Molecular biomarkers for prediction, diagnosis and monitoring of acute MS relapse

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Background

- The vast majority of **Multiple sclerosis (MS)** patients (85%) present with a **relapsing-remitting course (RRMS)**, featured by inflammatory attacks and periods of partial or complete remission in between

- The relapses could manifest as clinical exacerbation of symptoms, or only radiological findings of gadolinium-positive lesions in brain or spinal MRI

Aims

To assess the specific blood transcriptional profile of RRMS patients at relapse as compared to remission, and use this data for disease monitoring and prediction of future relapses

Study Design

- 1. Identifying the potential biomarkers of MS relapse using **paired analysis** of patients with one blood sample obtained at radiological relapse, and another obtained at remission

- 2. Using the obtained list of relapse associated biomarkers relapse for prediction of subsequent relapse in large cohort RRMS patients in remission

Methods

- A retrospective cohort study in which blood samples for Affymetrix Inc. microarray analysis were obtained as follows:

- Inclusion criteria:
  - Diagnosis of RRMS according to the 2010 McDonald criteria
  - Age 20-50
  - No steroid treatment for at least 1 month before obtaining the blood sample
  - For relapse biomarkers evaluation:

  a) MRI performed less than 2 months before or after obtaining the blood sample in relapse or remission

  b) In patients with acute MS relapse GD enchasing lesion in brain or spinal MRI

  For prediction analysis remitting stage confirmed by et least 1 month stable EDSS around blood sampling

Statistics

- Normalization will be done using R, an open source software environment for statistical computing. two methods of normalization will be applied:
  1) Single Channel Array Normalization (SCAN) – for normalization of individual samples
  2) Combining Batch (ComBat) – for solving batch effect on data

- Partek Genomics Software will be used for differential expression analysis

- Correction for multiple comparisons using FDR correction methods

Sample size calculation

- Our sample size was calculated using an online web tool developed for microarray studies developed by the M.D Anderson Cancer Center for microarray studies

- To obtain a gene expression difference of at least 2-fold, with a power of 80%, a standard deviation of 0.7 in a microarray chip containing about 22,000 probes and an expected false positive rate of 5%, a minimal sample size of 8 subjects per group is required. This gives an alpha value of 0.05 per gene

- We enrolled 38 pairs of patients that fulfill the inclusion criteria for biomarker evaluation analysis, and 560 patients in remission that fulfill the inclusion criteria for relapse prediction analysis

Thank you