



Team Progress Updates

SU2C-Dutch Cancer Society Colorectal Cancer Early Detection Dream Team: “Molecular Early Detection of Colorectal Cancer”



Colorectal cancer (CRC) is the third-most common cancer (after lung and breast) and the fourth-leading cause of death from cancer around the world. Patients can be effectively treated when the tumor is detected and removed early; however, colorectal cancer tends to develop without symptoms until it has reached an advanced stage.

Screening is the most effective strategy against colorectal cancer. Although testing for blood in stool (using the fecal immunochemical test, or FIT) is the standard approach, urgent improvements are needed as many cancers and precancerous lesions are missed by this test.

The Dream Team's first aim is to improve the current FIT screening test by looking for more specific tumor-related molecules in stool samples. Its second aim is to develop a molecular blood test to help identify patients who will benefit from chemotherapy after surgery.

In progress to date, the Dream Team has:

December 2018

- Team members have identified 12 DNA methylation markers for use in screening stool samples for early detection of colorectal cancer. They are adapting these assays for use in blood samples.
- The team has defined combinations of protein biomarkers that perform substantially better than current colorectal cancer screens and is developing antibody-based assays to leverage these combinations.
- The team has optimized its approach to detect circulating tumor DNA (ctDNA) in patients with early-stage cancer in order to identify those who would benefit from adjuvant chemotherapy after undergoing surgery.

June 2018

- The team has optimized the analytical performance for 10 protein markers, and clinical validation experiments have revealed that a three-protein marker panel results in a higher sensitivity for advanced adenomas and colon cancer.
- To increase the sensitivity of their methylation assays, the team implemented the DREAMING technology, which has proved to be more sensitive than the standard quantitative methylation-specific PCR (Q-MSP).





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- The team has identified 12 novel candidate DNA methylation markers for early detection of colorectal cancer.
- The observational Molecular Early Detection of Colon Cancer (MEDOCC) study within the Dutch colorectal cancer cohort (PLCRC) started in July 2016 in one hospital. Currently, 14 hospitals are open for inclusion. Initiation of the study is pending at five additional hospitals.
- The team has demonstrated that circulating tumor DNA can be detected in the majority of preoperative, treatment-naive stage II colorectal cancer patients and is studying the factors that cause the tumor to release DNA into the bloodstream.

December 2017

- Defined protein biomarker combinations that perform substantially better than the current test for population screening for colorectal cancer (CRC).
- Optimized approaches for detection of circulating tumor DNA and applied these for analysis in early stage patients with colorectal cancer and other tumor types
- Observed that circulating DNA can be used to predict whether a Stage II CRC patient will get CRC again, even after the cancer has been removed.

June 2016

- Developed a better test to detect CRC using stool samples. This newer test is superior to the Fecal Immunochemical Test (FIT) and Cologuard. The benefits of the test will be verified by analyzing more samples.
- Developed a much more sensitive method to analyze circulating tumor DNA from the blood of patients. This test is non-invasive and yields fewer false-positive results.
- Showed that measuring circulating tumor DNA can predict disease prognosis. In analyzing samples from CRC patients, observed that patients with higher circulating DNA in their blood had shorter progression-free and overall survival.

December 2015

- Identified and validated the top 10 protein biomarkers for CRC screening and collaborated with a biotech company for the assay development.
- Developed a bioinformatics platform, termed TEC-seq (Targeted Error Correction Sequencing) that has proven to non-invasively detect CRC among all stages, using liquid biopsies with over 80% sensitivity and over 99% specificity.



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June 2015

- Identified a list of 10 promising DNA methylation biomarkers to provide a sensitive method to detect colorectal cancer in stool samples.
- Reported approval of an amendment to the Dutch trial, the Prospective Dutch Colorectal Cancer Cohort Study (PLCRC), which will allow the team to move forward with testing how well liquid biopsies can identify stage II colorectal cancer patients who are high risk of disease recurrence after surgery.

December 2014

- Identified cancer-associated proteins that are more sensitive than current tests for detection of colorectal cancer and can therefore be used to improve the stool-based screening test.
- Established the DNA sequencing analysis methods to use in cancer tissue as well as blood samples in early stage colorectal cancer.