DNA methylation profiling

DNA methylation profiling is a technique used to identify and analyze the patterns of DNA methylation, which is the addition of a methyl group to the cytosine residue in DNA. This modification plays a crucial role in regulating gene expression, and abnormal DNA methylation patterns have been associated with many diseases, including cancer.

The profiling of DNA methylation involves the use of various technologies such as microarrays, bisulfite sequencing, and next-generation sequencing. Microarrays are used to measure the methylation status of pre-selected regions of the genome, while bisulfite sequencing and next-generation sequencing can provide more comprehensive information about the methylation status of the entire genome.

Bisulfite sequencing involves the treatment of DNA with sodium bisulfite, which converts unmethylated cytosine residues to uracil while leaving methylated cytosines intact. The treated DNA is then subjected to PCR amplification and sequencing, allowing for the identification of individual methylated cytosines in the genome.

Next-generation sequencing technologies can also be used for DNA methylation profiling, such as whole-genome bisulfite sequencing (WGBS) and reduced representation bisulfite sequencing (RRBS). WGBS provides a comprehensive view of the entire genome's methylation status, while RRBS focuses on specific regions of the genome that are enriched for CpG sites.

Overall, DNA methylation profiling has become an important tool for understanding the epigenetic regulation of gene expression and its role in disease development and progression.

Case series provide the support that tumor DNA methylation profiling adds meaningful classification information and may be beneficial to incorporate in clinical practice. The report also reveals that DNA methylation combined with WHO histology classification can more accurately predict tumor behavior than WHO classification alone [1)]

DNA methylation is one of the principal epigenetic mechanisms that control gene expression in humans, and its profiling provides critical information about health and disease. Current profiling methods require chemical modification of bases followed by sequencing, which is expensive and time-consuming.

Ferreyra Vega et al. investigated the potential utility of DNA methylation profiling to achieve molecular diagnosis in adult primary diffuse lower-grade glioma (dLGG) according to the World Health Organization Classification of Tumors of the Central Nervous System 2016. They also evaluated whether methylation profiling could provide improved molecular characterization and identify prognostic differences beyond the classical histological WHO grade together with IDH mutation status and 1p/19q co-deletion status. All patients diagnosed with dLGG in the period 2007-2016 from the Västra Götaland region in Sweden were assessed for inclusion in the study.

A total of 166 dLGG cases were subjected to genome-wide DNA methylation analysis. Of these, 126 (76%) were assigned a defined diagnostic methylation class with a class prediction score ≥ 0.84 and a

subclass score ≥ 0.50. The assigned methylation classes were highly associated with their IDH mutation status and 1p/19q codeletion status. IDH-wild-type gliomas were further divided into subgroups with distinct molecular features.

The stratification of the patients by methylation profiling was as effective as the integrated WHO 2016 molecular reclassification at predicting the clinical outcome of the patients. The study shows that DNA methylation profiling is a reliable and robust approach for the classification of dLGG into molecularly defined subgroups, providing accurate detection of molecular markers according to WHO 2016 classification [2)].

1)
Shen E, Leclair NK, Herlth K, Soucy M, Renzette N, Zhuo X, Kelly K, Omerza G, Onyiuke H, McNeill I, Wolansky L, Becker K, Li L, Wu Q, Bulsara KR. DNA methylation provides diagnostic value for meningioma recurrence in clinical practice. Acta Neurochir (Wien). 2023 Mar 15. doi: 10.1007/s00701-023-05550-5. Epub ahead of print. PMID: 36920663.
2)
Ferreyra Vega S, Olsson Bontell T, Corell A, Smits A, Jakola AS, Carén H. DNA methylation profiling for molecular classification of adult diffuse lower-grade gliomas. Clin Epigenetics. 2021 May 3;13(1):102. doi: 10.1186/s13148-021-01085-7. PMID: 33941250.