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Abstract

Portable Fluorescence Biosensing System for Low-Cost, Quantitative, and Multiplexed Allergen Screening†

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Abstract: A miniaturized multi-array system is being developed for immune-signature testing. The presented system includes microfluidic chips functionalized with allergens for IgEs detection and a custom-made portable reader for fast (~1 s), quantitative, and sensitive (500 dye molecules/μm²) detection, with a high spatial resolution (~50-100 μm). The developed solution enables the rapid sensing of allergic reactions at the point of care with a low-cost portable device.

Keywords: Biosensor; Allergy; Microfluidics; Point-of-care, Fluorescence; Optical Reader

1. Introduction

The incidence of immune-mediated diseases such as asthma and allergies is steadily increasing [1]. However, little is known yet about how genetics and environmental factors can influence the onset and progression of these diseases. Herein, we developed a portable multiarray system for allergy profiling. Such a platform could help to quickly screen various biomarkers, such as antibodies, related to immune-mediated diseases [2]. Based on microfluidic chips of the size of a standardized microscopy slide, the multiarray is embedded in a microfluidic channel with microstructures functionalized with allergen extract or recombinant proteins. An automated sample-on-chip processing system has been developed to ensure the reproducible detection of allergy-specific IgEs using fluorescence-labeled antibodies. In addition, a compact, low-cost, and fast fluorescence reader has also been fabricated for simple measurements of the fluorescence signals and automated quantification of the allergic response with a cross-platform software with a user-friendly interface.

2. Materials and Methods

The slide-shaped microfluidic system was fabricated by injection molding of polycarbonate, containing more than 300 micropillars (Figure 1(a), step 1). The slides are coated with a photo-linker polymer (OptoDex®), for immobilizing the allergens onto the micropillars, for passivating the surface to suppress non-specific bindings, and to hydrophilize the microfluidic channel. The allergen extracts and recombinant proteins (Timothy grass, cat and dog epithelium, house dust mite, and common birch, from Bühlmann Laboratories AG and Indoor Biotechnologies Limited) are added with a precision dispenser (GeSiM GmbH, Nanoplotter 2.0). After dispensing, a photo-immobilization is performed with a UV chamber (2 min at 20 mW/cm², Beltron GmbH). After lamination (Simport T329-1, US), control serum samples (PathTROL) were used to validate the multiarray. Parallelized sample handling (up to 6 slides) is performed using the custom IncaTrace technology (Figure 1(a), step 2), injecting 80 μL of serum sample per slide. Finally, detection antibodies (Mouse anti-hIgE) and AlexaFluor 647 Goat-Anti-mIgG (80 μL each) are flown in the system and subsequent fluorescence images can be acquired (Figure 1(a), step 3). Measurements were performed both with a commercial microarray reader (InnoScan 710) and with a custom-made portable reader (Figure 1(a), step 4) and the performance of the two devices was compared. The portable reader includes a dedicated software for device control and automated fluorescence image recognition, data extraction, and data analysis.

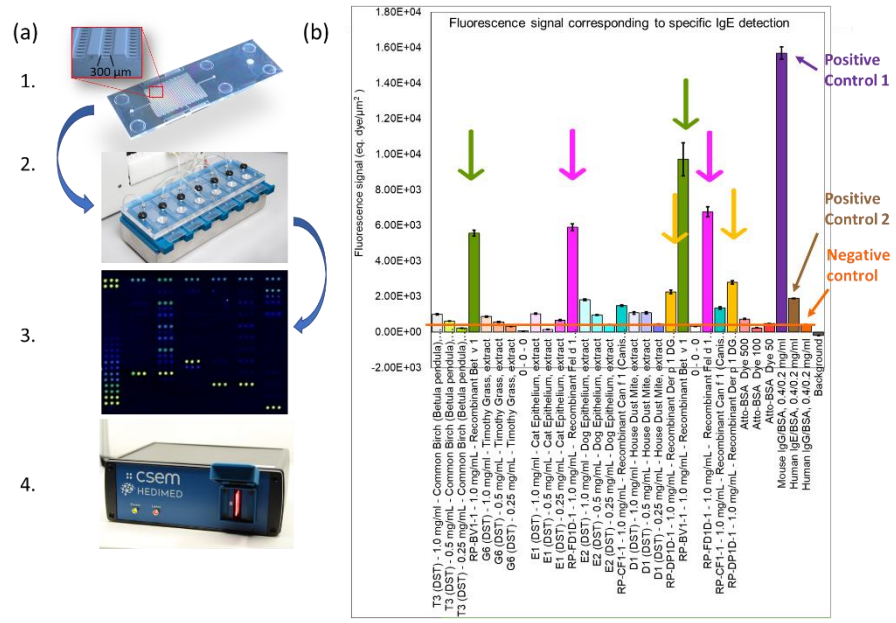

Figure 1. Multiplex system for allergen screening. (**a**) Images showing the microfluidic system (1.), the system for sample handling (2.), the fluorescent signals on the micropillars (3.), and the portable fluorescent reader (4.). (**b**) Signal corresponding to specific IgEs recorded with InnoScan reader.

The portable reader has a footprint of 20x16x7 cm, weighs 1.5 kg, and costs ~40 times less than commercial microarray readers, still reaching the performance needed for this assay. In contrast to commercial microarray scanners based on point scanning, the portable reader allows full slide imaging, significantly reducing the time needed for readout.

3. Discussion

The fluorescence signal from the microarray system is shown in Figure 1(b). The Mouse IgG and Human IgE positive control signals (purple and brown bars) and the negative control (Human IgG, orange bar) allow determining a crosstalk threshold of ~400 dye/µm². The results show that three positive allergic markers can be detected with the protein recombinant above the crosstalk threshold: common birch (green bars), cat epithelium (pink bars), house dust mite (Der. pteronyssinus, yellow bars). This agrees with the control serum being tested positive for cat and house dust mites. Common birch was not tested by the manufacturer and thus cannot be confirmed. Up to 88 different allergens could be tested in parallel with the system, opening new possibilities for allergen screening at the doctor's office.

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Conflicts of Interest: The authors declare no conflict of interest.

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