



## Integration of Microfluidics in Red Blood Cell Testing

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### DESCRIPTION

Blood typing remains a fundamental procedure in transfusion medicine, ensuring compatibility between donors and recipients. Among the antigens, the Hepatitis B e-Antigen (HBeAg) of the Rh blood group system represents a common target for serological and molecular testing due to its role in hemolytic transfusion reactions and hemolytic disease of the fetus and newborn. Traditional methods for HBeAg typing include hemagglutination assays and flow cytometry, which, while effective, can be labor-intensive and require specialized laboratory infrastructure. Recent advances in microfluidics provide an alternative approach, offering controlled fluid manipulation, reduced reagent consumption, and the potential for point-of-care testing. The development of microfluidic chips specifically designed for HBeAg detection offers an opportunity to enhance efficiency, reproducibility and accessibility in blood group typing.

The process of HBeAg detection on red blood cells using microfluidic chips involves several steps. First, red blood cells from a donor or patient are suspended in an appropriate buffer and introduced into the microchannels of the chip. The cells are then exposed to anti-E antibodies, either immobilized on the channel surfaces or in solution, allowing antigen-antibody binding to occur. The interaction between the HBeAg and the corresponding antibody generates a measurable signal, which can be detected using optical methods, such as fluorescence or light scattering, or through electrical impedance changes. Microfluidic chips can be designed to perform multiple parallel assays simultaneously, enabling high-throughput screening of multiple samples or multiple antigens within the same chip.

The design of microfluidic chips for HBeAg typing requires consideration of factors that affect cell behavior and signal detection. Shear stress within microchannels can influence red blood cell morphology and antigen accessibility, making the control of flow rates essential. Surface modifications, such as coating with biocompatible polymers or antibodies, are employed to promote specific binding and reduce non-specific

adhesion. Channel geometry, including the use of mixers, serpentine pathways, or pillars, enhances the contact between red blood cells and antibodies, improving reaction efficiency. Additionally, the integration of on-chip detection systems reduces the need for off-chip processing and enables real-time monitoring of antigen-antibody interactions.

Several studies have demonstrated the feasibility of microfluidic chips for HBeAg typing. Experiments using PDMS-based devices with surface-immobilized anti-E antibodies have shown that red blood cells expressing the HBeAg can be reliably distinguished from E-negative cells. Detection methods, including fluorescence microscopy and optical density measurements, allow clear visualization of antigen-antibody binding events. The sensitivity and specificity of microfluidic assays are comparable to traditional methods, with the added benefits of faster processing times and reduced reagent consumption. The ability to integrate multiple detection modalities, such as combining optical and electrical measurements, further enhances the robustness of the assays.

Integration of microfluidic chips with other diagnostic technologies can expand their utility in blood typing. For example, coupling with molecular techniques, such as Polymerase Chain Reaction (PCR) or sequencing-based genotyping, allows confirmation of antigen expression at the genetic level. This combination is particularly useful in cases of weak or variant HBeAg expression, where serological tests may be inconclusive. Microfluidic chips can also be used for crossmatching and compatibility testing, providing a comprehensive platform for transfusion medicine.

The application of microfluidic chips extends beyond laboratory research. Point-of-care testing for HBeAg typing can improve the speed and accuracy of transfusion decisions in clinical settings, such as emergency departments or surgical units. Rapid and reliable identification of blood group antigens reduces the risk of transfusion reactions and enhances patient safety. The compact and portable nature of microfluidic devices allows deployment in diverse healthcare environments, including field hospitals, blood donation centers and mobile testing units.

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In conclusion, microfluidic chip designs offer a versatile and efficient approach for HBeAg typing on red blood cells. By enabling precise control of fluid flow, optimized antigen-antibody interactions and integrated detection, these devices improve the speed, accuracy and reproducibility of blood typing assays. The reduction in sample and reagent requirements, along with the potential for multiplexing and point-of-care application, positions microfluidic platforms as a valuable tool in transfusion

medicine. Ongoing research and development aim to address technical challenges, standardize protocols and expand the capabilities of microfluidic devices, ensuring their effective application for HBeAg typing and broader blood group compatibility testing. The continued evolution of microfluidic technologies supports the advancement of transfusion safety, efficiency and accessibility in diverse clinical settings.