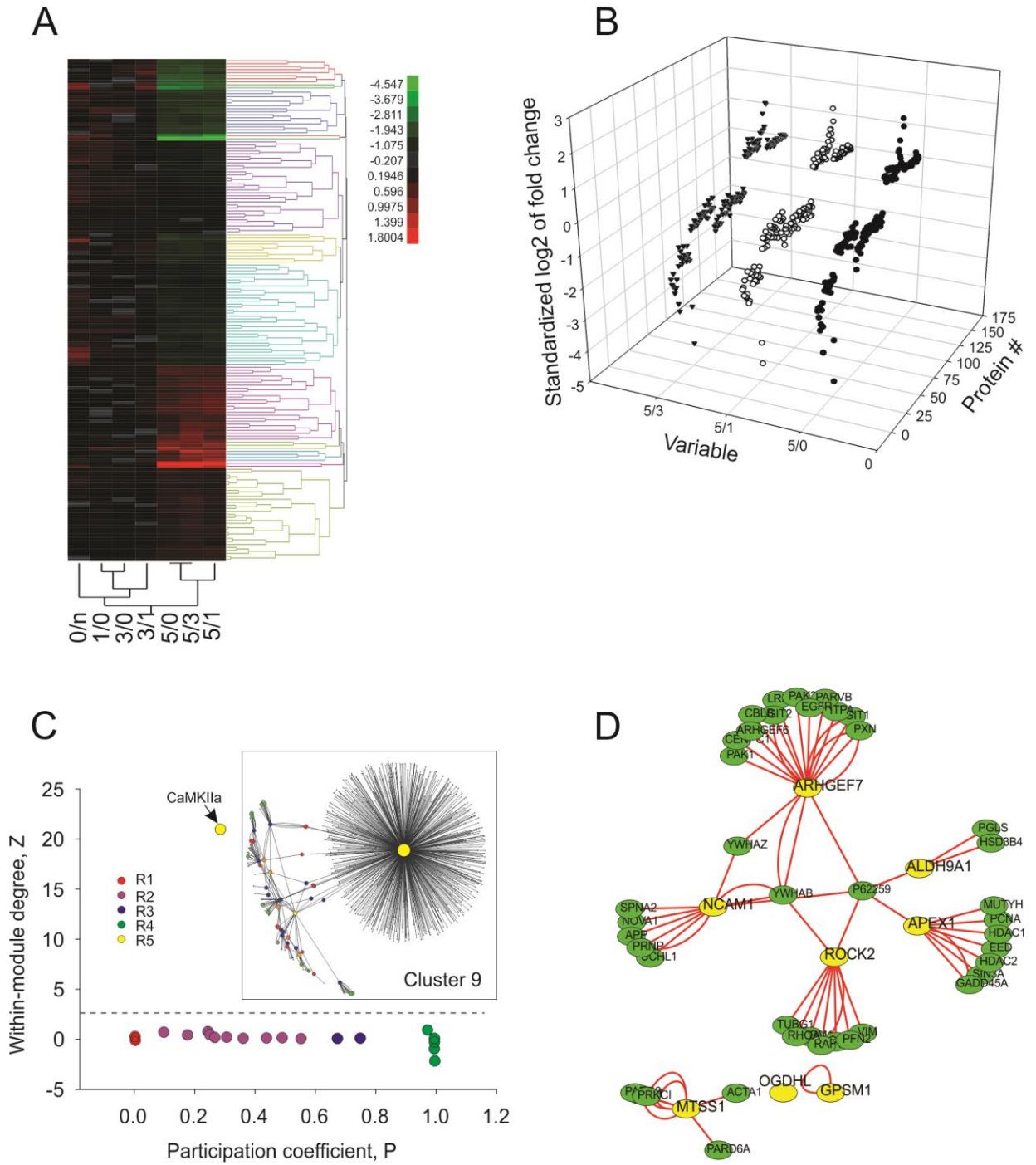
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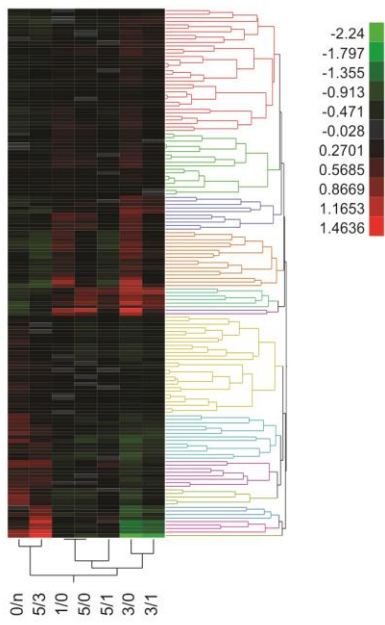


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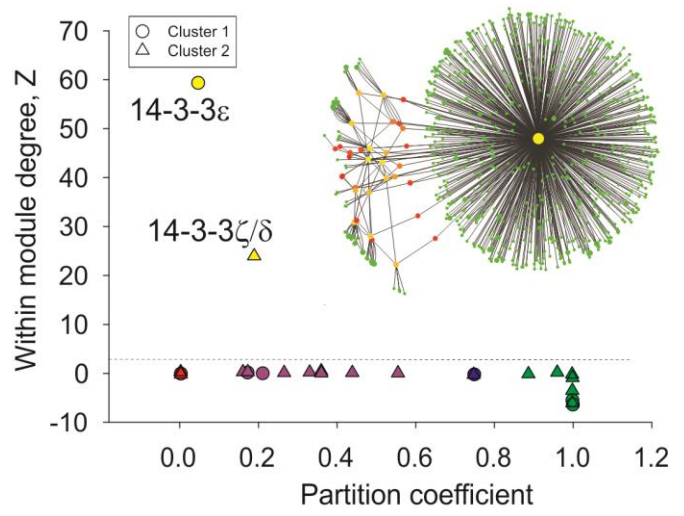


Suppl. Figure 4:

A

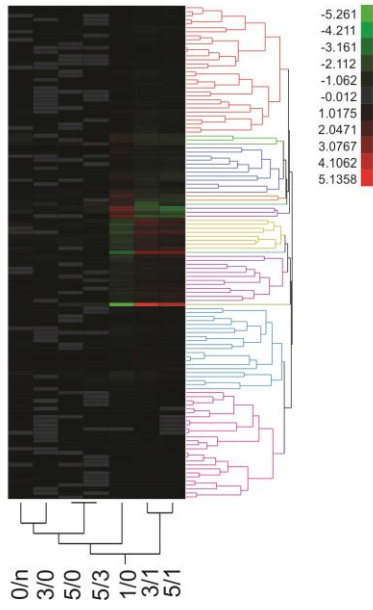


B



Suppl. Figure 5:

A



B

