

Clinical applications of methylation biomarkers.

Tomasz K Wojdacz

Independent Clinical Epigenetics Laboratory Pomeranian Medical University Szczecin, Poland

Email: tomasz.wojdacz@pum.edu.pl

Epigenetic mechanisms of gene expression regulation change gene expression without changing primary gene sequence. Referred to as DNA methylation, enzymatic addition of methyl groups to cytosines in DNA strand is one of the most important epigenetic mechanisms of gene expression regulation. In general terms methylation of gene promoter acts to repress gene expression and this mechanism is essential for normal development and tissue specific gene expression. Abnormal changes of methylation of genes contribute if not initiate malignant transformation. Thus, the phenotype of malignant neoplasia (e.g. aggressiveness or metastatic potential) to a large extent depends on the methylation changes acquired during carcinogenesis. Identification of the physiological processes disrupted by methylation during carcinogenesis allows not only for the discovery of the new treatment targets but also biomarkers for personalized medicine. There is an ample research evidence indicating that methylation biomarkers provide clinically useful information at all stages of the clinical disease management; from risk assessment through early diagnosis and treatment personalization to post treatment surveillance. In spite of that, the use of methylation biomarkers in clinical practice is still marginal and needs to be improved.

The process of identification of the methylation changes typically begins with a study that utilizes a technology allowing comparison of the genome wide methylation pattern of pathologically changed tissues and their healthy counterparts. Discovered in those analyses, methylation changes are subsequently validated for the clinical utility with more cost-effective technology such as PCR based techniques. In my talk I will review methylation biomarker discovery and clinical validation process using examples from my research in chronic lymphocytic leukemia (CLL) where we proposed improved stratification of CLL patients using methylation-based classifiers^{1,2}.

References:

¹ Wojdacz TK et al, Clinical significance of DNA methylation in chronic lymphocytic leukaemia patients: results from three UK clinical trials. **Blood Advances**, "in press".

² Hussmann D. et al, *IGHV*-related methylation changes significantly improve the prognostic power of *IGHV* mutation status of CLL patients. *Under review*.