Exploratory multivariate analysis of peripheral whole blood gene expression data in organ transplantation

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BACKGROUND: We have analyzed over a thousand samples of peripheral whole blood from organ transplantation patients using Affymetrix microarrays. These samples represent heart and kidney transplant patients from different demographic and clinical backgrounds as well as from various time points from end stage organ failure through the post transplantation period.
METHODS: We have undertaken exploratory multivariate data analysis of these samples using Principal Component Analysis (PCA) in order to reveal internal structure in the gene expression data in regards to clinical background, patient demographics, type of transplanted organ, and transplantation outcome. 3D real-time PCA (RGL R Plug-in) reduces the dimensionality of such complex data allowing for the most informative perspective of data to be visualized graphically. As an initial study we selected 154 organ-specific microarrays with a similar ratio of transplant rejection (R) and non-rejection (NR) in both acute (R:NR=1:2) and chronic instances (R:NR=1:1). This group included subjects of different ethnicity (119 Caucasians, 26 Asians, 4 North American Indians, 4 Multiracial, and one African American), age range (18 to 69 years) and sex (51 females). Of the 154 subjects, 47 were heart transplant patients, 87 were kidney transplant patients, and 20 were normal healthy subjects.
RESULTS: From this analysis we observed tight clustering of the microarray data from normal subjects. In contrast, microarray data from heart and kidney transplant patients was highly dispersed, regardless of the transplanted organ. Visually of most significance, clustering of data from acute rejecters of heart and kidney transplants is observed, distinct both from each other and normal healthy individuals.
FUTURE DIRECTION: We will use an extended cohort of 389 patient samples with time-course information to build upon our initial analysis. Correlation and projection of the time-course data will be tracked using PCA plots which may reveal predictive properties of the data. Finally, we will refine this analysis using data from biological relevant gene networks for a more targeted approach. We anticipate that this work will provide insight into global gene expression changes specific to organ transplantation outcome, highlighting the applicability of investigating highly complex multidimensional data for this purpose.