

# 5<sup>th</sup> International Conference on Biomarkers & Clinical Research

April 15-17, 2014 St. Hilda's College - University of Oxford, UK

## MicroRNA and colorectal cancer: Variations in miRNA binding site, genome-wide miRNA methylation, and the use of miRNA's as cancer biomarkers in different tissues

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MicroRNAs (miRNAs) are key gene regulators in most biological and pathological processes, including colorectal cancer (CRC). The association of miRNA-related polymorphisms with CRC incidence and prognosis, as well as the possibility of using circulating or fecal miRNA expression as noninvasive early detection biomarkers open interesting possibilities. miRNAs may be potential molecular classifiers, early detection biomarkers, and therapeutic targets for CRC. However, the underlying mechanisms of aberrant miRNA regulation, such as altered DNA methylation, are still poorly known.

We report our investigations on a) the role of variation in miRNA target binding sites on CRC risk and prognosis, focusing on DNA repair genes, b) genome-wide miRNA methylation levels in prediagnostic samples, c) the search of CRC biomarkers in surrogate specimens.

Variations in predicted binding sites in 3'UTR of nucleotide-excision repair pathway genes were associated with CRC risk; while a polymorphism in base-excision repair gene SMUG1 showing reduced gene expression *in vitro* was associated with increased survival in patients treated with 5-fluorouracil-based therapy. A miRNA signature discriminating CRC and precancerous lesions has been described in plasma samples, showing a dysregulation of miR-34a and miR-150. A pilot study on stool/plasma from healthy volunteers with different dietary habits has revealed differential expression of miR-92a among vegans, and subjects with omnivorous diet. A novel approach to analyse miRNA methylation from epigenome-wide DNA methylation levels measured in peripheral blood samples is described. The necessity to move on high-throughput techniques to globally define miRNA signatures involved in colorectal carcinogenesis in surrogate specimens is also briefly discussed.

### Biography

Alessio Naccarati has completed his Ph.D. in Human Molecular Genetics in 2003 at Pisa University (Italy). He has made his postdoc in the Department of Molecular Biology of Cancer (Academy of Sciences of the Czech Republic, Prague), where has also held a position of Head of Laboratory. He is currently Senior Scientist at the Molecular Genetic and Epidemiology Unit at Human Genetics Foundation (Torino, Italy). He has published 68 papers in peer reviewed impacted journals, participated in several international/national grants, both in Italy and Czech Republic. His main topics are colorectal cancer susceptibility, DNA repair and recently microRNAs.

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