Expression of p63 protein in anaplastic large cell lymphoma: implications for genetic subtyping

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Supplemental Materials

Supplemental Table 1 Correlation between copy numbers of *TP63* and *DUSP22* loci in ALCL (all WHO subtypes)

	DUSP22 genetic status – n (%)			
	Non-rearranged, no extra copies	Rearranged	Extra copies	Total
TP63 genetic status				
Non-rearranged, no extra copies	45 (58.4)	27 (35.1)	5 (6.5)	77
Rearranged	7 (70.0)	1 (10.0)	2 (20.0)	10
Extra copies	8 (29.6)	4 (14.8)	15 (55.6)	27
Total	60	32	22	114*

$p<0.0001$, Pearson χ^2 test.

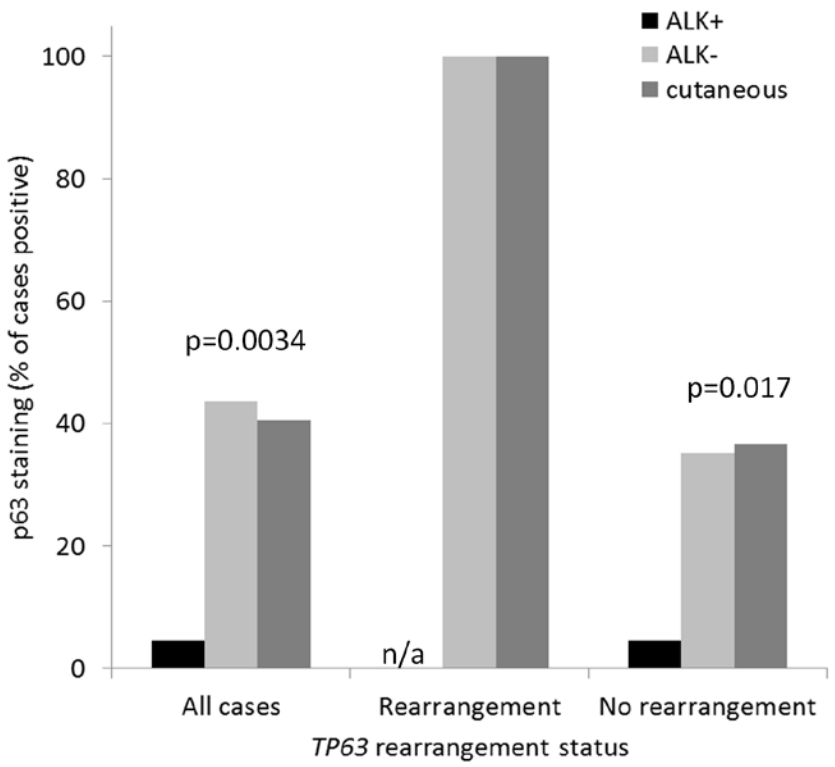
*Two ALCLs on which *DUSP22* FISH was not performed were excluded.

Supplemental Table 2 ALCLs tested for ΔNp63 expression by immunohistochemistry*

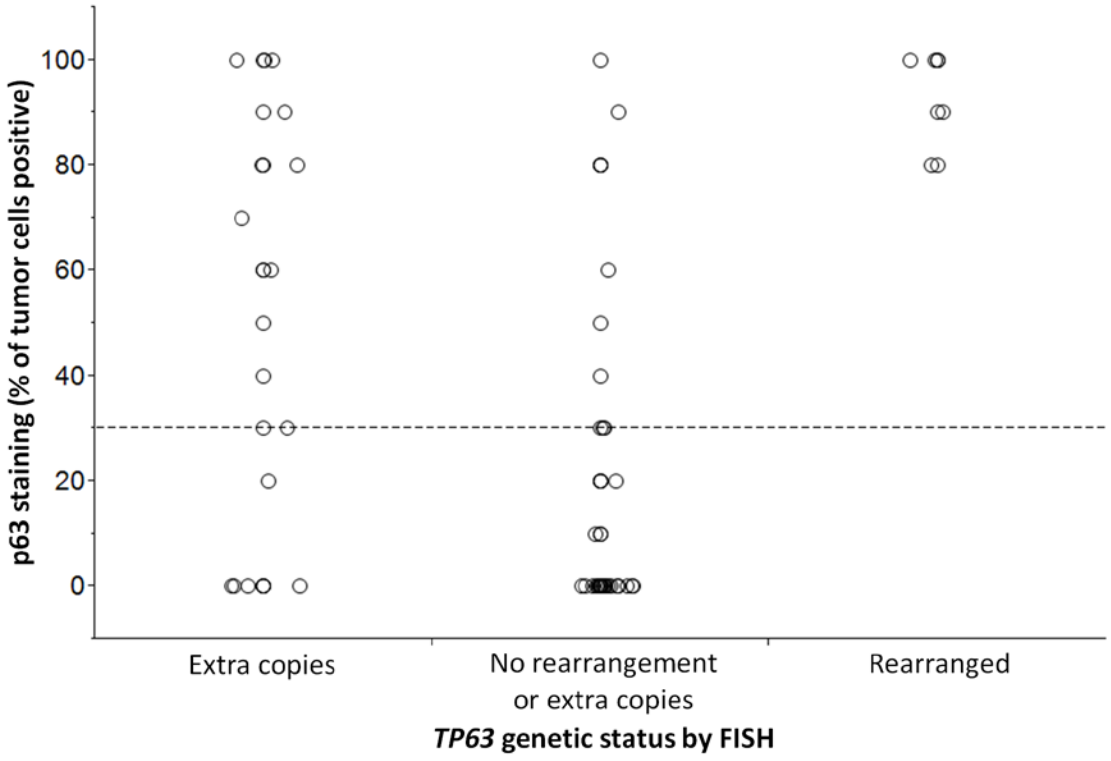
	WHO subtype			
	ALK-positive	ALK-negative	Primary cutaneous	Total
TP63 rearranged, p63 protein-positive	0	4	2	6
TP63 non-rearranged, p63 protein-positive	0	12	3	15
TP63 non-rearranged, p63 protein-negative	15	17	6	38

*No positive staining was seen in any case.

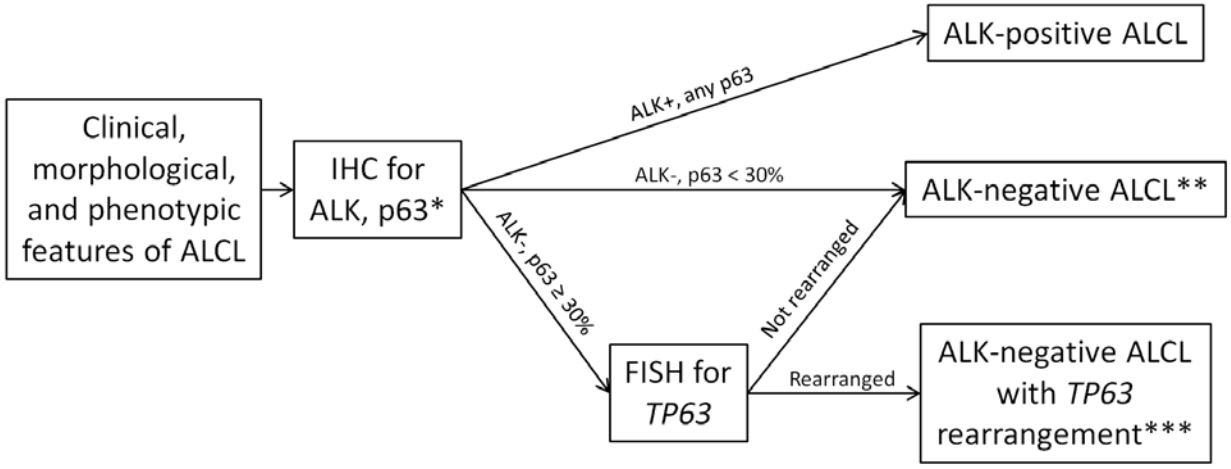
Abbreviations: ALCL: anaplastic large cell lymphoma; ALK: anaplastic lymphoma kinase; WHO: World Health Organization.



Supplemental Figure 1 Proportions of ALCLs positive for p63 by IHC (defined as positive staining in ≥30% of tumor cell nuclei), stratified by WHO subtype and *TP63* rearrangement status. n/a, not applicable (*TP63* rearrangements were not observed in ALK-positive ALCLs).



Supplemental Figure 2 Distribution of anaplastic large cell lymphomas (ALCLs) in the present study based on *TP63* genetic status by fluorescence *in situ* hybridization (FISH) and p63 immunohistochemistry results. All cases with *TP63* rearrangements showed strong nuclear staining in ≥ 80% of tumor cells. Although intensity of staining may be informative [1], it is difficult to assess reproducibly in clinical practice and may be affected by technical factors such as fixation. We propose performing FISH in cases with nuclear staining in ≥ 30% of tumor cells (dashed line), regardless of staining intensity. This cut-off has a sensitivity of 100% and a specificity of 71%. Although higher cut-off values also would have 100% sensitivity in this study, the more conservative value of 30% might identify additional positive cases with increasing experience, and could avoid the need for FISH in up to 65% of cases, depending on the patient population and practice algorithm adopted (see Supplemental Figure 3, below).



Supplemental Figure 3 Possible algorithm for use of p63 immunohistochemistry (IHC) and *TP63* fluorescence *in situ* hybridization (FISH) in the evaluation of anaplastic large cell lymphoma (ALCL).

**TP63* rearrangements have not been reported in ALK-positive ALCL; therefore, IHC for ALK and p63 could be sequential instead of concurrent, reserving p63 evaluation only for ALK-negative cases. However, cost savings would need to be weighed against increased turnaround time.

**FISH testing for *DUSP22* rearrangements should be considered in ALK-negative ALCL [1, 2].

***ALK-negative ALCL with *TP63* rearrangement is not a distinct entity in the World Health Organization classification system; the diagnosis is ALK-negative ALCL and the rearrangement should be mentioned because of its potential prognostic significance [1, 2].

Supplemental References

1. Parrilla Castellar ER, Jaffe ES, Said JW, et al. ALK-negative anaplastic large cell lymphoma is a genetically heterogeneous disease with widely disparate clinical outcomes. Blood 2014;124:1473-80.
2. Swerdlow SH, Campo E, Pileri SA, et al. The 2016 revision of the World Health Organization classification of lymphoid neoplasms. Blood 2016;127:2375-90.