



The Role of Cytogenetics in Pediatric Solid Tissue Tumors

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Tumors of infancy and childhood differ from adult tumors in both incidence and type. Aside from hematopoietic tumors, the most common pediatric neoplasms arise in nervous tissues, bones, soft tissues, and kidneys. Some examples of the most common neoplasms include neuroblastoma, Ewing's sarcoma, rhabdomyosarcoma, and Wilms tumor. These tumors are often primitive appearing histologically and consist of small, round, blue cells. Due to the overlapping morphology, cytogenetic analysis can be very useful in establishing the diagnosis. Also, cytogenetic findings are frequently predictors of prognosis. Cytogenetic analysis is achieved through both traditional karyotype analysis and fluorescent in situ hybridization (FISH). Conventional cytogenetics requires fresh, unfixed tissue, whereas FISH can be performed on fresh, frozen, or paraffin-embedded tissue.

In neuroblastomas, cytogenetics has a key role in determining prognosis. The most common karyotypic abnormality is partial gain of 17q. This finding occurs in up to 50% of neuroblastomas and is frequently due to an unbalanced translocation.¹ Gain of 17q is associated with poor prognosis as are deletions in the short arm of chromosome 1. Hyperdiploidy and triploidy are associated with a favorable prognosis. The most significant genetic prognostic predictor in neuroblastomas is *MYCN* amplification, and it is strongly associated with an adverse prognosis. Amplification can be seen on karyotype analysis as either double minutes (small accessory chromosomes) or homogeneously stained regions. However, FISH is the method more commonly performed to determine *MYCN* amplification status.

Soft tissue and bone tumors often times have characteristic translocations. These translocations can be detected by both FISH and karyotype analysis. Ewing's sarcoma was the first sarcoma to be defined by a specific translocation.² Ewing's sarcoma is most commonly associated with t(11;22) resulting in a *EWSR1/FLI1* gene fusion. This translocation will be detected in >90% of Ewing's sarcomas.³ Less commonly (approximately 5% of cases), t(21;22) (*EWSR1/ERG* fusion) is found in these tumors.³ Rhabdomyosarcomas are another pediatric sarcoma associated with characteristic translocations. Most cases of alveolar rhabdomyosarcomas will have a t(2;13), which results in a *PAX3/FOXO1A* gene

fusion and is associated with poor prognosis. More rarely, t(1;13) is found in alveolar rhabdomyosarcomas. Embryonal rhabdomyosarcomas do not display a characteristic translocation but are associated with abnormalities of chromosome 11p.

Wilms tumor is the most common renal tumor of childhood. The Wilms tumor-associated gene (*WT1*) is located at 11p13. Both deletions and translocations involving this gene are associated with the neoplasm. However, these abnormalities are more frequently seen in syndromic cases. Only 10% of sporadic Wilms tumors contain a *WT1* mutation.⁴ A second gene (*WT2*) has been identified at 11p15. Other chromosomal abnormalities more rarely associated with Wilms tumor include deletions of 1p and 16q, gains of 1q, and loss of 22.⁵

The cytogenetic abnormalities of many frequent pediatric solid tissue tumors are characteristic and well studied. Detection of a characteristic abnormality can aid in diagnosis as well as predict prognosis in many instances. Even in light of new molecular methods, the role of cytogenetics in pediatric neoplasia continues to be vitally important.

References:

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