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ORIGINAL ARTICLE

Reinventing immunological test Interpretation through Artificial Intelligence

Réinventer l'interprétation des bilans immunologiques par l'intelligence artificielle

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MOTS CLÉS

Intelligence artificielle ;

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Cytométrie en flux ;

Maladies auto-immunes

Résumé

Introduction : L'interprétation des bilans immunologiques est devenue plus complexe avec la diversification des techniques et l'augmentation des données biologiques à intégrer au contexte clinique.

Méthodes : Cette mise au point narrative repose sur une recherche bibliographique réalisée principalement dans PubMed, en privilégiant les publications de 2022 à 2025 sur l'intelligence artificielle appliquée à l'immunologie clinique.

Résultats : Les données récentes montrent que l'intelligence artificielle peut améliorer la lecture de l'immunofluorescence, l'analyse de la cytométrie en flux et l'identification de signatures immunologiques complexes.

Conclusion : L'intelligence artificielle constitue un outil prometteur d'aide à l'interprétation, mais son intégration nécessite une validation rigoureuse et une utilisation complémentaire de l'expertise clinique et biologique.

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KEYWORDS

Artificial intelligence;

Clinical immunology;

Flow cytometry;

Autoimmune diseases

Abstract

Introduction: The interpretation of immunological testing has become more complex because of the diversification of techniques and the increasing amount of laboratory data that must be integrated with clinical information.

Methods: This narrative review was based on a literature search conducted mainly through PubMed, with priority given to studies published between 2022 and 2025 on artificial intelligence in clinical immunology.

Results: Recent evidence suggests that artificial intelligence can improve immunofluorescence reading, flow cytometry analysis, and the identification of complex immunological signatures.

Conclusion: Artificial intelligence is a promising support tool for interpretation, but its implementation requires rigorous validation and use in combination with clinical and laboratory expertise.

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Introduction

Clinical immunology occupies a central position in contemporary medicine, at the intersection of laboratory medicine, pathophysiology, and clinical reasoning. Immunological testing is no longer limited to a few isolated assays; it now encompasses a broad range of investigations exploring humoral and cellular immunity, autoantibodies, complement, selected lymphocyte populations, soluble inflammatory mediators, and, increasingly, signatures derived from multiplex platforms. This growing informational density enhances the value of the laboratory, but it also increases the difficulty of interpretation, especially when abnormalities are partial, fluctuating, or only weakly specific [1].

In this context, artificial intelligence may be defined as the set of methods capable of learning from data in order to identify patterns, classify signals, or generate decision support. In practice, the tools most commonly used in immunology are supervised machine learning, deep learning applied to images, clustering approaches, and models capable of integrating several layers of information. Their value becomes particularly evident when conventional analysis reaches its limits in the face of large data volumes or complex biological relationships [2].

Autoimmune and systemic inflammatory diseases represent a particularly relevant field for such approaches. Their diagnosis rarely relies on a single marker; rather, it depends on a combination of clinical, immunological, temporal, and sometimes morphological data. Within this framework, artificial intelligence offers the possibility of recognizing global profiles, whereas classical reasoning often proceeds sequentially, one test at a time. This evolution does not eliminate medical judgment, but it changes the way available information is processed and interpreted [3].

A first highly concrete field of application concerns the reading of antinuclear antibodies by indirect immunofluorescence on HEP-2 cells. This test remains a reference standard in the screening of connective tissue diseases, but it remains exposed to significant inter-observer variability despite international harmonization efforts. The International Consensus on ANA Patterns has provided valuable standardization of nomenclature and patterns, yet expert reading remains crucial, particularly in mixed or weakly positive profiles [4].

Flow cytometry constitutes a second domain that is especially well suited to artificial intelligence.

It enables very fine multiparametric analysis of cell populations, but it generates complex data that are difficult to process rapidly and consistently through strictly manual interpretation.

In this setting, artificial intelligence appears not only as a tool for automation, but also as a lever for standardization and optimization of the analytical workflow [5].

Finally, the development of multiplex assays, cytokine signatures, and multi-omics approaches is driving immunology toward a precision-based paradigm. In this perspective, the added value of artificial intelligence lies not only in automation, but also in its ability to connect multiple layers of information and to bring out integrated immunological profiles that may be more useful for diagnosis, stratification, and follow-up [6].

The aim of this review is to examine current applications of artificial intelligence in the interpretation of immunological testing, to detail its practical contributions, to discuss its limitations, and to analyze innovations as well as short- and medium-term development prospects.

Methods

We conducted a narrative review focusing on artificial intelligence applied to the interpretation of immunological testing. The bibliographic search was performed mainly in PubMed, then complemented by targeted analysis of relevant references identified in the selected articles.

The search strategy prioritized publications from 2022 to 2025, while allowing occasional inclusion of earlier works when their methodological or conceptual value justified their presence in the analysis.

The keywords used, alone or in Boolean combinations, included: artificial intelligence, machine learning, clinical immunology, autoimmune diseases, antinuclear antibodies, indirect immunofluorescence, flow cytometry, cytokines, clinical laboratory, explainability, validation, and decision support.

Priority was given to original articles, narrative reviews, methodological reviews, validation studies, and governance-oriented works addressing assisted interpretation of autoantibodies, artificial intelligence applied to flow cytometry, identification of cytokine signatures, diagnostic support in autoimmune

diseases, and the conditions required for responsible integration of these tools into clinical practice.

Publications that were off-topic, redundant, insufficiently documented, or too distant from clinical immunology were excluded.

The final analysis was organized according to a thematic framework in order to provide a coherent synthesis of the available data.

Results

1. General contributions of artificial intelligence in clinical immunology

Recent evidence shows that artificial intelligence contributes to clinical immunology at three main levels: automation of repetitive tasks, identification of complex patterns, and integration of heterogeneous variables. This triple function is especially useful in a discipline in which the relevant signal is not always carried by a single test, but rather by a combination of biological and clinical parameters. In other words, artificial intelligence tends to shift analysis from a “test-by-test” logic toward a “profile-by-profile” logic [7].

This evolution does not mean that artificial intelligence replaces conventional laboratory practice. Rather, it acts as an additional layer of data exploitation. The more numerous, multidimensional, and interdependent the results become, the more relevant the use of learning-based tools becomes. The laboratory medicine literature nevertheless emphasizes that reported performances remain closely dependent on the quality of databases, signal preprocessing, and preanalytical and analytical standardization [8].

2. Assisted reading of antinuclear antibodies

The detection of antinuclear antibodies by indirect immunofluorescence is not a simple binary test. It requires morphological interpretation based on the pattern, intensity, sometimes the titer, and their consistency with the clinical context. This richness makes it a highly suitable field for image-based artificial intelligence approaches. The existence of a harmonized language through the international pattern consensus constitutes a major advantage for model training [4].

A recent pilot study compared conventional visual reading with reading assisted by an artificial intelligence system in a routine setting. The authors demonstrated good concordance for the distinction between positive and negative results, as well as promising performance for recognition of the most frequent patterns. Discordances persisted mainly in mixed or weakly intense profiles, suggesting that artificial intelligence is

already useful for pre-screening, but that it does not yet eliminate the need for expert validation [9].

Other studies have shown that artificial intelligence applications, when compared with commercial systems, may achieve useful performance for classification of selected immunofluorescence images.

These results open the door to more diversified solutions, including in lower-resource environments, provided that local validation is rigorous and that users maintain a critical view of algorithmic outputs [10].

3. Antineutrophil cytoplasmic antibodies

Antineutrophil cytoplasmic antibodies play an important role in the investigation of vasculitides associated with these autoantibodies.

Their interpretation by indirect immunofluorescence may be more challenging than that of antinuclear antibodies in some situations, particularly when signals are weak, atypical, or technically suboptimal.

Although the literature is less abundant, the same methodological principles apply: artificial intelligence may help segment the image, standardize initial classification, and reduce part of the human variability [2].

4. Artificial intelligence and flow cytometry

Flow cytometry allows multiparametric analysis of individual cells and is a key tool in immunodeficiency, immune dysregulation, certain hematologic disorders, and complex inflammatory contexts. Its main challenge is not the lack of data, but rather their abundance. Even when highly mastered, the succession of manual gating steps remains time-consuming, operator-dependent, and sometimes variable from one laboratory to another [5].

A clinical validation study published in 2024 developed an artificial intelligence-assisted flow cytometry workflow applied to immunological disorders. The model showed strong correlation with reference manual analysis for several lymphocyte subpopulations, with coefficients above 0.9, while significantly reducing processing time. This type of result suggests that artificial intelligence may already provide tangible routine benefits, especially in settings with a high analytical workload [11].

Recent syntheses in this field nevertheless stress an important point: artificial intelligence in flow cytometry should not be reduced to a final classifier.

It may also contribute to instrument standardization, panel design, quality control, artifact management, and sharing of analytical expertise.

In practice, it is therefore increasingly part of a complete analytical chain rather than a simple end-stage automation tool [12].

5. Cytokine signatures and integrated immunological profiles

Cytokines are central mediators of immune communication. Their isolated measurement is often of limited practical value because of considerable variability and sometimes low specificity.

By contrast, joint analysis of several cytokines or inflammatory proteins may reveal signatures that are more informative than the assessment of each marker separately. Artificial intelligence is particularly well suited to this type of integrated reading [6].

A recent study identified a five-protein signature capable of distinguishing several systemic inflammatory diseases with encouraging performance. This type of result illustrates the transition from analytical immunology to profile-based immunology, in which diagnostic value depends less on the isolated value of a biomarker than on the coherence of a set of signals [13].

In lupus and other systemic diseases, machine learning-based studies have also highlighted cytokine signatures associated with disease severity and with certain autoantibody profiles. Although these findings remain exploratory for some applications, they reinforce the idea that artificial intelligence may help better structure the biological heterogeneity of autoimmune diseases [14].

6. Routine laboratory data and explainable models

A recent trend has been to train models not only on specialized investigations, but also on routine laboratory data combined with other clinical variables.

The goal is not to provide an autonomous diagnostic truth, but rather calibrated probabilities or orientations consistent with real clinical logic.

This approach is particularly relevant in rheumatologic and autoimmune diseases, where biological profiles partially overlap [15].

Discussion

The available evidence confirms that artificial intelligence has not yet reached the same level of maturity across all domains of clinical immunology. It already appears credible in repetitive, well-defined, and highly standardized tasks, such as initial reading of immunofluorescence images or certain steps in flow cytometry. By contrast, its use becomes more delicate when dealing with weakly specific biological signals, incomplete clinical pictures, or models developed from monocentric datasets [8].

One of the most plausible short-term benefits is the reduction of human variability. In the reading of antinuclear antibodies, for example, artificial intelligence does not replace the expert, but it may homogenize initial triage, stabilize recognition of frequent patterns, and prioritize cases requiring specialized review. In a laboratory confronted with a high volume of analyses, this organizational benefit may be at least as important as the purely analytical gain [9].

In flow cytometry, the potential gains are even more structural. The issue is not only to move faster, but to achieve more reproducible interpretation between operators, between platforms, and ideally between centers. This, however, presupposes a robust quality infrastructure, because a model that performs well in a highly controlled environment may lose part of its value when confronted with other instruments, panels, or populations [11].

The most promising innovations probably concern integrative approaches. The future of artificial intelligence in immunology lies not only in a better algorithm for a given test, but in models capable of combining autoantibodies, flow cytometry, cytokines, routine laboratory data, clinical variables, and temporal trajectories. This evolution is part of the broader movement toward precision medicine in autoimmunity and rheumatology [3].

Several major projects and methodological developments are already underway. Continued enrichment of the ICAP framework for immunofluorescence patterns, the expansion of high-dimensional cytometry pipelines, the development of explainable models, and the gradual establishment of institutional frameworks for responsible use all show that the field is no longer confined to proof-of-concept research. It is progressively entering a phase of methodological and organizational structuring [16].

The regulatory dimension is also becoming unavoidable. The European environment has changed substantially with the Artificial Intelligence Act, whose implications for health

include risk classification, traceability, documentation, surveillance, and accountability. For laboratory professionals, this means that adopting an algorithmic tool cannot be regarded as merely adding another software program; it must be understood as integrating a potentially critical component into the decision chain [17].

Explainability lies at the center of this evolution. In a discipline where biological results sometimes guide major diagnostic or therapeutic decisions, trust does not depend only on overall performance, but also on the ability to understand, at least partly, why an algorithmic suggestion has been produced. Recent reflections on explainable artificial intelligence in healthcare clearly show that explainability is not a conceptual luxury, but a practical condition for clinical acceptability [18].

Ongoing projects on the use of generative artificial intelligence in healthcare add a new dimension to the debate.

In the future, such tools could help structure reports, synthesize heterogeneous data, or assist in contextualizing complex immunological results. However, recent frameworks proposed for evaluating these tools emphasize that their potential benefits must always be weighed against the risks of bias, hallucinated outputs, and poor integration into medical reasoning [19].

In practice, the most credible future is therefore not one of replacing the laboratorian or clinician, but one of structured collaboration between human expertise and algorithmic tools. This vision is consistent with recommendations put forward in allergy and immunology, which emphasize the need to involve specialists in the design, validation, implementation, and continuous evaluation of these systems. In other words, artificial intelligence has value only when integrated into a culture of quality, caution, and responsibility [20].

Conclusion

Artificial intelligence currently represents a credible development in the interpretation of immunological testing. Its most advanced applications concern assisted reading of immunofluorescence assays, analysis of selected flow cytometry data, and identification of complex biological signatures.

Its main value lies in its ability to strengthen standardization, reproducibility, and integration of data that have become increasingly numerous, multidimensional, and difficult to interpret in isolation. In practice, it should be regarded as a support tool intended to assist laboratorians and clinicians rather than replace their expertise.

Future perspectives are particularly important in multimodal approaches, precision immunology, explainable systems, and models capable of integrating biology, clinical context, and longitudinal data. However, the real value of these tools will depend on data quality, external validation, model explainability, and the robustness of their governance.

Thus, the most credible future for artificial intelligence in clinical immunology is not the replacement of the expert, but a structured collaboration between human expertise and algorithmic tools.

Declaration of interests

The authors declare that they have no conflicts of interest related to this work.

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