

Different biological characteristics of high-grade gliomas in children

Abstract

Central nervous system tumors represent the most common solid tumor malignancy of childhood, with high-grade gliomas forming one of the most aggressive subgroups. Despite advances in pediatric oncology, the prognosis of children with high-grade gliomas remains unfavorable, underscoring the need for a deeper understanding of their biology and the development of new therapeutic approaches. The diagnosis of pediatric central nervous system tumors is complex and involves clinical, radiological and pathological investigations, including the latest molecular biological techniques, which play a key role in accurate classification and prognosis. The 2021 WHO classification of central nervous system tumors represents more than 100 histopathological entities, with significant expansion of knowledge on molecular characteristics including genetic and epigenetic alterations. This dissertation focuses on a comprehensive molecular characterization of a cohort of pediatric patients with high-grade gliomas, identifying key oncogenic mutations, secondary alterations and methylation classes with the aim of identifying novel therapeutic targets. A detailed analysis of the molecular, radiological and clinical characteristics of radiotherapy-induced gliomas that represent a significant late sequela of radiotherapy and are part of a cohort of high-grade gliomas was performed. A major contribution of this work is to highlight the heterogeneity of high-grade gliomas in children and to reveal specific molecular biological patterns that may serve as potential therapeutic targets. Furthermore, the detailed molecular characterization of radiotherapy-induced gliomas has provided important information to differentiate these tumors from primary high-grade gliomas and recurrences of primary disease. Thus, this work provides new insights into the molecular pathogenesis of high-grade pediatric gliomas, highlights the importance of integrating histopathological, molecular-genetic and radiological data for accurate diagnosis and selection of optimal therapy, and suggests directions for future research in pediatric neuro-oncology.