Mass Spectrometry Used To Define Plasma Protein-Based Classifiers That Discriminate Patients With Colon Polyps or Adenomas As Compared to Colonoscopy.


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This study demonstrates the feasibility of identifying blood plasma-based proteins on a mass spectrometer (MS)-based platform that distinguish patients with colon polyps or adenomas from those without. Large portions of the population age 50 and older do not undergo a recommended screening colonoscopy for colon cancer. A simple blood-based test for polyps may help physicians encourage those patients to follow the recommendation. Blood plasma samples were collected from patients undergoing colonoscopy. The patient’s reasons for undergoing the procedure (e.g., routine screening, personal or familial history, or clinical symptoms) were not used as inclusion or exclusion criteria. After standard dietary restriction and bowel preparation protocols, and prior to colonoscopy, a blood sample was obtained and processed to plasma under a standardized protocol. Medical history and clinical data for each patient were recorded, and the colonoscopy procedure and pathology reports were obtained. 100 age- and gender-matched paired-samples with complete data were used in this analysis: 50 patients demonstrated to have one or more polyps or adenomas based on pathology reports, and 50 patients without any observed polyps or adenomas as controls. There was no filtering for polyp number, size, location, or appearance. The group size was chosen to ensure that the desired study power would be achieved. The selected plasma samples were thawed and lipids and particulate matter were removed by filter centrifugation. Abundant proteins were removed by immunoaffinity depletion. Remaining proteins were separated into fractions by reverse-phase HPLC prior to peptide conversion by trypsin-TFE digestion. Quantitative data on the peptide-based features were collected on an HPLC, tandem-mass spectrometer (ESI-QTOF) platform. Approx. 150,000 protein molecular features were observed in at least 50% of the samples in at least one study group. Molecular feature data were normalized to reduce systematic variation. Ten rounds of 10-fold cross validation using Elastic Net feature selection, top 100 feature ranking, and SVM(linear
kernel) classifier assembly were performed. The average cross-validated AUC was $0.92 \pm 0.12$ for the 100 total rounds, indicating a high degree of predictive performance. Random re-assignment of sample classifications was employed to test for over-fitting; the resulting AUC of $0.48 \pm 0.22$ confirms the robustness of the earlier result. These results demonstrate the feasibility of blood-based protein tests to help manage colonoscopy screen compliance.