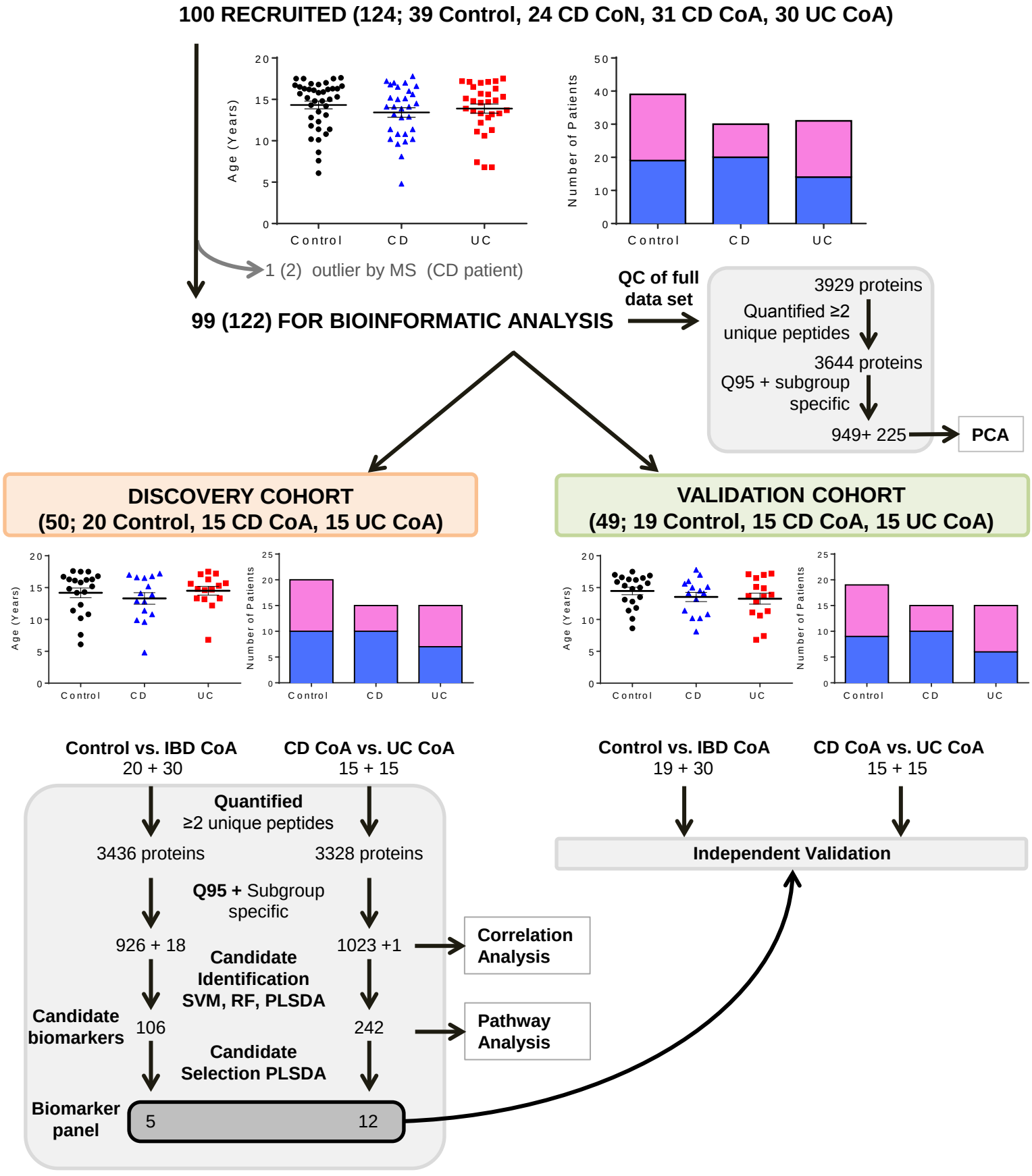
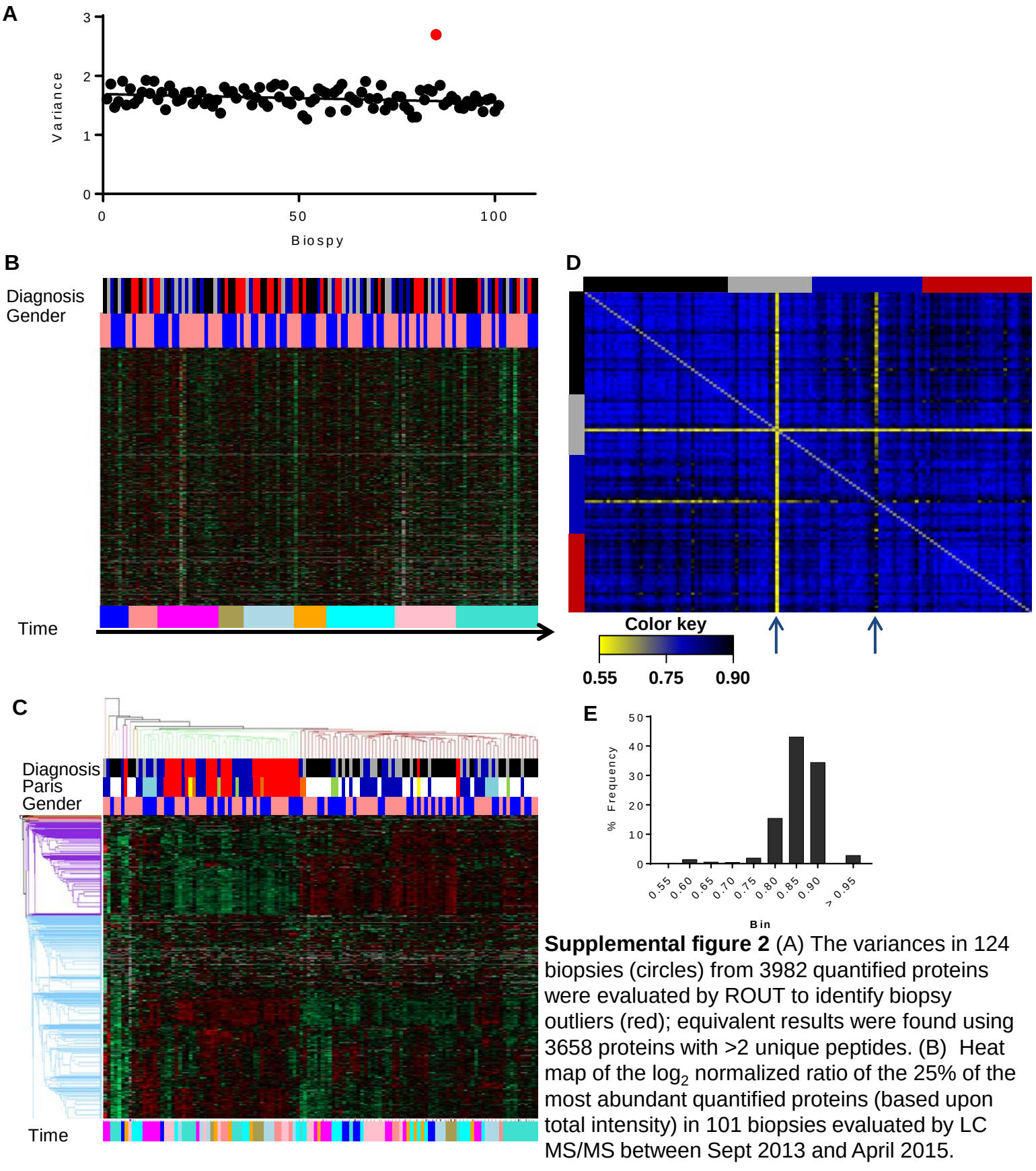
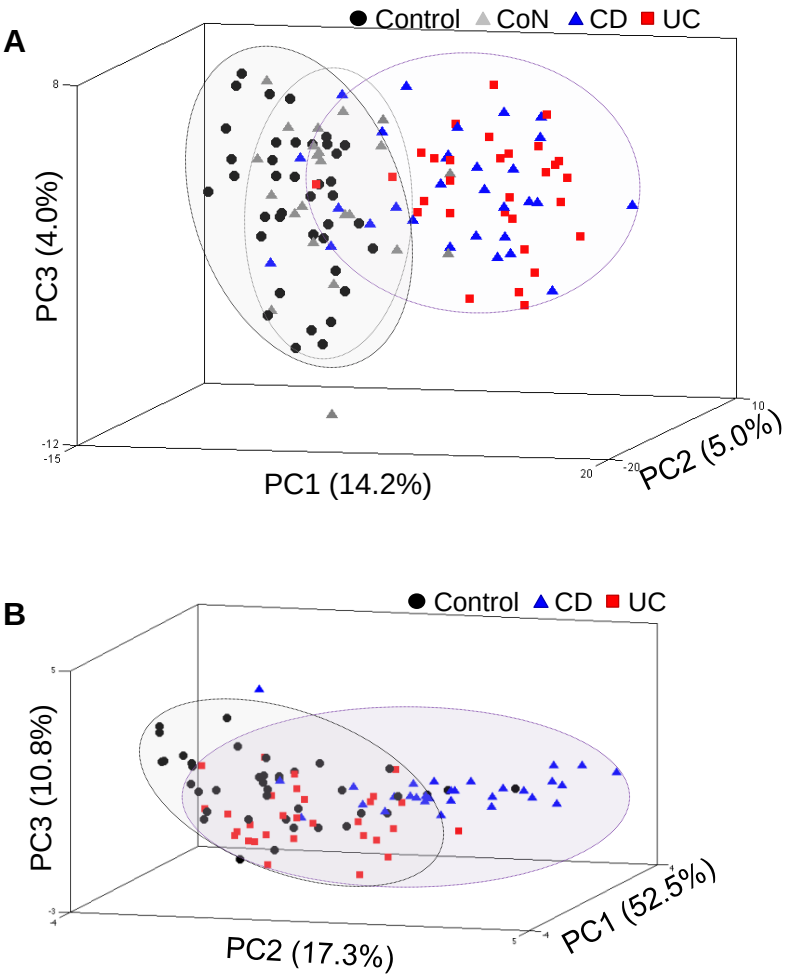


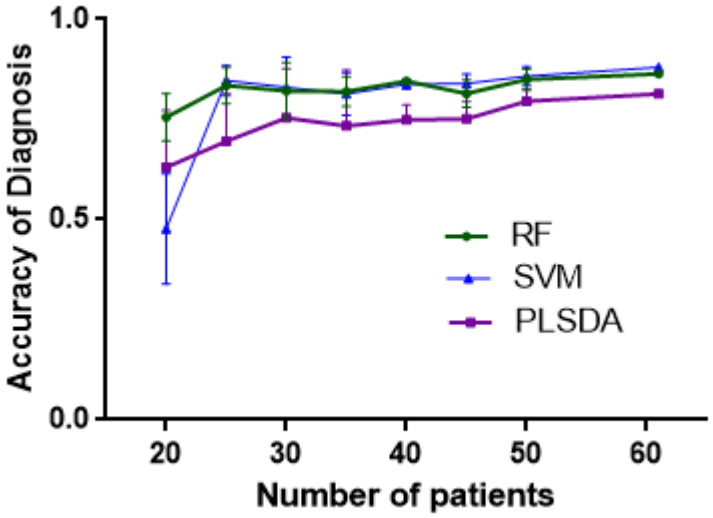
Supplemental figure 1 Schematic representation of study design. The number of patients (biopsies) is indicated at each step. Graphs indicate the age of control (black), CD (blue) and UC (red) patients, and gender distribution (male, blue; female, pink). A subset of patients was included in the Discovery phase, and a second independent set for Validation.



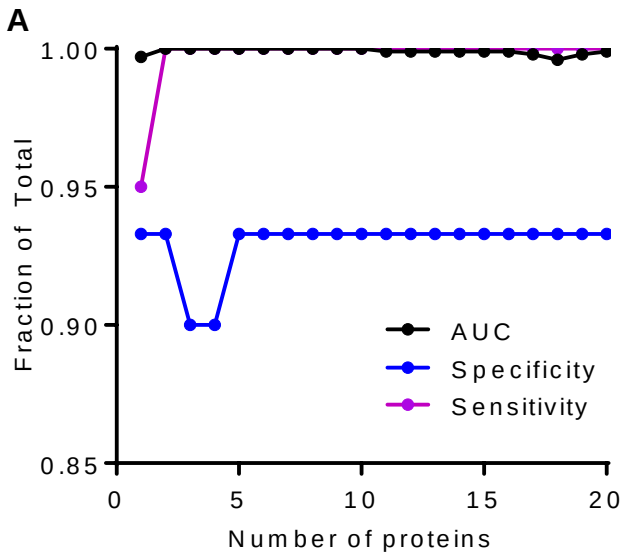
Supplemental figure 2 (A) The variances in 124 biopsies (circles) from 3982 quantified proteins were evaluated by ROUT to identify biopsy outliers (red); equivalent results were found using 3658 proteins with >2 unique peptides. (B) Heat map of the $\log_2$ normalized ratio of the 25% of the most abundant quantified proteins (based upon total intensity) in 101 biopsies evaluated by LC MS/MS between Sept 2013 and April 2015. Each MS run is represented at the bottom of the heat map by a colour bar. Indicated by separate colour bars at the top are the Diagnosis (Black = control, Gray=CoN, Blue = CD, Red = UC), Paris classification (Green = L1; Light blue = L2, Blue = L3; Yellow = E2, Orange = E3, Red = E4), and Gender (Blue = male; Pink = female) associated with each biopsy. (C) Hierarchical clustering of the data shown in B indicates a lack of pattern due to MS date. (D) Heat map of Pearson correlation score from low (yellow) to high (black); arrow indicating one patient (both CoN and CoA biopsies) with low correlation, and (E) histogram of Pearson correlation indicate the similarity of proteomes between MS runs.

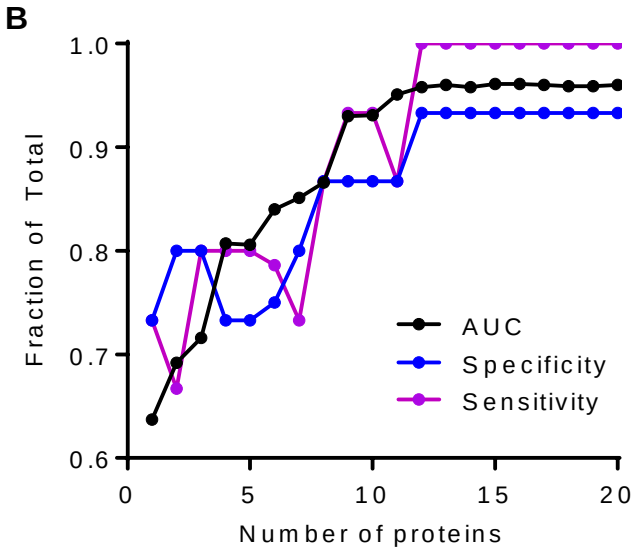


Supplemental figure 3 PCA was performed (A) using Q95 proteins after removal of proteins identified as involved in immunological processes, or (B) using patient data for blood-based biochemical parameters, including hemoglobin, albumin, C-reactive protein, erythrocyte sedimentation rate, hematocrit, and counts for platelets, white blood cells, neutrophils, lymphocytes and eosinophils.

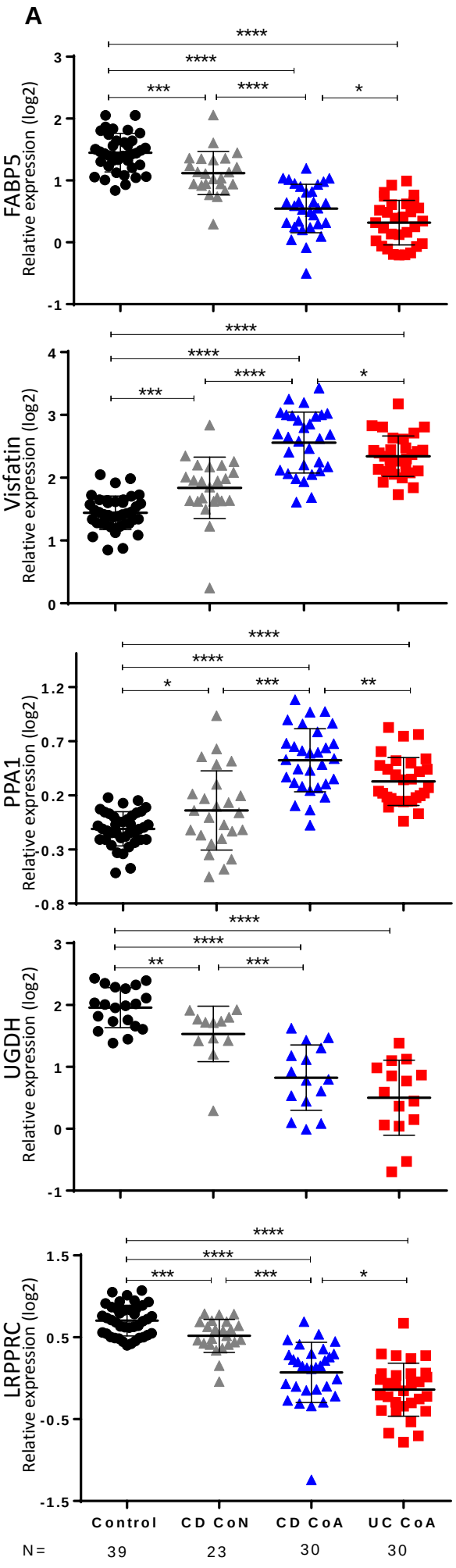


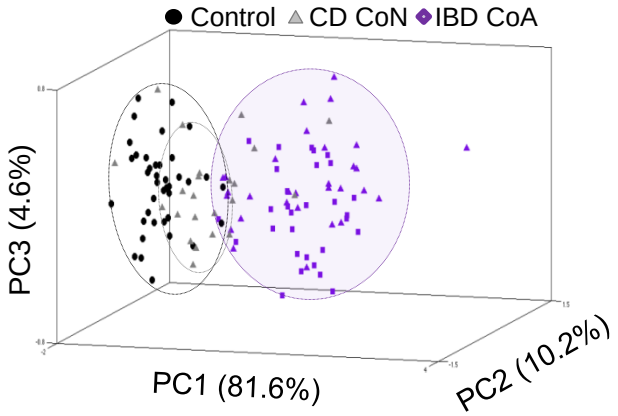
Supplemental figure 4 To evaluate the number of patients required for the Discovery stage of biomarker identification, the accuracy of diagnosis was evaluated with increasing number of total patients (where CD and UC were equally represented) by random forest (RF), support vector machine (SVM) and partial least squares discriminant analysis (PLSDA). In each model, two-thirds of patients are used for training and one-third for testing, with 100 Monte Carlo cross-validations; each model was evaluated 3 times. There is an observed increase in error and decrease in accuracy below 30 patients with each of the models, therefore it was determined that the patient population would be divided equally between Discovery and Validation.

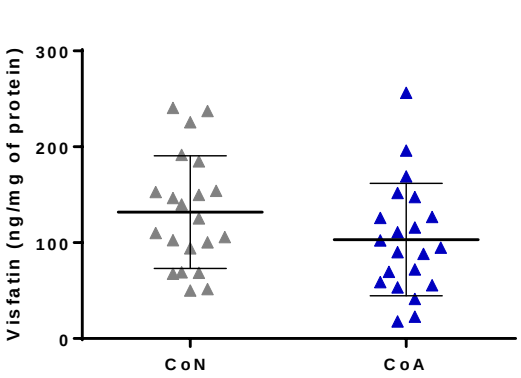




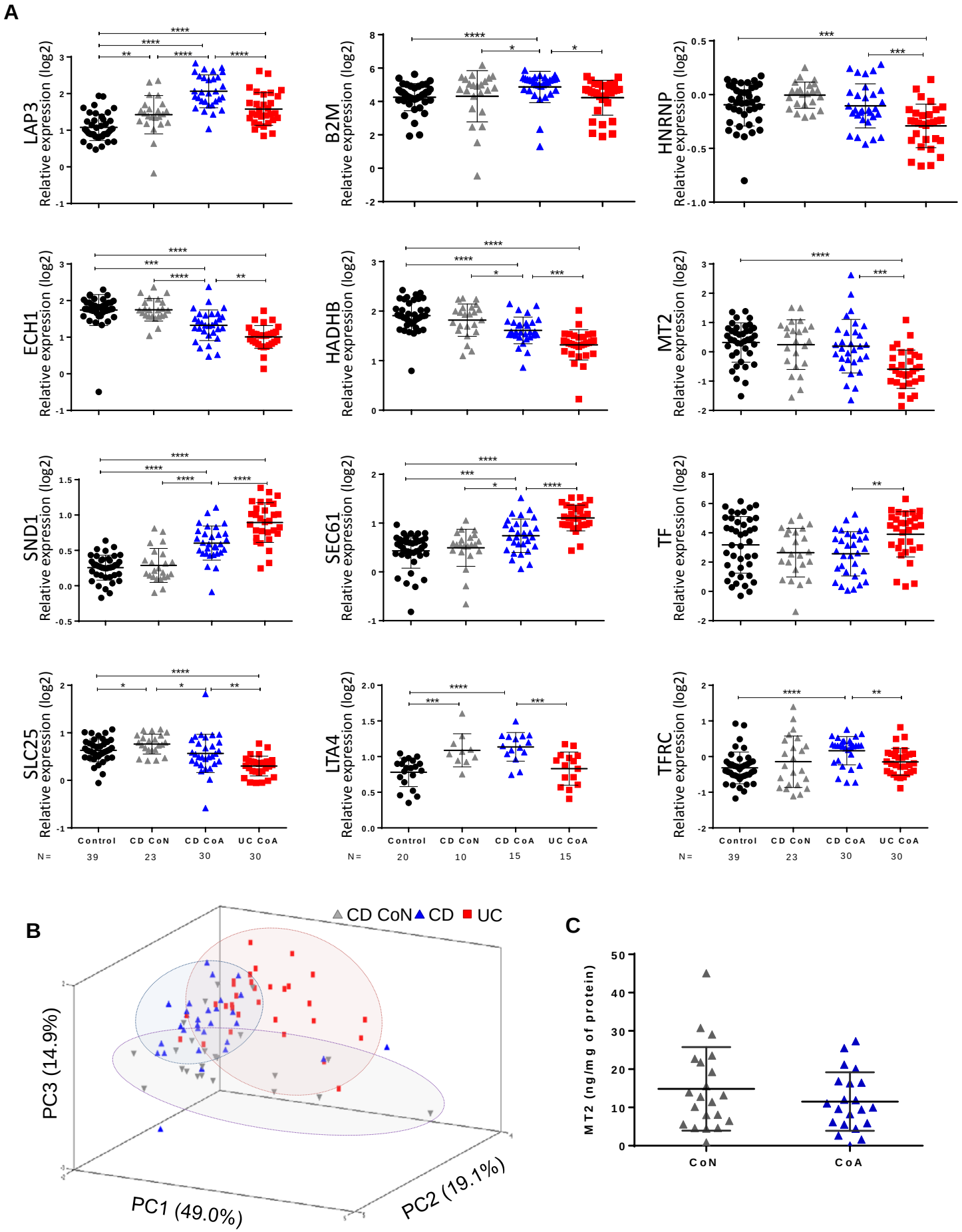
Supplemental figure 5 Plot of the AUC, sensitivity, specificity values obtained by cross-validation of step-forward addition of candidate biomarkers (based upon AUC rank) to the PLSDA model for classification of discovery cohort patients for (A) Control from IBD, or (B) CD from UC.







Supplemental figure 6 (A) The relative expression (log2) levels of Panel 1 proteins as determined by proteomic analysis. (B) PCA analysis of all patients based on five proteins. Control (black), CD CoN (gray), IBD CoA (purple). (C) Comparison of visfatin absolute levels in paired CD CoN and CD CoA biopsies as determined by ELISA.



Supplemental figure 7 (A) The relative expression levels of Panel 2 proteins as determined by proteomic analysis. (B) PCA analysis of all patients based on 12 proteins. CD CoN (gray), CD CoA (blue), UC CoA (red). (C) Comparison of MT2 absolute levels in paired CD CoN and CD CoA biopsies as determined by ELISA.