



Recommended Cell Markers in Lymphoproliferative Diagnosis: A Delphi Poll

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INTRODUCTION

Multi-parametric flow cytometry plays a key role in the diagnosis of lymphoproliferative disorders (LPD). Various flow labs across the UK provide immunophenotyping reports on blood and bone marrow samples for suspected LPD, however there is no UK based general consensus for the mandatory and recommended cell markers required for diagnosis. A Delphi technique is a well-established approach to answering a research question through the identification of a consensus view across experts [1]. It allows for reflection among participants, who are reconsider their opinion based on the anonymised opinions of others and utilises the knowledge and expertise of its practitioners [1].

AIM

To assess the degree of consensus in the composition of Lymphoproliferative Disease (LPD) panels amongst flow cytometry laboratories in the UK.

METHOD

An online questionnaire was sent to 17 UK laboratories to obtain information on the composition of B-cell and T-cell LPD panels. A 2-stage Delphi poll was then conducted to convert individual opinion into a group consensus. The Delphi expert panel experts consisted of haematologists and scientists specialising in immunophenotyping of haematological disorders and represented all 17 laboratories. In the first stage a list of LPD cell markers from the questionnaire, was rated for utility by the panel. To be classified as a mandatory cell marker for an LPD panel, 75% Delphi experts must have voted it as mandatory. To be classified as recommended for subtyping, 70% Delphi experts voted it as mandatory and/or recommended for subtyping. Using these results, consensus for mandatory and recommended markers was further assessed by a second stage Delphi poll.

RESULTS

Most of the laboratories (14 of 17) used a screening tube when processing a suspected LPD sample. From the questionnaire, 32 B-cell LPD markers were used by 1 or more of the 17 laboratories for screening and/or LPD panels. Experts were asked to comment on the utility of 6 cell markers used by 5-7 flow labs; CD305, CD27, CD81, CD49d, CD123 (Table 1). There were 7 cell markers classified as mandatory for a B-cell LPD Panel; CD45, CD19, CD20, surface kappa, surface lambda, CD5 and CD10 with 100% consensus for CD45, CD19, CD20, kappa, lambda and CD5. A further 10 cell markers were classified as recommended for B-LPD subtyping; CD79b, CD23, CD200, CD38, CD103, CD11c, CD25, CD123, CD43, CD22 with 100% consensus reached for CD79b, CD23 and CD200. (Table 2).

With regards to T cell LPD markers, 31 markers were in use by the 17 laboratories. Experts were asked to comment on the utility of 3 cell markers used by 5-7 flow labs; CD11c, CD103, CD30 (Table 3). Of these, 6 were classified as mandatory for a T-LPD Panel; CD45, CD2, CD3, CD4, CD7 and CD8. 100% consensus was reached that CD45, CD3, CD4, CD7 and CD8 should be included in the T-LPD Panel. Ten further cell markers were classified as recommended (for T-LPD subtyping; CD5, CD56, CD16, TCR-AB, TCR-GD, CD25, CD10, CD30, TRBC1, CD57, CD26 with a 100% consensus reached for CD5 and CD56. (Table 4).

REFERENCES

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- Nasa P, Jain R, Juneja D. Delphi methodology in healthcare research: How to decide its appropriateness. World Journal of Methodology 2021;11(4):116-29.

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RESULTS

Cell Marker	Expert Comments
CD305	' One of the best general markers for separating non chronic lymphocytic leukaemia (CLL) LPD from normal B-cells'
CD27	' For differentiating hairy cell leukaemia (HCL) from HCL variant'
CD81	' Used for CLL Minimal residual disease (MRD)'
CD49d	'Prognosis in CLL'
CD123	' Used for HCL'

Table 1: Expert comments for B-cell markers used infrequently in panels

Cell Markers	CATEGORY BY 1 ST STAGE VOTING (PROCEEDED TO 2 ND STAGE)	2 ND STAGE	
		MANDATORY	RECOMMENDED
CD45	MANDATORY	100%	
CD19	MANDATORY	100%	
CD20	MANDATORY	100%	
KAPPA	MANDATORY	100%	
LAMBDA	MANDATORY	100%	
CD5	MANDATORY	100%	
CD10	MANDATORY	94%	
CD79B	RECOMMENDED		100%
CD23	RECOMMENDED		100%
CD200	RECOMMENDED		100%
CD103	RECOMMENDED		94%
CD11C	RECOMMENDED		94%
CD25	RECOMMENDED		94%
CD43	RECOMMENDED		94%
CD22	RECOMMENDED		88%
CD38	RECOMMENDED		81%
CD123	RECOMMENDED		75%

Table 2: Delphi poll for B-cell markers

Cell Markers	CATEGORY BY 1 ST STAGE VOTING (PROCEEDED TO 2 ND STAGE)	2 ND STAGE	
		MANDATORY	RECOMMENDED
CD45	MANDATORY	100%	
CD3	MANDATORY	100%	
CD4	MANDATORY	100%	
CD8	MANDATORY	100%	
CD7	MANDATORY	100%	
CD2	MANDATORY	94%	
CD5	RECOMMENDED		100%
CD56	RECOMMENDED		100%
CD16	RECOMMENDED		94%
CD57	RECOMMENDED		94%
CD25	RECOMMENDED		88%
CD26	RECOMMENDED		88%
TCR-GD	RECOMMENDED		87%
TCR-AB	RECOMMENDED		86%
CD10	RECOMMENDED		81%
TRBC1	RECOMMENDED		80%
CD30	RECOMMENDED		75%

Table 4: Delphi poll for T-cell markers

CONCLUSIONS

This Delphi study provides a valuable insight into the composition of LPD Panels used across UK flow cytometry laboratories and consensus for core/recommended markers. The cell marker TRBC1 was deemed particularly useful with some laboratories commenting that it should be included in the screening tube and is essential and cost saving for detecting clonality of immunophenotypically distinct T-cell populations.

