Stellingen

behorend bij het proefschrift

High-throughput DNA methylation analysis in colorectal cancer and childhood leukemia

Eddy H. J. van Roon, 20 juni 2012

1 - The association between high levels of promoter methylation and *BRAF* mutations in colorectal cancer is a result of selective pressure on neoplastic cells for epigenetic inactivation of genes associated with BRAF-induced senescence. (This thesis)

2 - The high specificity and sensitivity in Lynch syndrome associated colon tumors imply a possible utility for *PTPRGint1* methylation in new or existing colon-specific methylation marker panels for colon cancer screening. (This thesis)

3 - To filter out methylation changes with minimal expected effects on transcription and thereby tumorigenesis one must exclude differential methylation targets that have repressive histone modifications in the cells from which they originate. (This thesis)

4 - The high levels of methylation and correlation with expression suggest an epigenetic block of B-cell differentiation in t(4;11)- and t(11;19)- positive infant ALL patients. (This thesis)

5 - Infant ALL patients with t(4;11)- and t(11;19) translocations have high levels of DNA methylation and could be considered for DNA methylation inhibiting therapies. (This thesis)

6 - "Many of the CpG islands that become methylated in cancer are located in promoters of genes that are repressed before transformation or are located in non-promoter regions, making it unlikely that these particular modifications significantly influence tumor biology." (Schlesinger *et al*., 2007. Nature Genetics 39:232-6)

7 - "In the light of the recent paradigm shift toward 3-D genome regulation, the traditional regulatory functions of CTCF, including transcriptional activation, repression, insulation and imprinting, may all be secondary effects of its primary, ubiquitous, and essential role as a genome-wide organizer of chromatin architecture." (Phillip *et al*., 2009. Cell. 137:1194-1211)

8 - "If optimal sensitivity and specificity is gained through the identification of markers that show the highest differences in methylation between the cancer and the background, testing for methylated DNA in blood or stool samples may have great potential as a new screening marker for CRC as well as a tool for disease monitoring in colon cancer patients." (Kim *et al*., 2010. Cancer Metastasis Rev. 29:181-206)

9 –"Targeting individuals and populations with a low fruit and vegetable intake might be most effective for colorectal cancer prevention." (Aune *et al*., 2011. Gastroenterology. 141:106–118)

10 - Boxing is a relatively healthy way to cope with the setbacks encountered in your scientific research.

11 - The complexity of epigenetic regulation of gene expression is daunting. You can only wonder if man will ever truly understand the molecular mechanisms that allow his body to function.