WHITEPAPER

Reliable Rheumatoid Arthritis Diagnosis Validated through WHO ACPA Controls

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Human
Diagnostics Worldwide

Summary

Rheumatoid arthritis (RA) is a chronic autoimmune disease characterized by inflammation and joint damage. It is not just a disease of the joints—it is a systemic autoimmune disorder that, if left undiagnosed or untreated, can lead to severe disability, cardiovascular complications, and reduced life expectancy.

Early and precise diagnosis is a game-changer in RA management, enabling timely intervention and better long-term treatment outcomes. In this regard, ACPA are closely linked to RA and may play a key role in its pathogenesis, acting as a trigger that sustains the disease's chronic nature.

Specific ACPA Profiling with IMTEC-Arthritis-LIA Enhances Diagnostic Accuracy in RA

To ensure timely and accurate diagnosis of rheumatoid arthritis (RA), the integration of multiple serological parameters is essential. Among these, Anti-Citrullinated Protein Antibodies (ACPAs) stand out as highly specific markers and are now part of the American College of Rheumatology (ACR) classification criteria for RA. Their presence often precedes clinical symptoms, making them valuable tools for early diagnosis and intervention.

Figure 1 illustrates the clinical relevance of ACPA testing and highlights the capability of the IMTEC-Arthritis-LIA assay to detect specific ACPA targets through the CP4 peptide series—offering improved diagnostic precision and differentiation within autoimmune profiling.

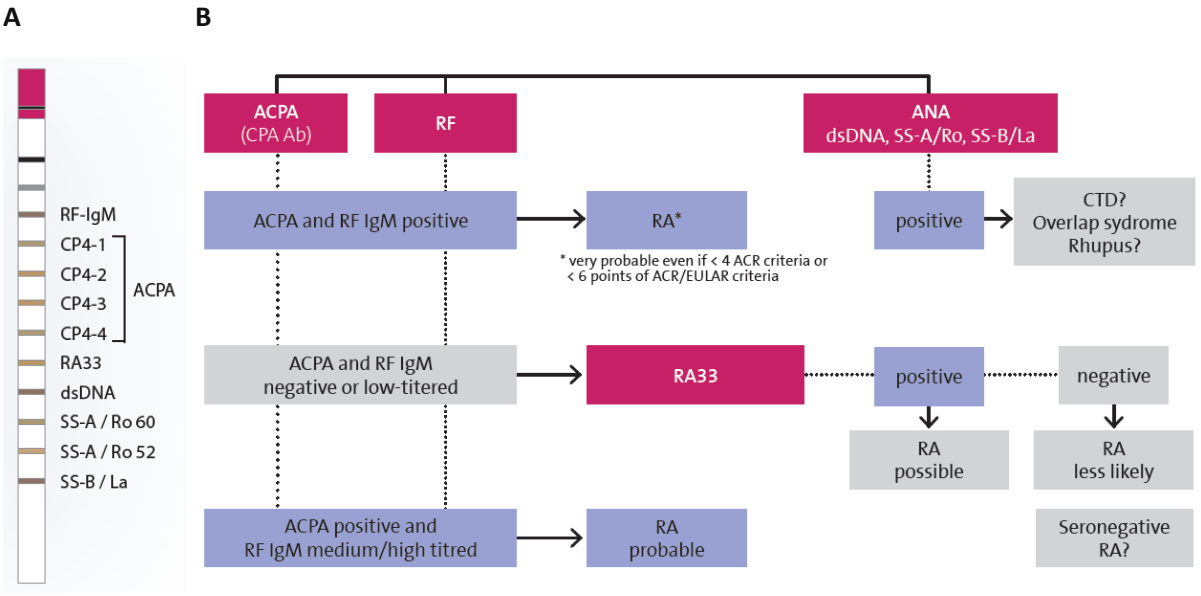

Figure 1: (A) ACPA antibodies, part of the ACR criteria for RA, are widely used in clinical practice (top left). **(B)** IMTEC-Arthritis-LIA enables specific ACPA detection with four selected CP4 peptides. The other parameters identifiable by IMTEC Arthritis-LIA are highlighted in red (adapted from 4)

The Role of ACPA and CP4 Peptide Profiling

To ensure timely and accurate diagnosis multiple parameters can be used for aid in diagnosis. ACPAs testing has long been a cornerstone in RA diagnosis (2) (Figure 1). ACPA can recognize different citrullinated antigens, which trigger that ignites the RA (Figure 2). In this regard, autoreactive T cells stimulate B cells to produce ACPA. Dendritic cells present peptides via HLA class II, activating T cells, which in turn promote B cell activation (Figure 2).

The CP4 series (citrullinated peptides; CP4-1, CP4-2, CP4-3, CP4-4) on IMTEC Arthritis LIA (Figure1) are recognized targets of ACPAs, which are specific markers for rheumatoid arthritis and play a pivotal role in its pathogenesis. The CP4 series on Human Arthritis LIA offers additional benefits aiding in terms of specificity, early detection, differentiation from other conditions and disease severity assessment. Utilizing these specific peptides can enhance diagnostic accuracy and improve patient outcomes through more tailored and timely interventions.

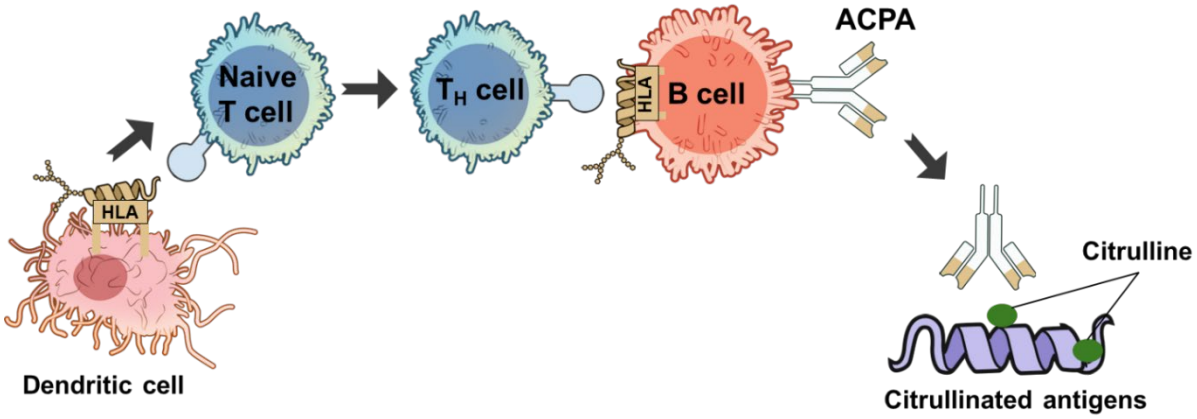

Figure 2: ACPA targets diverse citrullinated antigens. Dendritic cells activate T cells via HLA II, which then stimulate B cells to produce ACPA (adapted from 1).

Conclusion and outlook

Recently, inclusion of available WHO ACPA standard controls (3) as part of HUMAN quality improvement process, ensured that the CP4 series in the HUMAN LIA test functions optimally, confirming the detection and reliability of CP4 antigens.

WHO ACPA controls played a dual role here: they ensure the overall accuracy of detecting ACPAs while specifically validating the performance of the CP4 antigens within the Arthritis LIA. This approach may enhance arthritis diagnostics and support improved patient care worldwide.

References

1. Willemze, A., et al. (2012). The influence of ACPA status and characteristics on the course of RA. Nature Reviews Rheumatology, 8(3), 144–152. https://doi.org/10.1038/nrrheum.2011.204

2. Aletaha, D., Neogi, T., Silman, A. J., Funovits, J., Felson, D. T., Bingham, C. O. 3rd, Birnbaum, N. S., Burmester, G. R., Bykerk, V. P., Cohen, M. D., Combe, B., Costenbader, K. H., Dougados, M., Emery, P., Ferraccioli, G., Hazes, J. M., Hobbs, K., Huizinga, T. W., Kavanaugh, A., ... Hawker, G. (2010). 2010 rheumatoid arthritis classification criteria: An American College of Rheumatology/European League Against Rheumatism collaborative initiative. Annals of the Rheumatic Diseases, 69(9), 1580–1588. https://doi.org/10.1136/ard.2010.138461

3. World Health Organization. (2023). Proposed first WHO international standard for anti-citrullinated peptide antibodies (ACPA). WHO ECBS Document, 1, 1–24.

4. Conrad, K., et al. (2015). Autoantibodies in systemic autoimmune diseases – A diagnostic reference (Vol. 2, 3rd ed.). Pabst Science Publishers.

About HUMAN

Founded in 1972, HUMAN has been one of the global players in the IVD industry for more than 50 years.

Its broad and steadily growing portfolio ranges from classical clinical chemistry to innovative molecular diagnostic methods as well as special applications like assays for autoimmunity testing. With its worldwide service and delivery capacities and a broad network of long-standing distributors, HUMAN supports medical laboratories in over 160 countries and is a recognized partner to numerous governmental and non-governmental organizations.

HUMAN has its headquarters in Wiesbaden, Germany, and maintains regional sales offices in the United Arab Emirates, Singapore, China, India, Panama. It has local HUMAN representatives in many other countries.

Sustainability is a particular concern for HUMAN as a responsible and future-oriented company. A certified environmental management system has been established that meets the requirements of the international ISO 14001 standard and the European EMAS directive.