OMIC-06. MOLECULAR SUBGROUPING OF MEDULLOBLASTOMA VIA LOW-DEPTH WHOLE GENOME BISULFITE SEQUENCING

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Abstract: Genome-wide DNA methylation profiling has emerged as an important diagnostic tool that complements histopathology for CNS tumors in children and adults. Literature describing its application in Asian countries is nonetheless limited. Herein, we report the feasibility and utility of adopting such a platform for children diagnosed with CNS tumors in Hong Kong. A multi-institutional cohort (n=94, 97% of Chinese ethnicity) with CNS embryonal or high grade neuroependelial tumors (HGNET) diagnosed in Hong Kong from 1999 to 2021 was assayed based on tissue availability. DNA was extracted from FFPE tumor material (median 301ng, range 13-1000ng), bisulfite converted and profiled with the Infinium Methylation Epic BeadChip kit. Raw data were analyzed on the German Cancer Research Center MNP 2.0 classifier and through unsupervised dimensionality-reduction analysis (t-SNE) referencing a published CNS tumor reference dataset (GSE90496). The radiologic diagnosis included medulloblastoma (n=65), AT/RT (n=9), pineal parenchymal tumors (n=7), ETMR (n=5), CNS-PNET (n=4) and other embryonic tumor fifteenth and NPKD (n=4). t-SNE was performed with 137 input features estimated where possible. Finally, comprehensive subgroup-specific DNA methylation data was compared with Methyl Chip data. Machine-learning WGBS-based subgroup classifiers were retrained and profiled with the Infinium Methylation EPIC BeadChip kit. Raw data were analyzed on the German Cancer Research Center MNP 2.0 classifier and t-SNE was used to visualize the data.

OMIC-08. COMPOUND HETEROZYGOSITY OF POLE AND PMS2 LEADS TO CMMRD-LIKE PHENOTYPE – ‘POLYCH’ SYNDROME

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OMIC-07. FEASIBILITY AND EPICEPHALIC PROFILING FOR CHILDMHOOD CNS TUMORS IN HONG KONG

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OMIC-05. COMPOUND HETEROZYGOSITY OF POLE AND PMS2 LEADS TO CMMRD-LIKE PHENOTYPE – ‘POLYCH’ SYNDROME

OMIC-06. MOLECULAR SUBGROUPING OF MEDULLOBLASTOMA VIA LOW-DEPTH WHOLE GENOME BISULFITE SEQUENCING

Intational consensus recognises four molecular subgroups of medulloblastoma, each with distinct molecular features and clinical outcomes. The current gold-standard for subgroup assignment is DNA methylation microarray. There is an unmet need to develop platform-independent subgrouping assays which are both non-proprietary and compatible with rapidly-expanding WGS capacity in healthcare. Whole Genome Bisulfite Sequencing (WGBS) enables the assessment of genome-wide methylation status at single-base resolution. Previously, WGBS adoption has been limited by cost and sample quality/quantity requirements. Its application for routine detection of medulloblastoma subgroups has not been reported. Here, we present a novel WGBS assay for medulloblastoma diagnose and genotyping within the clinical setting. Methylation status was assessed in paired DNA methylation microarray. Group 4 MBs most closely resembled differentiated neuronal cells and revealed new insights into subgroup enriched pathways and kinase activity in MB.

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