Commentary

Translocations in Malignant Tumors

Avery A. Sandberg

*St. Joseph's Hospital and Medical Center
Phoenix, Arizona*

In general, the development and biology of epithelial tumors, carcinomas, and adenocarcinomas are associated with an array of orchestrated genetic changes characterized by a successive process of loss of heterozygosity. On the other hand, tumors of mesodermal origin (bone and soft tissue tumors) are often associated with translocations thought to be causally related to the development of the neoplasia. Often, the translocation is the only cytogenetic change observed in these tumors (Table 1). The occurrence of translocations as a sole karyotypic event in carcinomas, as indicated by the authors of the article by French et al,¹ is extremely rare.

There is general consensus that the translocations shown in Table 1 and their associated molecular events are not only diagnostic of these tumors, regardless of their site of origin and variability of the histology, but also, as already mentioned, the genetic changes resulting from these translocations are responsible for the genesis of these tumors. Furthermore, therapeutic approaches, akin to those found effective in leukemias associated with specific translocations, eg, t(9;22) in chronic myelocytic leukemia and t(15;17) in acute promyelocytic leukemia, hold much promise for the treatment of these tumors.

The present article by French et al¹ points to the strong possibility that a somewhat heterogeneous group of rare carcinomas may be characterized by a t(15;19) and the molecular events associated with this translocation. The heterogeneity is related to the reported breakpoints on

chromosome 15 (q11, q12, q13, q15, and p12) and the somewhat anatomical variability of the tumor sites, though the tumors appear to be mediastinal or thoracic in their location. However, these carcinomas as a group do share a poor prognosis and an apparently similar histology.

Although the studies of French et al¹ have not yet revealed the presumptive oncogenic fusion product associated with the t(15;19), they have established that the *BRD4* gene on chromosome 19 is interrupted by the translocation and that a 9 kb region containing the *Nop10p* gene on chromosome 15 is affected by the translocation break. Thus, it remains imperative to ascertain the exact gene affected on chromosome 15 and to determine the structure and transforming mechanisms of the fusion product of the t(15;19). It is equally important to evaluate further whether the above-mentioned variability in the breakpoints on chromosome 15 is real and thus raises concerns regarding the specificity of the t(15;19) in these tumors. Obviously, more carcinomas with t(15;19) will have to be studied to more firmly establish their cytogenetic and molecular aspects.

Reference

1. French C, Miyoshi I, Aster JC, Kubonishi I, Kroll TG, Dal Cin P, Vargas SO, Perez-Atayde AR, Fletcher J: BRD4 bromodomain gene rearrangement in aggressive carcinoma with translocation t(15;19). *Am J Pathol* 2001, 159:1987–1992

Accepted for publication September 26, 2001.

Address reprint requests to Avery A. Sandberg, M.D., Department of DNA Diagnostics, St. Joseph's Hospital and Medical Center, 350 West Thomas Rd., Phoenix, AZ 85013.

Table 1. Specific Chromosomal Translocations Established Cytogenetically and the Corresponding Gene Changes in Bone and Soft Tissue Tumors

Tumors	Translocation	Gene changes
Alveolar rhabdomyosarcoma	t(2;13)(q35;q14)	PAX3-FKHR
Alveolar soft part sarcoma	t(1;13)(p36;q14)	PAX7-FKHR
Clear cell sarcoma (malignant melanoma of soft parts)	t(X;17)(p11.2;q25)	ASPL-TFE3
Congenital fibrosarcoma and mesoblastic nephroma	t(12;22)(q13;q12)	ATF1-EWS
Dermatofibrosarcoma protuberans (giant cell fibroblastoma)	t(12;15)(p13;q25)	ETV6-NTRK3
Desmoplastic round cell tumor	t(17;22)(q22;q13)	COL1A1-PDGFB
Endometrial stromal sarcoma	t(11;22)(p13;q12)	WT1-EWS
Ewing sarcoma and peripheral primitive neuroectodermal tumors	t(7;17)(p15;q21)	JAZF1-JJAZ1
	t(11;22)(q24;q12),	EWS-FLI1
	t(21;22)(q22;q12)	EWS-ERG
	t(7;22)(p22;q12)	EWS-ETV1
	t(17;22)(q12;q12)	EWS-E1AF
	t(2;22)(q33;q12)	FEV-EWS
Inflammatory myofibroblastic tumor	t(2;19)(p23;p13.1)	ALK-TPM4
	t(1;2)(q22-23;p23)	TPM3-ALK
Myxoid chondrosarcoma, extraskeletal	t(9;22)(q22;q12)	EWS-CHN(TEC)
	t(9;17)(q22;q11.)	RBP56-CHN(TEC)
	t(9;15)(q22;q21)	TEC/TCF12
Myxoid liposarcoma	t(12;16)(q13;p11)	TLS(FUS)-CHOP
	t(12;22)(q13;q12)	EWS-CHOP
Synovial sarcoma	t(X;18)(p11;q11)	SYT-SSX1
		SYT-SSX2