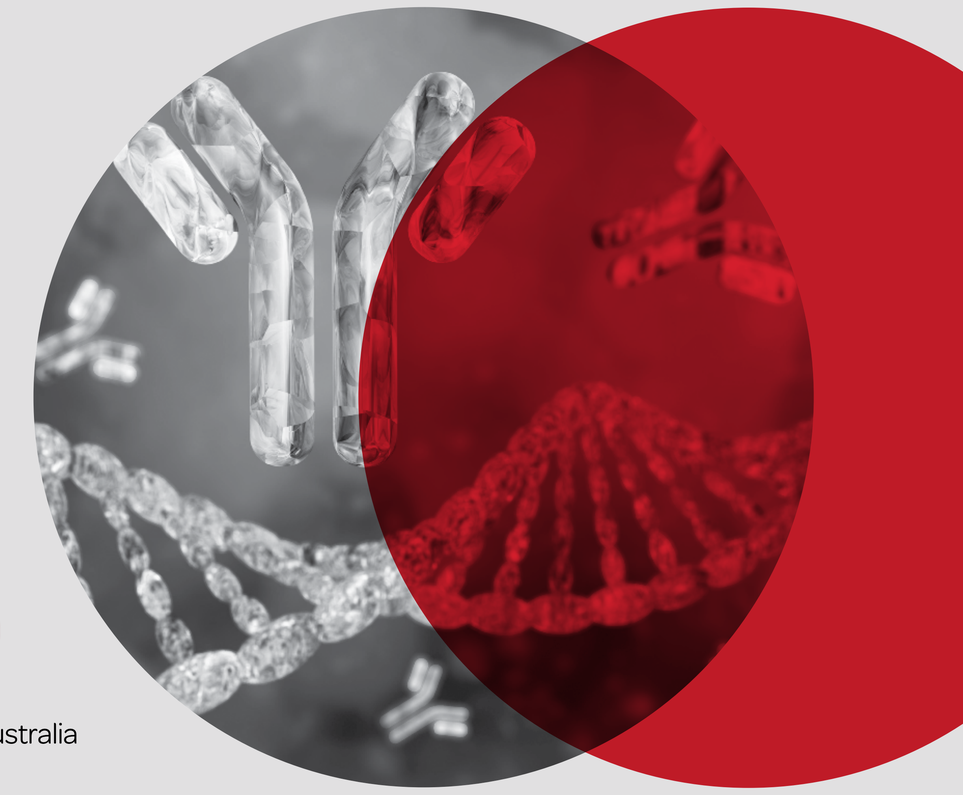
Evaluation of method discordance in a double-stranded DNA antibody external quality assurance program



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Introduction

Systemic lupus erythematosus (SLE) is characterised by the presence of elevated antibodies to double stranded DNA (dsDNA) in the serum of patients (Isenberg, 2007). Anti-dsDNA antibodies are also a laboratory criterion in the classification of SLE.

Multiple studies have demonstrated a decline of anti-dsDNA antibodies following treatment (Fu, 2015), leading to its widespread use as a marker for the diagnosis and monitoring of SLE.

However, this practice has been called into question over recent years due to the lack of a pathological mechanism and because not all anti-dsDNA antibody isotypes are pathogenic (Isenberg, 2007).

Aim

Correlate the results of anti-dsDNA antibodies assays submitted to the Royal College of Pathologists of Australasia Quality Assurance Program (RCPAQAP) with the immunosuppressive regimes of the donors at the time of collection.

Methods

Survey material for RCPAQAP's anti-dsDNA antibodies external QAP program were derived from single source patient donations. If possible, clinical history and treatment information were recorded at the time of collection.

Aliquots were provided to participating laboratories who tested for the presence of anti-dsDNA antibodies using a variety of assays (*Crithidia luciliae* immunofluorescence, enzyme-linked immunoassays, radio-immunoassays).

The presence of anti-dsDNA antibodies (Positive/Negative) was defined by 80% consensus reporting by participants.

Data submitted between 2017-2021 were collated and correlated with the presence and type of immunosuppression of the donor at the approximate time of sample collection.

Results and Discussion

For the 40 surveys reviewed between 2017–2021:

- consensus reporting for the presence of anti-dsDNA antibodies (Positive/Negative) was observed in 25 (63%) surveys (Table 1).
- variable qualitative reporting was observed both within and between method groups. This was even noted in 4/25 (16%) surveys where a consensus result was found, suggesting differences in assay specificity and/or sensitivity.
- donor history was available for 33/40 (83%) surveys (Table 1).

Of the 33 surveys with donor history available:

- 15 (45%) had no consensus in qualitative reporting (Positive, Negative) for the presence of anti-dsDNA antibodies.
- the majority of surveys with non-consensus results were derived from patients on active treatment (14/15, 93%). Of these, nine donors (64%) were on combination therapy and six (43%) were on a single agent at the time of sample collection.
- immunosuppressive therapy was less frequent in surveys with consensus qualitative reporting with 10/18 (56%) surveys obtained from donors undergoing treatment. Of these, nine (90%) were from donors on combination therapy, and one (10%) on a single agent.

Conclusion

Our preliminary data indicates that anti-dsDNA assay performance and subsequent qualitative reporting of these antibodies, will vary in the presence of patient treatment. This suggests that while anti-dsDNA antibodies testing may be useful for SLE diagnosis when the clinical presentation is suggestive of disease, the clinical utility of long-term disease monitoring may be limited once a patient has been treated.

Table 1. Summary of RCPAQAP samples for each year (2017-2021) including current immunosuppression at the time of collection and consensus reporting for presence of anti-dsDNA antibodies.

✓ Indicates ≥80% consensus in qualitative reporting of anti-dsDNA antibodies
× Indicates <80% consensus in qualitative reporting of anti-dsDNA antibodies
Greyed out indicates no donor history available.

Year	Survey	Immunosuppression	Anti-dsDNA Antibody Reporting Consensus
2021	1	Nil	✓
	2	Prednisone, Mycophenolate	×
	3	Nil	✓
	4	Nil	✓
	5	Nil	✓
	6	Prednisone, Mycophenolate	×
	7	Nil	✓
	8	Prednisone	×
2020	1	Prednisone, Mycophenolate	×
	2	Mycophenolate	×
	3	Prednisone, Mycophenolate	✓
	4	Mycophenolate	×
	5	Prednisone, Mycophenolate	×
	6	Nil	×
	7	Not available	✓
	8	Not available	✓
2019	1	Prednisone	✓
	2	Mycophenolate	×
	3	Prednisone	✓
	4	Nil	×
	5	Prednisone, Mycophenolate	×
	6	Prednisone	×
	7	Nil	×
	8	Prednisone, Mycophenolate	×
2018	1	Prednisone, Mycophenolate	✓
	2	Nil	×
	3	Prednisone, Mycophenolate	✓
	4	Prednisone, Mycophenolate	✓
	5	Nil	✓
	6	Nil	✓
	7	Prednisone	✓
	8	Prednisone, Mycophenolate	✓
2017	1	Not available	✓
	2	Not available	✓
	3	Not available	✓
	4	Prednisone	✓
	5	Prednisone, Mycophenolate	✓
	6	Not available	✓
	7	Prednisone, Mycophenolate	✓
	8	Not available	✓

References:

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Fu SM, Dai C, Zhao Z, Gaskin F, Anti-dsDNA antibodies are one of the many autoantibodies in systemic lupus erythematosus. *F1000 Research* 2015;4;939.
Isenberg DA, Mason JJ, Ehrenstein MR, Rahman A, Fifty years of anti-dsDNA antibodies: are we approaching journey's end? *Rheumatology*, 2007;46(7) 1052-1056.

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