

## DIAGNOSTIC BRIEF

# Immunohistochemical classification of T cell and NK cell neoplasms

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In the new World Health Organisation (WHO) classification of haematological malignancies, immunophenotypical analysis plays an important role in the subclassification of lymphomas.<sup>1</sup> In the past decade, many new antibodies have become available that can be used on routinely fixed, paraffin wax embedded tissue sections. At present, it is possible to make a correct subclassification of T cell lymphomas in most cases using a relatively restricted set of markers in combination with clinical presentation. However, in some cases it may be difficult to differentiate a benign T cell response from a malignant T cell proliferation. In these cases, clonality analysis based on the presence of monoclonal T cell receptor rearrangements is indicated.

In table 1 the most discriminating markers are depicted in relation to the different entities, as recognised by the WHO classification.

### REFERENCES

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- 3 Pulford K, Lamant L, Morris SW, et al. Detection of anaplastic lymphoma kinase (ALK) and nucleolar protein nucleophosmin (NPM)-ALK proteins in normal and neoplastic cells with the monoclonal antibody ALK1. *Blood* 1997;89:1394-404.
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### Key points

- CD3, CD4, CD8, CD56, and CD30 all give a predominantly membranous staining. However, in extranodal NK/T cell lymphoma, nasal type, CD3 staining is usually cytoplasmic. In other entities cytoplasmic CD3 is unusual.
- Staining with granzyme B, perforin, and TIA-1 always gives characteristic granular cytoplasmic staining reflecting expression in the cytotoxic granules.<sup>2</sup>
- Terminal deoxynucleotidyl transferase staining is strictly nuclear.
- ALK staining is most frequently both nuclear and cytoplasmic, but may be membranous or only cytoplasmic.<sup>3,4</sup>
- The presence of the Epstein Barr virus (EBV) in the tumour cells can only be determined reliably using RNA in situ hybridisation detecting the abundantly transcribed EBV encoded RNAs (EBER). Expression of EBV encoded latent membrane 1 is frequently undetectable in EBER positive T cell lymphomas.

Table 1 Interpretation of immunohistochemistry

	TdT	CD3	CD4	CD8	GB/P	TIA1	CD56	EBV	CD30	ALK	Characteristic feature(s)
Predominantly leukaemic											
Precursor T lymphoblastic leukaemia	+	+	+/-	+/-	-	-	-	-	-	-	Frequent presentation with mediastinal mass
T cell PLL	-	+	+/-	-/+	-	-	-	-	-	-	Multi-organ involvement including the skin
T cell large granular lymphocytic leukaemia	-	+	-/+	+/-	+	+	+/-*	-	-	-	Indolent behaviour
Aggressive NK cell leukaemia	-	+	-/+	+	+	+	+	+	-	-	Multi-organ involvement, highly aggressive
Adult T cell lymphoma/leukaemia (HTLV 1+)	-	+	+	-	-	-	-	+/-	-	-	Usually widely disseminated, very rare in non-endemic areas
Predominantly extranodal											
Extranodal NK/T cell lymphoma, nasal type	-	+	-	-/+	+	+	+/-	+	-/+	-	Nearly always primary nasal localisation
Enteropathy-type T cell lymphoma	-	+	-	-/+	+	+	-/+	-/+	-/+	-	Usually, but not always associated with coeliac disease
Hepatosplenic γ <sub>T</sub> T cell lymphoma	-	+	-	-	+	+	+	-	-	-	Involvement of liver, spleen, and bone marrow
Predominantly cutaneous											
Blastic NK cell lymphoma†	-/+	-	+	-	-/+	-/+	+	-	-	-	Difficult distinction from T cell acute lymphoblastic leukaemia and myeloblastic leukaemia
Subcutaneous panniculitis-like T cell	-	+	-	+	+	+	-/+	-	-	-	Rimming of adipocytes
Mycosis fungoides/Sézary syndrome	-	-	+	-/+	-/+	-/+	-	-	-	-	Epidermotropism and Pautrier abscess formation
ALCL primary cutaneous	-	-/+	+/-	-/+	+/-	+/-	-	-	+	-	Distinction with lymphomatoid papulosis only on basis of clinical behaviour
Predominantly nodal											
ALCL systemic	-	-/+	+/-	-/+	+/-	+/-	-	-	+	+/-	ALK positive cases demonstrate favourable clinical outcome
Peripheral T cell lymphoma, NOS	-	+	+/-	-/+	-	-	-	-	+/-	-	Usually generalised disease
Angio immunoblastic T cell lymphoma	-	+	+	+	-	-	-	+	-	-	Aggregates of CD21 positive dendritic cells, outside follicle centres. EBV positive B cells

\*The T cell origin of this entity is disputed; these tumours are usually CD57+.

†ALCL, anaplastic large cell lymphoma; EBV, Epstein-Barr virus; GB, granzyme B; HTLV1, human T cell lymphotropic virus 1; NK, natural killer; NOS, not otherwise specified; P, perforin; PLL, polymorphous leukaemia; TdT, terminal deoxynucleotidyl transferase; +, positive; -, negative; +/-, usually positive, sometimes negative; -/+ , usually negative, sometimes positive.