Immunodiagnostics: today's trends shaping tomorrow's healthcare

Introduction

Since the development of the radioimmunoassay (RIA) in the 1950s, immunodiagnostic assays have been transforming healthcare – helping clinicians to achieve accurate diagnoses with unprecedented speed and simplicity.

Immunodiagnostics rely on specific binding between antigens and antibodies to detect and quantify analytes of interest. Because antibodies can be engineered to bind an immense variety of antigenic structures, immunoassays can be developed to measure almost any clinically relevant analyte, including proteins, antibodies, hormones, and pathogens.

Immunoassay techniques have developed substantially since the early days of RIAs. From enzyme-linked immunosorbent assays (ELISAs) to fluorescence spectroscopy and more, recent innovations such as multiplex assays and biosensors have enabled the development of highly sensitive and specific assays for a broad and ever-growing range of analytes.

Today, immunoassays are an indispensable resource across numerous branches of medicine, including oncology, cardiology, infectious diseases, and more. They provide a rapid, sensitive, and cost-effective means of disease detection and monitoring.

As the world of immunodiagnostics evolves, emerging technologies such as microfluidics, nanotechnology, and artificial intelligence are bringing the next generation of immunoassays. Characterized by augmented accuracy, speed, and simplicity, these advancements promise to streamline and enhance testing processes further than ever before.

In this whitepaper, we will explore the rapidly evolving landscape of immunodiagnostics that holds the potential to transform healthcare systems worldwide. Through investigating current and emerging technologies, market trends, and future prospects, we will consider the opportunities and challenges that lie ahead.

The current landscape of immunoassays

Immunodiagnostic assays are an indispensable tool for healthcare providers. Let's take a look at some of the most popular immunoassay types used in clinical diagnostics today.

ELISA: the benchmark immunoassay

The ELISA is by far the most commonly implemented immunodiagnostic method. It is the foundation on which many alternative immunoassays have been developed (1). Since breaking into the clinic, the impact of the ELISA on healthcare systems is unparalleled. From screening for infectious diseases such as HIV and hepatitis to assessing cardiac biomarkers indicative of myocardial infarction, ELISA plays a crucial role across disease detection and medical care.

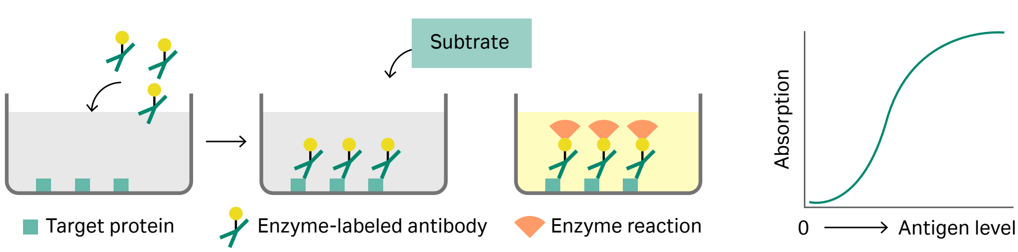

Fig 1. In a direct ELISA, immobilized antigens capture an enzyme-labeled antibody, which is detected via an enzyme-catalyzed reaction (2).

To detect and quantify antigen-antibody interactions, ELISAs rely on the catalytic activity of enzymes (Fig 1). A main advantage of ELISAs is their sensitivity, which allows for the detection of complex biological analytes, even at minute concentrations.

Various ELISA formats have been developed, including direct, indirect, sandwich, and competitive ELISA, which vary in terms of antigens, antibodies, substrates, and experimental conditions. These formats have helped to broaden their uses and applications, including diagnosing infectious diseases, allergy profiling, and monitoring biomarkers for chronic conditions. Also, the ability to miniaturize and automate ELISAs makes the technique well-suited for high-throughput screening, providing a rapid and cost-effective means of analyzing large groups of people (3).

Traditional ELISA limitations

Despite its widespread adoption and valuable advantages, the ELISA is not without its limitations. One of its biggest drawbacks is its susceptibility to nonspecific binding, which can lead to a high background signal that compromises assay specificity and accuracy (4). Additionally, the antigen-antibody reaction requires a long incubation period, with diagnostic results generally provided in 4 to 6 hours.

Recent advancements in immunodiagnostics aim to address these time and specificity challenges, and further enhance the sensitivity of immunoassays. These advances include the development of immunoassay variants, including chemiluminescent and fluorescence immunoassays, along with the integration of nanotechnology and surface-enhanced Raman spectroscopy.

Learn more about the benchmark ELISA immunoassay

Enhancing sensitivity with chemiluminescent immunoassays

Chemiluminescent immunoassays (CLIAs) are a highly sensitive and versatile alternative to the ELISA. There are several different types of CLIAs, including those that use luminophore markers (direct chemiluminescence methods) and those that use an enzyme-catalyzed process such as horseradish peroxidase/luminol oxidation (indirect chemiluminescence methods) (5).

Opting for a luminescent signal makes CLIAs less susceptible to background interference, with an enhanced signal-to-noise ratio that boosts assay specificity. CLIAs can also detect analytes at trace-level concentrations, which is particularly advantageous for identifying biomarkers associated with early-stage diseases or monitoring disease progression (6).

Additionally, CLIAs offer rapid assay kinetics, reducing incubation times and accelerating time-to-result compared to ELISA, helping to enhance workflow efficiency in clinical labs. The technique is also well-suited for high-throughput analysis, supporting large-scale studies and screening campaigns (7).

In clinical practice, CLIAs find utility across a broad spectrum of diagnostic applications, from cancer to fertility biomarker detection, endocrinological conditions, autoimmune disorders, and more.

Easy multiplexing with fluorescent immunoassays

Fluorescence immunoassays (FIAs) are another popular class of immunodiagnostics. In FIAs, detection occurs using fluorophore-labeled antibodies or antigens. Like CLIAs, FIAs offer reduced background noise and enable the highly specific and sensitive detection of numerous biomarkers, pathogens, drugs, and more (8).

The evolution of fluorescent labeling techniques along with advancements in analytical technologies has given rise to a diverse array of FIA diagnostic protocols. These new-and-improved FIAs incorporate novel fluorescent compounds and sophisticated detection systems that enable higher resolution, greater sensitivity, and the capacity for multiplexing (9,10).

By using fluorophores that emit at different excitation wavelengths, multiplex FIAs can simultaneously quantify multiple analytes within a single sample. Multiplexing enhances efficiency, saving time and resources while requiring minimal sample volumes. The multiplexing capabilities of FIAs make them well-suited for applications where multiple markers need to be detected such as in screening for drugs of abuse (11).

Latest innovations in immunodiagnostics

Immunodiagnostics is constantly evolving to incorporate new technologies and materials, helping to enhance the sensitivity, specificity, and efficiency of diagnostic assays, and expand their applications to address unmet clinical needs. These innovations include nanotechnology, microfluidic chips, and surface-enhanced Raman spectroscopy.

Nanotechnology

Nanotechnology is a game-changer for immunodiagnostics. It integrates nanoparticles containing unique optical, electronic, or magnetic properties to improve assay performance.

When integrated into immunoassays, nanotechnology offers high-throughput biosensing with high sensitivity and specificity, allowing for the detection of targets at lower concentrations than ever before. As a result, advances in immunodiagnostic nanotechnology are facilitating earlier disease detection and improved disease monitoring (12,13).

To date, nanotechnology used in immunodiagnostic tests includes gold nanoparticles, which can be harnessed to enhance the visual detection of assay results, and quantum dots, which offer sharp, stable fluorescence signals for FIAs.

Streamlining immunoassays with magnetic beads

Magnetic beads, or magbeads, are a type of nanotechnology that can address many challenges associated with conventional immunoassays like ELISAs and CLIAs. Magbeads are particles of iron oxides that give them superparamagnetic properties. Magbeads can be engineered with variety of surface chemistry options. They can be used for several purposes in immunodiagnostics, including as biomolecule carriers, reaction support phases, and separation tools (14).

To streamline immunoassays, magbeads can be coated with specific antibodies or antigens that bind to the target analyte. A magnetic field is then applied to separate the magbead-bound complexes from the rest of the sample; an effective process that reduces background noise and enhances assay sensitivity.

Learn more about how magnetic beads are used in immunoassay development

Magbead technology is an elegant solution for clinical immunoassays, bringing a variety of benefits including (14–16):

- **Reduced sample volume and reagent use:** ELISAs and CLIAs typically require large volumes of samples and reagents, which can be particularly challenging when dealing with rare or scarce sample material. Because magbeads provide a high surface area-to-volume ratio, they allow for effective analyte binding in much smaller volumes, reducing the amount of sample and reagents needed.
- **Minimized nonspecific binding:** Magbeads enable high-precision washing steps, helping to reduce nonspecific binding. The result is cleaner backgrounds, thereby enhancing the sensitivity and specificity of the assay.
- **Streamlined assay steps:** Traditional immunoassays can be labor-intensive and time-consuming, with multiple steps of washing, incubation, and separation required. Magnetic separation simplifies these steps, allowing for rapid, reliable, and automated processing. Automation not only saves time but also reduces the potential for human error and contamination in assay preparation and execution.

Learn more about enhancing ELISAs with magnetic beads

Microfluidic chip technology in immunodiagnostics

Microfluidic chips are the latest innovation to transform immunodiagnostics and are used across a broad range of diagnostic applications. This technology incorporates microscale channels and reservoirs that enable precise manipulation of samples and reagents.

Often involving a magbead component, microfluidic chip technology can be used to perform a wide array of immunodiagnostic processes, including sample preparation, reagent mixing, and signal detection and quantification, all within a compact and integrated platform (17).

One of the stand-out advantages of microfluidic chips is their ability to drastically reduce the volumes of samples and reagents required in immunoassays. Smaller volumes conserve valuable biological samples while the high surface-to-volume ratio of micro-channels accelerates antibody-antigen binding. Faster binding helps to substantially shorten the time to result.

Microfluidic chips are revolutionizing immunodiagnostic testing with their rapid turnaround times, portability, and user-friendliness. Moreover, the integration of microfluidic technology with digital systems and connectivity options further enhances their use in clinical settings, allowing for real-time data analysis and sharing (18).

Another key benefit of microfluidic chip technology is the ability to integrate complex, multiplexed immunoassays to simultaneously test for multiple pathogens, toxins, or biomarkers from a single sample. This multiplexing ability is particularly valuable in the diagnosis of complex diseases like cancer where multiple biomarkers need to be analyzed to make an accurate diagnosis or to tailor personalized treatment plans (19,20).

Integration of surface-enhanced Raman spectroscopy

Microfluidic immunoassays commonly integrate immunoassay techniques such as FIAs or CLIAs due to their high sensitivity and multiplexing capabilities (21,22). More recently, however, developers are incorporating surface-enhanced Raman spectroscopy (SERS) into immunodiagnostic devices. SERS is a powerful spectroscopic technique that harnesses Raman scattering to obtain ultrasensitive chemical information on a sample.

Compared to FIA and CLIA, SERS exhibits vastly improved detection limits for various analytes, boosting assay sensitivity. SERS also minimizes the photobleaching effect associated with fluorescent labels and allows for a broader excitation wavelength range. The result is a more robust and versatile diagnostic platform.

SERS also enables the simultaneous detection of multiple targets without the need for multiple fluorescent labels simplifying assay design. Combined with SERS technology, microfluidic immunoassays can improve the performance of immunoassays in terms of sensitivity, response time, throughput, and overall cost (23,24).

Immunodiagnostics market insights and trends

Exploring immunodiagnostics market trends provides valuable insight into the emerging technologies and their applications. The immunodiagnostics market is rapidly expanding. It is predicted to grow from USD 17.44 billion in 2022 to USD 31.43 billion by 2030 (25).

This market growth is being fueled by several demand drivers, including:

- **Global demographic changes:** The global increase in life expectancy has led to a larger elderly population who are more susceptible to chronic and infectious diseases. An aging global population requires more frequent and comprehensive diagnostic testing to manage health conditions effectively.
- **Increasing burden of infectious and chronic diseases:** The rising incidence of chronic diseases (such as cancer, diabetes, and cardiovascular disorders) and infectious diseases (like HIV/AIDS and COVID-19) has heightened the need for disease detection and monitoring tools.
- **Increased emphasis on early detection:** Detecting diseases at an early stage is key to enhancing treatment effectiveness and minimizing healthcare costs. This increased need for early detection has driven the demand for high-sensitivity immunoassays.
- **Demand for personalized medicine:** There is a growing trend toward personalized medicine. In personalized medicine, treatments are tailored to the individual characteristics, needs, and preferences of a person. Immunodiagnostics play a crucial role in facilitating personalized medicine by enabling the sensitive identification of biomarkers that inform therapeutic strategies.

Immunodiagnostics market segments by application

In the current immunodiagnostic market, infectious diseases represent the largest application. This emphasis is thanks to the increasing incidence of infectious disease globally, particularly following the COVID-19 pandemic.

However, another rapidly growing application area in the immunodiagnostics space is in oncology. Immunodiagnostics are crucial for the screening, detection, prognosis, and monitoring of cancer treatments. Consequently, substantial expansion in the oncology segment is anticipated in the near future (26).

Future prospects for clinical immunodiagnostics

Looking to the future, novel technologies will bring new opportunities in immunodiagnostics. From artificial intelligence (AI) to an increased emphasis on point-of-care (POC) testing, future innovations and approaches promise to enhance diagnostic precision, expand accessibility, and accelerate the delivery of personalized healthcare solutions.

Integration with digital technology

As with all clinical diagnostic approaches, immunodiagnostics is set to become more integrated with digital technology. Increased connectivity with electronic health records (EHRs), digital imaging, as well as mobile health applications is predicted, aiding the seamless collection, storage, and sharing of diagnostic data.

Several microfluidic immunoassay devices have been developed that can be operated via smartphone apps. An example includes a CLIA-based device that detects a prostate-specific antigen, with the chemiluminescent signal observed using a conventional smartphone camera (27) (Fig 2).

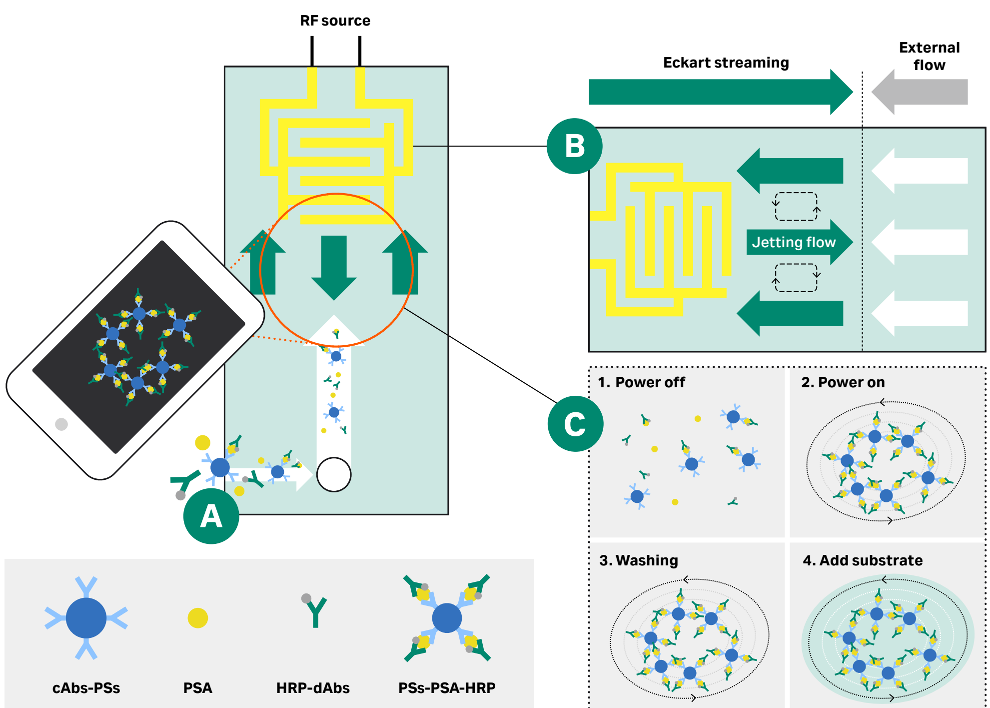

Fig 2. Example of a microfluidic CLIA device that enables signal detection via a conventional smartphone camera.

The integration of AI technology into immunodiagnostics is another exciting prospect for the future of healthcare. AI algorithms are increasingly being employed to interpret complex diagnostic data. AI has the ability to improve test performance, sensitivity, specificity, and diagnostic turnaround.

For example, a team has recently developed a microfluidic immunodiagnostic that uses AI to control various microfluidic assay steps. Operable via smartphones, the device was designed to perform ELISAs for a broad range of applications. The platform featured an integrated bubble trap, activated by AI, to eliminate any bubbles — preventing potential false signals during the ELISA (28).

Increased testing at the point of care

The expansion of POC testing represents a significant shift towards decentralized immunodiagnostic approaches. POC immunoassays, such as lateral-flow assays (LFAs), have become highly popular in diagnostics, with LFAs showing enormous potential during the COVID-19 pandemic. By enabling diagnostic tests to be performed at or near a person's location, POC testing can significantly reduce the time from testing to result interpretation, which leads to rapid clinical decision-making (29).

The transition from lab-based to POC immunodiagnostics is set to continue at pace. Microfluidic technologies and digitalized diagnostic devices are at the forefront of this shift, offering compact, easy-to-use platforms for a wide range of immunodiagnostic tests. By eliminating the need for sophisticated instrumentation, these devices have the potential to improve access to immunodiagnostic testing, particularly in resource-limited settings. Looking to the future, the shift towards POC testing will be especially crucial in managing infectious diseases and cancers, where timely diagnosis can dramatically affect health outcomes.

Learn more about the latest developments in membrane-based POC testing

Conclusion

The recent advancements in immunodiagnostics, particularly through the integration of nanotechnology, microfluidics, and digital technology have heralded a new era in healthcare diagnostics. These innovations promise to improve the speed, sensitivity, and specificity of immunodiagnostic tests, all while minimizing costs and resource use. These improvements are transforming medical care including the development of more personalized and accessible healthcare solutions.

With a host of exciting possibilities on the horizon for immunodiagnostics, why not join us in embracing innovation and shaping the future of healthcare?

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