

Detector-C: A blood-based IVD with high sensitivity and specificity for early detection of colorectal cancer.

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Abstract:

Background: Colonoscopy is the gold standard for screening of colorectal cancer (CRC). However, only 20%-30% of the screening population aged 55-75 years use colonoscopy due to its inconvenience and invasive nature. There is a need for an accurate, noninvasive blood test. **Methods:** We randomized 572 PAX-RNA blood samples from two prospective, multicentre clinical studies. CRC cases originated from the MSKK study, controls from the CRC.SCR.2 study which enrolled healthy individuals from a screening population undergoing colonoscopy. Blood was drawn prior to surgery or prior to colonoscopy. RNA was isolated, QC checked, hybridized onto the Affymetrix U133 2.0 Plus arrays, and QC checked. Clinical data were monitored. **Results:** After all QCs data of 462 pts remained. Data from 119 pts (55 cases, 64 controls) were utilized for discovery of gene signatures using a double nested bootstrap with random forest and SVM as feature selection methods. The best signature, Detector-C, discriminating between cases and controls contained 202 probe sets and resulted in a prospective sensitivity (S+) of 85.3% and a prospective specificity (S-) of 93.3%. The hypothesis for the prospective performance evaluation (validation) of Detector-C was to show a S+ of > 70% and a S- of > 80% with a one-sided alpha of 2.5% and a power of 97.5%. In order to test this hypothesis at least 122 cases and at least 109 controls would be needed. We used the remaining 210 cases and 133 controls for the prospective validation. S+ was 90% (95% CI: 0.851-0.937) and S- was 88% (95% CI: 0.812-0.930). S+ by UICC stage was: stage I: 0.89 (95% CI: 0.774-0.958), stage II: 0.90 (95% CI: 0.788-0.961), stage III: 90% (95% CI: 0.805-0.959) and stage IV: 93% (95% CI: 0.765-0.991). Detector-C also identified high-grade intraepithelial neoplasia with S+ of 66%. Multivariate analysis showed no significant effect of stage, age, gender, tumor localization, or RNA quality on correct prediction. **Conclusions:** Detector-C measures the host response (host defense, immune answer, wound healing, inflammation) of white blood cells to tumor lesions and is highly suited for screening of CRC due its easy of use, noninvasiveness and its high sensitivity for early-stage CRC/neoplastic lesions.

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