Late Breaking Abstracts

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Is there a role of circulating tumor cells (CTCs) as an independent prognostic factor in locally advanced rectal cancer?

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Background: CTCs detected at baseline and at disease-evaluation time-point in locally advanced rectal cancer seems to be an indipendent prognostic factor in metastatic rectal cancer. Aim of the study is to detect CTCs' evolution after combined neoadjuvant therapy plus curative surgery in locally advanced rectal cancer.
Materials and Methods: In a prospective single institution study, cT3−4 and/or N+ rectal cancer patients are submitted to capecitabine with concomitant radiotherapy followed by surgery with total mesorectal excision (TME). Primary endpoints are evaluation in 120 patients of CTCs at baseline (t0), after neoadjuvant therapy and before surgery (t1), within 7 days after surgery (t2) and at 6 month follow-up (t3) and its correlation with disease free and overall survival. CTCs are enumerated with immunomagnetic separation in 7.5 mL peripheral blood at the above-mentioned time-points (CellSearch System, Veridex Inc.).
Results: From July 2008 to June 2011 67 patients underwent t0 sampling. Among these, 52 completed neoadjuvant therapy (CT+RT) and therefore underwent t1 and t2 sampling. Thirty-eight patients at that time have their t3 sampling completed. At t0, t1, t2 and t3 patients presenting at least 1 CTC (detection rate) were 13/67 (19%), 5/51 (10%), 3/52 (6%) and 2/38 (5%) respectively ($p = 0.07$ t0 vs t2).
Conclusion: CTCs $\geqslant 1$ are present in 23% of our patients at baseline. It seems that neoadjuvant CT−RT followed by radical surgery has an impact on CTCs reduction. At this time the study recruitment is still open for achieving sample size objective.

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Validation of a plasma based miRNA PCR test for early detection of colorectal cancer

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Background: Colorectal cancer (CRC) is a major cause of mortality in the western world. Early detection of CRC improves survival and screening for CRC has been clinically proven to lower CRC-related mortality in the screening population. However, although population screening programs have been implemented in a number of countries, screening rates among the 50−75 year olds are unsatisfactory. There is therefore a clear unmet need for a quick, sensitive, specific, and minimally invasive screening assay to select at risk individuals for definitive diagnosis by colonoscopy.
Materials and Methods: In order to detect microRNA (miRNA) biomarkers for CRC in blood plasma, we developed an LNA-enhanced miRNA RT-qPCR platform with high sensitivity and linearity for optimal quantitation of miRNAs from limited plasma samples. A clinical reference-lab compatible workflow that allows for the entire procedure from sample preparation through data acquisition and QC to test result to be completed within one working day was established. A reference melting curve database has been implemented to ensure the integrity of each data point, and appropriate controls monitor plate-to-plate and day-to-day variation. State-of-the-art normalization protocols have been evaluated to ensure optimal normalization of datasets prior to data analysis.
Results: We previously determined a miRNA signature in a multi hospital discovery cohort that is differentially expressed between healthy individuals and stage II CRC patients. Here we report on the validation of this miRNA signature in an independent set of 105 plasma samples from CRC patients and healthy volunteers. We have counter-screened the miRNA signature in a set of patients with other prevalent diseases, including hypertension, diabetes, diverticulitis, and others. In addition, we report on our progress on the next large-scale validation in samples from a clinical trial of 3,000 symptomatic patients undergoing first-time colonoscopy.
Conclusion: A plasma miRNA signature for early detection of CRC from patient plasma was developed and validated in an independent clinical sample set. The signature was specific with respect to other diseases prevalent in the screening population. A second large-scale validation project is on-going. We conclude that plasma miRNA biomarkers can constitute an effective minimally invasive approach to population-wide CRC screening.

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Studying the impact of nanog and other trascription factors in stemness pathway

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Background: The last few years, there is great evidence that malignant tumors are initiated by a small population of cells that share similar hallmarks with normal stem cells. The cancer stem cell's hypothesis is based on the fact that this population has the ability to differentiate into any of the three germ layers (pluripotency) as well as to self-renew using the asymmetric cell division. Regulators in this process are many transcription factors such as nanog, oct3/4 and sox2 which may play a key role in stemness pathway. This project attempts to prove if there is a synergistic role between nanog, oct3/4, sox2 as well as other transcription factors such as nestin and cd34 gene in stemness pathway.
Materials and Methods: Three different methods have been chosen in order to prove the above hypothesis. Firstly, a siRNA-based method was used for repressing the nanog gene. The second panel of the test included molecular based-methods in order to test the gene and protein expression of the transcription factors that were mentioned above and to prove that nanog is the cornerstone in the activation of cancer stem cell-like cells. For these experiments, two different populations of breast cancer stem cells were used and cultivated. The first population was isolated from patients who suffered from breast carcinoma and the second was a commercial breast cancer stem cell population.
Results: In the first panel of the experiment, it has been shown that the expression level of nanog gene was reduced as it was expected, after siRNA knocking down. In the second panel of the test, it has been proved that when there was a reduction in nanog's expression, there was also a reduction in the other stemness markers.
Conclusion: The present scientific attempt indicates that in this particular case, there is a great correlation between nanog and oct3/4, sox2, nestin as well as cd34 gene concerning the expression level.