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Mobility fellowships

# 13.as Jornadas de Formación del Centro de Investigación Biomédica en Red de Enfermedades Respiratorias (CIBERES)

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## EFFECTS OF DIESEL EXHAUST PARTICLES ON ALLERGIC AND CHEMICAL-INDUCED ASTHMA

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**Introduction:** Air pollution is known to exacerbate and induce asthma pathophysiology, but the immunological effects of diesel exhaust particles (DEP) are still not well characterized and seem to differ depending on the pre-existing asthma endotype. Nowadays, asthma is classified into a type 2 (T2), further subdivided into Th2 and ILC2-driven; a non-T2; and a mixed Th2/Th17 endotype. Fellowships at Centre for environment and Health, working under the supervision of Dr. Peter Hoet and Dr. Jeroen Vanoirbeek, may be an opportunity to acquire new techniques and foster new collaborative projects.
**Objectives:** To learn new procedures used in the research of asthma, to design and use a specific flow cytometry panel, and to collaborate in the different research projects carried out by the group.
**Methods:** The selected institution was the Catholic University of Leuven, one of the leading centers on respiratory research in Europe. Centre for environment and Health is involved in the research of air pollutants and the respiratory system. Thanks to the funding obtained from CIBER, a six-week stay was possible and resulted in an enriching experience.
**Results:** The applicant standardized a flow cytometry panel able to analyse the proportion of several leukocytes in lung tissue; learned new ways to analyse lung function in asthmatic mice with the FlexiVent; joined in one project to test the effect of ketotifen in swimming pool-induced asthma; and had the opportunity to upgrade current protocols of optical projection tomography (OPT). This knowledge has been used in two recently published research articles, where the authors evaluate the effects of DEP on allergic and chemical-induced asthma.
**Conclusions:** CIBER mobility fellowship favours the interaction and synergies with strategic external research groups and is key for increasing the scientific production and internationalization of CIBER groups.

## TACKLING BACTERIAL INFECTIONS WITH PHAGE LYSINS BY USING HIGH THROUGHPUT SYNTHETIC BIOLOGY APPROACHES

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**Introduction:** Phage-encoded lytic enzymes, also called lysins, are one of the most promising alternatives to common antibiotics in this approaching post-antibiotic era. Their potential as novel antimicrobials to tackle antibiotic resistant bacteria not only arises from features such as a lower chance to provoke resistance, but also from their versatility as synthetic biology parts. Functional modules or fragments derived from lysins are currently being used for the design of novel antimicrobials with desired properties. This way, several engineered lysins have been designed to tackle bacterial infections caused both by Gram-positive (such as chimeric lysin Cpl-711) (Diez-Martinez et al. J Antimicrob Chemother. 2015;70:1763-73) or Gram-negative (such as the so-called 'artilysins') (Briers et al. mBio. 2014;5:e01379-01314).
**Objectives:** The aim of this work was to generate a library of protein variants made up of shuffled lysin domains, in order to check their ability to attack both the respiratory pathogen Streptococcus pneumoniae and some Gram-negative pathogens that often appear in polymicrobial infection settings.
**Methods:** We used the high-throughput 'VersaTile'genetic engineering platform (Gerstmans et al. Sci Adv. 2020;6:eaaz1136) to semi-randomly shuffle a collection of previously constructed and 'ad hoc' prepared lysin domains. Both the VersaTile platform and the domains collection were available at the Laboratory of Applied Biotechnology, in Ghent University (Belgium).
**Results:** We obtained up to four different libraries, of which two have been screened against S. pneumoniae, Moraxella catarrhalis and Haemophilus influenzae. Several protein variants have been found to be active against S. pneumoniae and are now being thoroughly tested against both pneumococci and other pathogens.
**Conclusions:** The VersaTile high-throughput strategy allows to obtain different chimeric protein constructs maximizing the chances of success, in terms of obtaining a protein that expresses well, is soluble and active, minimizing at the same time the experimental efforts that typically lead to many trial-and-error dead ends.
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