Detector C 2.0:  
A highly accurate blood-based IVD test for early detection of colorectal cancer with sensitivity and specificity over 90%  

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Background:  
The EU-5 and US screening population (39.9 million people) is growing, with approximately 1 million colorectal cancer cases (CRC) per year. Traditional colorectal cancer screening involves flexible sigmoidoscopy or colonoscopy, with FOBT and gGFOBT. Colonoscopy achieves high sensitivity but is invasive, carries a risk of complications, and is low due to the limitations of the test and the difficulties of excluding colorectal specimens.  

Unmet Clinical Need in Colorectal Cancer Screening:  
Colorectal cancer screening in Germany;  
10,5 million fecal tests (p.a.);  
5 million screening colonoscopies (10 years)  
Cumulative Cancer estimates: Sensitivity: 91.6% (95% confidence interval (CI): 86.3-95.4) and specificity: 94.8% (95% CI 77.3-99.4).  

Methods:  
Prior to the 483 Affymetrix U133 plus 2.0 expression data were used for discovery and validation of Detector C, which selected 45  
expression data set of 491 CRC cases and 503 controls of 451 CRC cases for discovery of Detector C.  

Table 2: Overview of Expected Number of Patients in Study CRC.SCR.4  
<table>
<thead>
<tr>
<th>Patient Group</th>
<th>Patients with carcinoma in situ</th>
<th>Patients with high-grade intraepithelial neoplasia</th>
<th>Patients without any pathological finding</th>
<th>Patients with carcinoma in situ or high-grade intraepithelial neoplasia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cancer patients in screening arm</td>
<td>60</td>
<td>60</td>
<td>720</td>
<td>180</td>
</tr>
<tr>
<td>Cancer patients in surgery arm</td>
<td>60</td>
<td>60</td>
<td>60</td>
<td>60</td>
</tr>
</tbody>
</table>

Figure 1: Second Order Unbiased Estimates for Sensitivity and Specificity by Number of Probesets (Gene) in the Signature  

Conclusion:  
Using a three-tiered discovery set for Detector C 2.0 that for Detector C 2.0 with improved cancer detection sensitivity (cancer detection rate) by 1,9% to 4,5%. The most consistent outcome is the high specificity of 94,4% at Detector C 2.0. This is in line with the published results, even though Detector C 2.0 has been prospectively validated with very good results, it could not be expected that a larger screening test would be as effective in a large-scale screening setting.  

Figure 2: Hierarchical Sequence of Tests  

Outlook:  
For the first time a large randomized patient enrollment, data entry, and powering of studies CRC.COE 2.0. The expected number of patients are listed in Table 2.  

Figure 3: testing platform allows for multiple tests on a single chip  

Detector C 2.0 and Detector C 3.0 will be prospectively validated in multiple, large-scale performance matched clinical studies.  

Study CRC.COE 2.0 also gives the opportunity to discover and validate additional RNA-based markers for different adenomas, carcinoma in situ, and high-grade epithelial neoplasia. It might even be possible to classify a validated RNA-based test for different histotypes like minor adenomas, or even cancerous adenomas, or benign adenomas.  

Such additional tests would be performed side-by-side, see Figure 3. The chip platform allows for multiple tests on a single chip.