

TB-17. A COMPREHENSIVE PAN-CANCER ANALYSIS OF CHILDHOOD MALIGNANCIES

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Genomic profiling of individual tumours by next-generation sequencing has led to an improved understanding of tumour biology and allows patient stratification into clinically relevant molecular subtypes. Recently, large-scale integrative analyses across various adult cancer types revealed further insights into

cancer aetiologies by identifying for example significantly mutated genes and mutational processes underlying cancer types. To transfer this approach to childhood cancers, we have compiled a comprehensive pediatric Pan-Cancer dataset containing genome and exome sequencing data of 925 patients from 22 distinct molecular entities. CNS tumours are the most aggressive and second most common pediatric cancers and thus contribute a significant proportion of the samples. Raw sequencing data were processed with a standardised workflow and subjected to mutation calling, including single nucleotide variants and insertions/deletions, as well as copy number variation analysis. Mutation loads are lowest in hepatoblastoma and pilocytic astrocytoma, highest in Burkitt Lymphoma and DIPG, and are mostly independent from patient age. Based on recurrence and functional significance, we identified the most important driver genes of childhood tumours per cancer type and across entities. We unravelled the mutational processes inherent in pediatric cancers by deciphering mutational signatures, including very common signatures shared between many cancer types, but also specific ones that even differentiate on subtype level, e.g. between Medulloblastoma subgroups. Moreover, this novel Pediatric Pan Cancer compendium enabled us to investigate the relevance of hereditary cancer predispositions in children and to assess the druggability of childhood cancers based on mutations in targetable genes or pathways from a clinical perspective.