A comparison of clinical expert to software analysis of T-cell receptor gamma gene rearrangement capillary electrophoresis datasets

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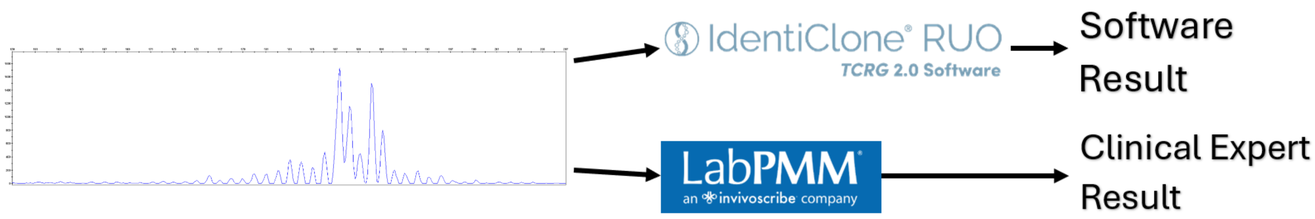
INTRODUCTION

The detection of clonal T-cell populations is key to the diagnosis of suspected T-cell lymphoproliferative disorders. Polymerase chain reaction (PCR) based assays followed by fragment analysis using capillary electrophoresis are frequently used for the detection of clonal T-cell populations. Analysis of capillary electrophoresis datasets involves expert interpretation that is subjective and time consuming. The IdentiClone® RUO *TCRG* 2.0 Software provides a research tool to quickly and objectively determine clonality status of capillary electrophoresis data. The IdentiClone® RUO *TCRG* 2.0 Software is for Research Use Only (RUO) and is not intended for medical diagnostic purposes.

METHOD

A capillary electrophoresis dataset from 68 (42 positive, 26 negative) de-identified Formalin-Fixed Paraffin-Embedded (FFPE) specimens was generated using the Invivoscribe® T-Cell Receptor Gamma Gene Rearrangement Assay 2.0 (*TCRG* 2.0). The *TCRG* 2.0 results were analyzed by a clinical expert and the IdentiClone® RUO *TCRG* 2.0 Software. Clinical expert results and Software results were both compared to medical diagnosis and next-generation sequencing (NGS) results (LymphoTrack® *TRG* Assay) for concordance. Clinical expert and Software results were then compared to each other.



CONCORDANCE TO REFERENCE METHODS

SOFTWARE

IdentiClone RUO *TCRG* 2.0 Software	Medical Diagnosis	
	Positive	Negative
Positive	37	0
Negative	5	26
Total	42	26
Positive Percent Agreement	88.1% (95% CI: 74.4% - 96.0%)	
Negative Percent Agreement	100.0% (95% CI: 86.8% - 100.0%)	

IdentiClone RUO *TCRG* 2.0 Software	NGS Method	
	Positive	Negative
Positive	36	1
Negative	4	27
Total	40	28
Positive Percent Agreement	90.0% (95% CI: 76.3% - 97.2%)	
Negative Percent Agreement	96.4% (95% CI: 81.7% - 99.9%)	

CLINICAL EXPERT

Clinical Expert	Medical Diagnosis	
	Positive	Negative
Positive	36	1
Negative	6	25
Total	42	26
Positive Percent Agreement	85.7% (95% CI: 71.5% - 94.6%)	
Negative Percent Agreement	96.2% (95% CI: 80.4% - 99.9%)	

Clinical Expert	NGS Method	
	Positive	Negative
Positive	36	1
Negative	4	27
Total	40	28
Positive Percent Agreement	90.0% (95% CI: 76.3% - 97.2%)	
Negative Percent Agreement	96.4% (95% CI: 81.7% - 99.9%)	

Both the Software and Clinical Expert achieve greater than 85% Positive Percent Agreement (PPA) and 96% and Negative Percent Agreement (NPA) when using Medical Diagnosis or NGS as the reference method. The Software achieved a better PPA and NPA compared to Clinical Expert when using medical diagnosis as the reference method.

CLINICAL EXPERT TO SOFTWARE COMPARISON

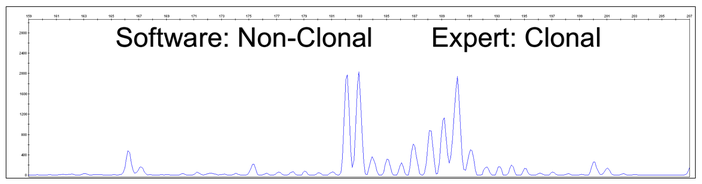
IdentiClone RUO *TCRG* 2.0 Software	Clinical Expert	
	Positive	Negative
Positive	34	3
Negative	3	28
Total	37	31
Positive Percent Agreement	91.9% (95% CI: 78.1% - 98.3%)	
Negative Percent Agreement	90.3% (95% CI: 74.2% - 98.0%)	

CONCLUSIONS

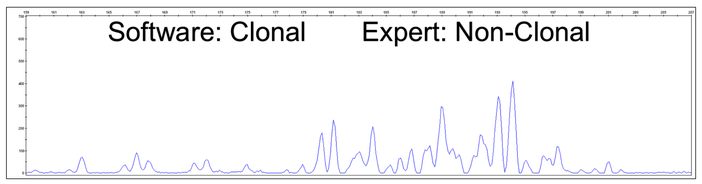
- The clinical expert achieved a PPA of 85.7% and NPA of 96.2% to diagnosis. The Software achieved a PPA of 88.1% and NPA of 100.0% to diagnosis.
- The clinical expert achieved a PPA of 90.0% and NPA of 96.4% to NGS. The Software achieved a PPA of 90.0% and NPA of 96.4% to NGS.
- When comparing Software results to clinical expert results, a PPA of 91.9% and NPA of 90.3% was achieved.
- Of the 6 discordant calls between Software and the clinical expert, 4 Software calls correctly matched the medical diagnosis.
- The Software removes subjectivity involved in human analysis and significantly decreases analysis turnaround time from hours to seconds.
- The IdentiClone® RUO *TCRG* 2.0 Software is for Research Use Only (RUO) and is not intended for medical diagnostic purposes.

DISCORDANT ELECTROPHEROGRAMS – SOFTWARE VS CLINICAL EXPERT

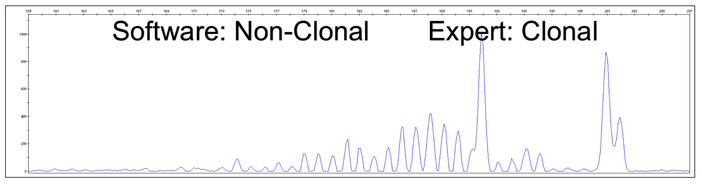
(CLONAL : POSITIVE, NON-CLONAL : NEGATIVE)



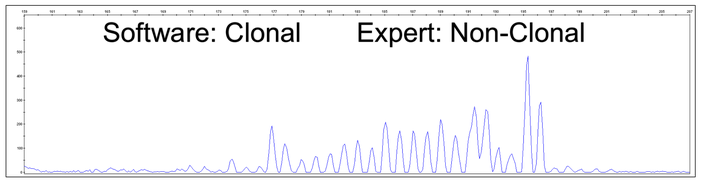
Medical Diagnosis: Positive



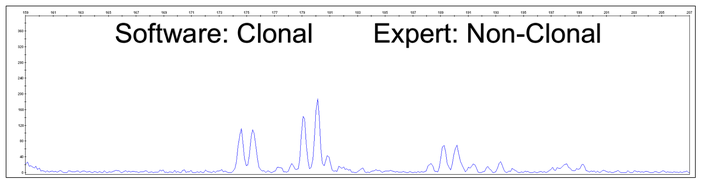
Medical Diagnosis: Positive



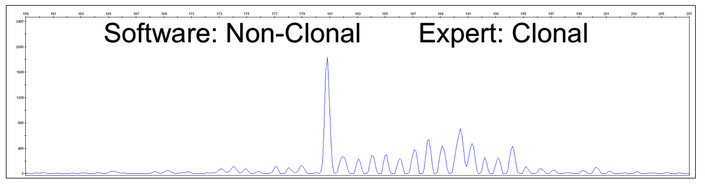
Medical Diagnosis: Positive



Medical Diagnosis: Positive



Medical Diagnosis: Positive



Medical Diagnosis: Negative