A protein-based blood panel test for the early detection of colorectal cancer and advanced neoplasia

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Background:
Early detection of colorectal cancer (CRC) is key to survival. CRC screening compliance is still low because of either the invasive procedure (colonoscopy) or the so-called "ick factor" (stool-based tests). Stool-based tests also lack of ability to detect advanced adenoma (CRC precursor). A blood-based test could improve adherence to screening guidelines, but no one has so far been recommended due to a lack of sufficient sensitivity and specificity. Here we report the potential clinical utility of a blood-based biomarker panel providing high sensitivity (SE) and specificity (SP) for CRC and advanced adenomas (AA) as a screening triage option addressing positive patients to colonoscopy.

Methods:
A total of 241 retrospective serum samples (179 CRC, 22 adenoma, 40 healthy controls) were obtained from the Cooperative Human Tissue Network (CHTN) biobank and tested with a proprietary sandwhich ELISA that detects dual CRC specific biomarkers (BF7 and CC3). A standard curve was generated and biomarkers concentration in the samples were calculated using a 4-parameter logistic method. The median biomarker concentration values in each patient group were compared to determine whether differences were statistically significant ($p< 0.05$). Statistical analysis of two-group and multi-group comparisons was carried out using the non-parametric Mann-Whitney U test and the Kruskal-Wallis test, respectively. Receiver operating characteristic (ROC) curves were calculated to evaluate the diagnostic performance, by determining sensitivity (SE), specificity (SP), area under the curve (AUC), and confidence interval (CI). Statistical analysis, ROC curves and scatter plots were performed with GraphPad Prism 7.0.

Results:
Both biomarker's median concentration difference between CRC versus healthy samples groups were found to be statistically significant ($p<0.05$). Both biomarkers were also elevated in AA as compared to healthy samples, but difference in median concentration was only statistically significant for CC3 ($p<0.0001$). BF7 serum levels in cancer patients were significantly associated with TMN stage ($p=0.019$), N stage ($p=0.039$) and M stage ($p=0.0006$). No significant associations were found between this biomarker levels and other clinical characteristics of the CRC patients including age. Our test discriminated CRC (all stages) from healthy individuals with a SE of 80% and a SP of 90%. Sensitivity for early (n=95) and late-stage CRC (n=80) was 79% and 84%, respectively. Our test was also able to detect 81% of serum from advanced adenoma patients who are at increased risk of CRC.

Conclusion:
This study illustrates the potential clinical utility of our blood-based assay for the early detection of CRC which has a better sensitivity for advanced adenoma than stool-based tests in current clinical use. A large prospective cohort study is planned to further validate the clinical performance of this test.