Web COBIOPHAD – MAY 19

1. CONGRESS

1. International Conference on Allergy Asthma & Immunology
   June 05 – 06, 2019
   London, United Kingdom.
   https://allergy.scitechconferences.com/

2. Japanese Society of Allergology 68th Annual Meeting 2019
   June 14 – 16, 2019
   Tokyo, Japan
   http://www.c-linkage.co.jp/jsa68/

3. Federation of Clinical Immunology Societies Annual Meeting 2019
   June 18 – 21, 2019
   Boston , MA, United States
   http://www.focisnet.org/#

4. AIS 2019 — 7th Antibody Industrial Symposium
   June 24 – 25, 2019
   Tours, France
   https://aiscongress.com

5. Euro Summit on Immunology & Infectious Diseases
   July 08 – 09, 2019
   Valencia, Spain
   https://www.immunochemistryconference.com/

6. DGfI 2019 — II Joint Meeting of the German Society for Immunology (DGfI) and the Italian Society of Immunology, Clinical Immunology and Allergology (SIICA)
   September 10 – 13, 2019
   Munich, Germany
   http://www.immunology-conference.de/

7. 17th International Congress of Immunology
   19-23 October, 2019
   Beijing, China
   https://iuis2019.org/

8. Allergologie Update Refresher
   November 04 – 05, 2019
   Vienna, Austria
   https://www.fomf.at/allergologie-update-refresher-wien-1119

9. Immunology2019 — International Summit on Immunology conference
November 07 – 08, 2019
London, UK.
https://www.royalmarsden.nhs.uk/user-guide-cancer-immunotherapy-november-2019

2. NEWS

1. Suspected case of measles at Sylvania school, stepfather claims allergic reaction
https://www.13abc.com/content/news/Health-Department-investigating-suspected-case-of-measles-at-Sylvania-school-510076691.html

2. CD-style device to detect antibiotic allergies.
https://www.labonline.com.au/content/life-science-clinical-diagnostics-instruments/news/cd-style-device-to-detect-antibiotic-allergies-591270593

3. ARTICLES

[1] - Sánchez-Gómez FJ, González-Morena JM, Vida Y, Pérez-Inestrosa E, Blanca M, Torres MJ, et al. Amoxicillin haptenates intracellular proteins that can be transported in exosomes to target cells. Allergy Eur J Allergy Clin Immunol. 2017;72(3):385–96.

Abstract:

Allergic reactions to β-lactams are among the most frequent causes of drug allergy and constitute an important clinical problem. Drug covalent binding to endogenous proteins (haptenation) is thought to be required for activation of the immune system. Nevertheless, neither the nature nor the role of the drug protein targets involved in this process is fully understood. Here, we aim to identify novel intracellular targets for haptenation by amoxicillin (AX) and their cellular fate. Methods: We have treated B lymphocytes with either AX or a biotinylated analog (AX-B). The identification of protein targets for haptenation by AX has been approached by mass spectrometry an d immunoaffinity techniques. In addition, intercellular communication mediated by the delivery of vesicles loaded with AX-B-protein adducts has been explored by microscopy techniques. Results: We have observed a complex pattern of AX-haptenated proteins. Several novel targets for haptenation by AX in B lymphocytes have been identified. AX-haptenated proteins were detected in cell lysates and extracellularly, either as soluble proteins or in lymphocyte-derived extracellular vesicles. Interestingly, exosomes from AX-B-treated cells showed a positive biotin signal in electron microscopy. Moreover, they were internalized by endothelial cells, thus supporting their involvement in intercellular transfer of haptenated proteins. Conclusions: These results represent the first identification of AX-mediated haptenation of intracellular proteins. Moreover, they show that exosomes can constitute a novel vehicle for haptenated proteins, and raise the hypothesis that they could provide antigens for activation of the immune system during the allergic response.

DOI: 10.1111/all.12958

[2] - Barbero N, Fernández-Santamaría R, Mayorga C, Martin-Serrano Á, Salas M, Bogas G, et al. Identification of an antigenic determinant of clavulanic acid responsible for IgE-mediated reactions. Allergy Eur J Allergy Clin Immunol. 2019;(February):1–12

Abstract:

Background: Selective reactions to clavulanic acid (CLV) account for around 30% of immediate reactions after administration of amoxicillin-CLV. Currently, no immunoassay is available for detecting specific IgE to CLV, and its specific recognition in patients with immediate reactions has only been demonstrated by basophil activation testing,

however with suboptimal sensitivity. The lack of knowledge regarding the structure of the drug that remains bound to proteins (antigenic determinant) is hampering the development of in vitro diagnostics. We aimed to identify the antigenic determinants of CLV as well as to evaluate their specific IgE recognition and potential role for diagnosis.

Methods: Based on complex CLV degradation mechanisms, we hypothesized the formation of two antigenic determinants for CLV, AD-I (N-protein, 3-oxopropanamide) and AD-II (N-protein, 3-aminopropanamide), and designed different synthetic analogs to each one. IgE recognition of these structures was evaluated in basophils from patients with selective reactions to CLV and tolerant subjects. In parallel, the CLV fragments bound to proteins were identified by proteomic approaches.

Results: Two synthetic analogs of AD-I were found to activate basophils from allergic patients. This determinant was also detected bound to lysines 195 and 475 of CLV-treated human serum albumin. One of these analogs was able to activate basophils in 59% of patients whereas CLV only in 41%. Combining both results led to an increase in basophil activation in 69% of patients, and only in 12% of controls.

Conclusion: We have identified AD-I as one CLV antigenic determinant, which is the drug fragment that remains protein-bound.

DOI: 10.1111/all.13761

[3] - Ariza A, Mayorga C, Salas M, Donã I, Martín-Serrano Á, Pérez-Inestrosa E, et al. The influence of the carrier molecule on amoxicillin recognition by specific IgE in patients with immediate hypersensitivity reactions to betalactams. Sci Rep. 2016;6(October):1–10.

Abstract:

The optimal recognition of penicillin determinants, including amoxicillin (AX), by specific IgE antibodies is widely believed to require covalent binding to a carrier molecule. The nature of the carrier and its contribution to the antigenic determinant is not well known. Here we aimed to evaluate the specific-IgE recognition of different AX-derived structures. We studied patients with immediate hypersensitivity reactions to AX, classified as selective or cross-reactors to penicillins. Competitive immunoassays were performed using AX itself, amoxicilloic acid, AX bound to butylamine (AXO-BA) or to human serum albumin (AXO-HSA) in the fluid phase, as inhibitors, and amoxicilloyl-poli-L-lysine (AXO-PLL) in the solid-phase. Two distinct patterns of AX recognition by IgE were found: Group A showed a higher recognition of AX itself and AX-modified components of low molecular weights, whilst Group B showed similar recognition of both unconjugated and conjugated AX. Amoxicilloic acid was poorly recognized in both groups, which reinforces the need for AX conjugation to a carrier for optimal recognition. Remarkably, IgE recognition in Group A (selective responders to AX) is influenced by the mode of binding and/or the nature of the carrier; whereas IgE in Group B (cross-responders to penicillins) recognizes AX independently of the nature of the carrier.

DOI: 10.1038/srep35113

[4] - Strohmeier O, Keller M, Schwemmer F, Zehnle S, Mark D, Von Stetten F, et al. Centrifugal microfluidic platforms: advanced unit operations and applications. Chem Soc Rev [Internet]. 2015;44(17):6187–229. Available from: http://dx.doi.org/10.1039/C4CS00371C.

Abstract:

Review on miniaturization, integration, and automation of laboratory processes within centrifugal microfluidic platforms. For efficient implementation of applications, building blocks are categorized into unit operations and process chains.Centrifugal microfluidics has evolved into a mature technology. Several major diagnostic companies either have products on the market or are currently evaluating centrifugal microfluidics for product development. The fields of application are widespread and include clinical chemistry, immunodiagnostics and protein analysis, cell handling, molecular diagnostics, as well as food, water, and soil analysis. Nevertheless, new fluidic functions and applications that expand the possibilities of centrifugal microfluidics are being introduced at a high pace. In this review, we first present an up-to-date comprehensive overview of centrifugal microfluidic unit operations. Then, we introduce

the term “process chain” to review how these unit operations can be combined for the automation of laboratory workflows. Such aggregation of basic functionalities enables efficient fluidic design at a higher level of integration. Furthermore, we analyze how novel, ground-breaking unit operations may foster the integration of more complex applications. Among these are the storage of pneumatic energy to realize complex switching sequences or to pump liquids radially inward, as well as the complete pre-storage and release of reagents. In this context, centrifugal microfluidics provides major advantages over other microfluidic actuation principles: the pulse-free inertial liquid propulsion provided by centrifugal microfluidics allows for closed fluidic systems that are free of any interfaces to external pumps. Processed volumes are easily scalable from nanoliters to milliliters. Volume forces can be adjusted by rotation and thus, even for very small volumes, surface forces may easily be overcome in the centrifugal gravity field which enables the efficient separation of nanoliter volumes from channels, chambers or sensor matrixes as well as the removal of any disturbing bubbles. In summary, centrifugal microfluidics takes advantage of a comprehensive set of fluidic unit operations such as liquid transport, metering, mixing and valving. The available unit operations cover the entire range of automated liquid handling requirements and enable efficient miniaturization, parallelization, and integration of assays.

DOI: 10.1039/c4cs00371c

[5] - Park JM, Cho YK, Lee BS, Lee JG, Ko C. Multifunctional microvalves control by optical illumination on nanoheaters and its application in centrifugal microfluidic devices. Lab Chip. 2007;7(5):557–64.

Abstract:

Valving is critical in microfluidic systems. Among many innovative microvalves used in lab-on-a-chip applications, phase change based microvalves using paraffin wax are particularly attractive for disposable biochip applications because they are simple to implement, cost-effective and biocompatible. However, previously reported paraffin-based valves require embedded microheaters and therefore multi-step operation of many microvalves was a difficult problem. Besides, the operation time was relatively long, 2-10 s. In this paper, we report a unique phase change based microvalve for rapid and versatile operation of multiple microvalves using a single laser diode. The valve is made of nanocomposite materials in which 10 nm-sized iron oxide nanoparticles are dispersed in paraffin wax and used as nanoheaters when excited by laser irradiation. Laser light of relatively weak intensity was able to melt the paraffin wax with the embedded iron oxide nanoparticles, whereas even a very intense laser beam does not melt wax alone. The microvalves are leak-free up to 403.0 ± 7.6 kPa and the response times to operate both normally closed and normally opened microvalves are less than 0.5 s. Furthermore, a sequential operation of multiple microvalves on a centrifugal microfluidic device using a single laser diode was demonstrated. It showed that the optical control of multiple microvalves is fast, robust, simple to operate, and requires minimal chip space and thus is well suited for fully integrated lab-on-a-chip applications.

DOI: 10.1039/b616112j

[6] - Lutz S, Weber P, Focke M, Faltin B, Hoffmann J, Müller C, et al. Microfluidic lab-on-a-foil for nucleic acid analysis based on isothermal recombinase polymerase amplification (RPA). Lab Chip. 2010;10(7):887–93.

Abstract:

For the first time we demonstrate a self-sufficient lab-on-a-foil system for the fully automated analysis of nucleic acids which is based on the recently available isothermal recombinase polymerase amplification (RPA). The system consists of a novel, foil-based centrifugal microfluidic cartridge including prestored liquid and dry reagents, and a commercially available centrifugal analyzer for incubation at 37 ?C and real-time fluorescence detection. The system was characterized with an assay for the detection of the antibiotic resistance gene mecA of Staphylococcus aureus. The limit of detection was <10 copies and time-to-result was <20 min. Microfluidic unit operations comprise storage and release of liquid reagents, reconstitution of lyophilized reagents, aliquoting the sample into #30 independent reaction cavities, and mixing of reagents with the DNA samples. The foil-based cartridge was produced by blow-molding and sealed with a self-adhesive tape. The demonstrated system excels existing PCR based lab-on-a-chip platforms in terms

of energy efficiency and time-to-result. Applications are suggested in the field of mobile point-of-care analysis, B-detection, or in combination with continuous monitoring systems.

DOI: 10.1039/b921140c

[7] - Al-Faqheri W, Ibrahim F, Thio THG, Moebius J, Joseph K, Arof H, et al. Vacuum/Compression Valving (VCV) Using Parrafin-Wax on a Centrifugal Microfluidic CD Platform. PLoS One. 2013;8(3):2–10.

Abstract:

This paper introduces novel vacuum/compression valves (VCVs) utilizing paraffin wax. A VCV is implemented by sealing the venting channel/hole with wax plugs (for normally-closed valve), or to be sealed by wax (for normally-open valve), and is activated by localized heating on the CD surface. We demonstrate that the VCV provides the advantages of avoiding unnecessary heating of the sample/reagents in the diagnostic process, allowing for vacuum sealing of the CD, and clear separation of the paraffin wax from the sample/reagents in the microfluidic process. As a proof of concept, the microfluidic processes of liquid flow switching and liquid metering is demonstrated with the VCV. Results show that the VCV lowers the required spinning frequency to perform the microfluidic processes with high accuracy and ease of control.

DOI: 10.1371/journal.pone.0058523

[8] - Aeinehvand MM, Ibrahim F, Harun SW, Al-Faqheri W, Thio THG, Kazemzadeh A, et al. Latex micro-balloon pumping in centrifugal microfluidic platforms. Lab Chip. 2014;14(5):988–97.

Abstract:

Centrifugal microfluidic platforms have emerged as point-of-care diagnostic tools. However, the unidirectional nature of the centrifugal force limits the available space for multi-step processes on a single microfluidic disc. To overcome this limitation, a passive pneumatic pumping method actuated at high rotational speeds has been previously proposed to pump liquid against the centrifugal force. In this paper, a novel micro-balloon pumping method that relies on elastic energy stored in a latex membrane is introduced. It operates at low rotational speeds and pumps a larger volume of liquid towards the centre of the disc. Two different micro-balloon pumping mechanisms have been designed to study the pump performance at a range of rotational frequencies from 0 to 1500 rpm. The behaviour of the micro-balloon pump on the centrifugal microfluidic platforms has been theoretically analysed and compared with the experimental data. The experimental data show that the developed pumping method dramatically decreases the required rotational speed to pump liquid compared to the previously developed pneumatic pumping methods. It also shows that within a range of rotational speed, a desirable volume of liquid can be stored and pumped by adjusting the size of the micro-balloon.

DOI: 10.1039/c3lc51116b