



# INNOVATIONS TO FIGHT RESPIRATORY DISEASES

*Prevention, research and treatments*

December 3-4th 2024

Biocitech Paris-Romainville

Session **#Keynote lecture**

**Maladies respiratoires = un réel enjeu de santé publique en 2024**

**Claire ANDREJAK, CHU Amiens-Picardie, Présidente SPLF (Société de Pneumologie de Langue Française)**

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## Session #1 - Research and Innovations

Prepared for the next virus pandemic: The APPEAL project

**Olivier MONCORGÉ**, IRIM - UMR9004 (Institut de Recherche en Infectiologie de Montpellier)

The APPEAL project, funded by the European Union, aims to identify broad spectrum host-directed antiviral drugs as therapeutic options against a panel of viruses, including respiratory viruses. The APPEAL consortium is using a gene selection pipeline following a high-tech strategy and several state-of-the-art approaches to identify key host factors used by some emerging and re-emerging viruses and viruses with pandemic potential. The aim of this presentation is to present the objectives of the APPEAL consortium but also the scientific reasons behind the creation of this project.

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## **Session #1 - Research and Innovations**

### **Metabolic control of lung inflammation**

**Mustapha SI-TAHAR, INSERM, Université de Tours**

Le métabolisme et l'immunité, historiquement des domaines de recherche cloisonnés, ont récemment convergé sous le concept d'immunométabolisme.

Dans le contexte de l'infection par le virus de la grippe, mon équipe a montré que la muqueuse pulmonaire subit une reprogrammation métabolique, conduisant à l'accumulation de métabolites spécifiques appelés metabokines. Nous avons révélé la double fonctionnalité de certaines metabokines, qui régulent les réponses des cellules immunitaires de l'hôte par la modulation des signaux inflammatoires et l'induction de modifications post-traductionnelles. Simultanément, ces composés perturbent directement ou indirectement la réplication du virus de la grippe. Ces découvertes offrent un potentiel majeur pour le développement de traitements innovants ciblant l'inflammation et les virus.

*Metabolism and immunity, historically siloed research domains, have recently converged under the concept of immunometabolism.*

*In the context of influenza virus infection, we have shown that the lung mucosa undergoes metabolic reprogramming, leading to the accumulation of specific metabolites known as metabokines. We revealed the dual functionality of certain metabokines as they regulate host immune cell responses through the modulation of inflammatory signaling and the induction of post-translational modifications. Simultaneously, these compounds directly or indirectly disrupt influenza virus replication. These major findings offer significant potential for innovative treatments targeting inflammation and viruses.*



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## **Session #1 - Research and Innovations**

### **Lung microbiota: a new frontier in diagnosing and treating respiratory diseases**

**Geneviève HÉRY-ARNAUD, INSERM U1078, CHU Brest, Faculté de Médecine, Université de Brest**

Long considered sterile, the lungs, like other mucous membranes, are proving to be a privileged niche for bacterial development. Studies of the lung microbiota have revealed its many specific features, in particular the presence of large numbers of anaerobic bacteria. The importance of the lung microbiota in immune homeostasis is increasingly recognized, as it plays a crucial role in maintaining the balance of the airway immune system. The development of immunotherapy in pneumology, particularly for the treatment of lung cancer, raises the question of the impact of the pulmonary microbiota on therapeutic success. In the age of personalized medicine, the lung microbiota is a potential source of biomarkers for diagnosing, prognosing or monitoring respiratory diseases. The lung microbiota is also an essential lever for preventing respiratory diseases with an infectious or inflammatory component, such as cystic fibrosis, asthma and COPD (chronic obstructive pulmonary disease). Finally, the lung microbiota opens up new avenues for innovative therapies for chronic respiratory diseases, for which there is a strong 'unmet medical need' and which represent the third leading cause of death worldwide. The characterization of commensal pulmonary species has indeed revealed the beneficial properties of certain bacterial strains, which could ultimately constitute potential live biotherapeutic products for an innovative, targeted approach to respiratory diseases.





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Session #2 - Experimental models

Applications of 3D tissue engineering of the human upper and lower respiratory system in basic and applied research

Jan MARKUS, MatTek

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## Session #2 - Experimental models

### **Advances in In Vitro Modeling of Lung Diseases: Focus on Precision-Cut Lung Slices (PCLS) Model**

**Hanan OSMAN-PONCHET, PKDERM**

Hanan Osman-Ponchet<sup>1</sup>, Manon Barthe<sup>1</sup>, Jean-Paul Thénot<sup>1</sup>, Ines Metatla<sup>2</sup>, Kevin Rogers<sup>2</sup>, Ida Chiara Guerrera<sup>2</sup>, Agnes Choppin<sup>3</sup>, and Franck Chiappini<sup>3</sup>.

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Diffuse alveolar damage is a key factor in the inflammation associated with various pulmonary diseases. This damage can result from infections like COVID-19 or from diseases of unknown origin, such as idiopathic pulmonary fibrosis (IPF), a severe and progressive lung disorder. Understanding the mechanisms underlying IPF is crucial for advancing research in this area. A range of in vitro models, including 2D, 3D, and ex vivo lung models, are instrumental in bridging the knowledge gap regarding IPF mechanisms. Among these, precision-cut lung slices (PCLS) stand out as a valuable ex vivo model for respiratory disease research and drug development. PCLS retain the lung's native 3D architecture and include all lung cell types, making them particularly useful for studying lung diseases and evaluating the safety, toxicity, and efficacy of new therapies.

The generation of human PCLS (hPCLS) is a meticulous process that requires precise techniques. This presentation will delve into the methods for preparing accurate and reproducible hPCLS from surgical lung resections. We will discuss effective strategies for inducing fibrosis in this model using a specific profibrotic cocktail, as well as methodologies for detailed hPCLS characterization and the evaluation of antifibrotic drug candidates. Notably, hPCLS can remain viable for at least 14 days, making them ideal for studies involving repeated dosing.

In summary, this presentation will highlight the significant role of human precision-cut lung slices in the investigation of respiratory diseases like IPF. Their ability to maintain viability and replicate the lung's natural structure makes hPCLS an excellent tool for studying disease mechanisms, testing potential therapies, and assessing the impact of repeated dosing.



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## **Session #2 - Experimental models**

### **Developing a digital twin of the human respiratory system**

**Andrea BENASSI, Chiesi**

The current state of the art in the development of digital twins of patient respiratory system will be reviewed, with particular focus on the capability of the models to quantitatively predict therapeutic aerosol transport and deposition. Different modelling techniques will be discussed from high fidelity computational fluid dynamics simulations to simplified statistical deposition models. Current bottlenecks and limitations will be discussed for both the modelling/simulation aspects and the experiments/measurements needed to validate and challenge the models.



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**A preclinical platform for the investigation of respiratory viral infections in the NHP model**

**Erwan CORCUFF, Cynbiose**

**Respiratory viral infection models in NHP, against hRSV Infection and SARS-CoV-2.**

Cynbiose is the only Contract Research Organization (CRO) of its kind in Europe.

The company is specialized in non-GLP preclinical research services with a core expertise and focus on the non-human primate (NHP) model to accelerate time to clinics for drug candidates:

- Exploratory DMPK, early tox studies
- PoC studies: off-the-shelf or on-demand clinically relevant efficacy models

We combine both flexible and highly-skilled teams, predictive models, knowhow and techniques with high ethical standards (AAALAC-accredited since 2015).

With a complete and achieved BSL3 capability, we provide an efficient preclinical tool to evaluate Immunotherapies for example, against **SARS-CoV-2 and Bimervax efficacy study**.





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**Session #3 - Innovative therapeutics and diagnostics approaches**

**The vascular NMDA receptor in PAH (Pulmonary Arterial Hypertension), an out-of-the-box academic scientific strategy towards therapeutic innovation**

**Sylvia COHEN-KAMINSKY**, Directrice de recherche CNRS, Inserm UMR\_S999,  
Université Paris Saclay

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## **Session #3 - Innovative therapeutics and diagnostics approaches**

### **Lessons Learned from Using the FilmArray Pneumonia Panel Plus in the Field**

**Thomas GUILLARD, Université de Reims Champagne-Ardenne, Inserm UMR-S 1250 P3Cell, CHU de Reims, Laboratoire de bactériologie-Virologie-Hygiène hospitalière, Reims, France**

#### **Identification rapide des pathogènes respiratoires au lit du malade. Retour d'expérience sur l'utilisation du FilmArray Pneumonia Panel Plus.**

L'approche moléculaire syndromique en bactériologie est une méthode innovante qui a considérablement amélioré le diagnostic des maladies infectieuses. Cette approche repose sur la détection simultanée de plusieurs pathogènes potentiels responsables d'un syndrome infectieux spécifique, grâce à un seul test. Les pneumonies sont une cause de mortalité importante en France et dans le monde. Les PCR syndromique peuvent permettre d'identifier l'agent infectieux responsable de pneumonie plus rapidement. Ainsi, la prise en charge du patient peut être améliorée. Cette présentation rapporte le retour d'expérience de l'utilisation du FilmArray® BIOFIRE Pneumonia Plus au CHU de Reims au travers de deux articles publiés dans des journaux internationaux à comité de lecture.

#### **Rapid identification of respiratory pathogens at patient's bedside. Feedback of FilmArray Pneumonia Panel Plus use**

The syndromic molecular approach in bacteriology is an innovative method that has significantly enhanced the diagnosis of infectious diseases. This approach relies on the simultaneous detection of multiple potential pathogens responsible for a specific infectious syndrome, all through a single test. Pneumonia remains a leading cause of mortality both in France and worldwide. Syndromic PCR can rapidly identify the infectious agent responsible for pneumonia, leading to improved patient management. This talk discusses the use of FilmArray® BIOFIRE Pneumonia Plus at Reims University Hospital, based on two articles published in international peer-reviewed journals.



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## **Session #3 - Innovative therapeutics and diagnostics approaches**

**Advancing tuberculosis drug resistance diagnosis  
with targeted next-generation sequencing**

**Nelly BADALATO, [GenoScreen](#)**

Targeted next-generation sequencing (tNGS) was a groundbreaking innovation just a few years ago, revolutionizing the diagnosis of drug-resistant tuberculosis. This technology rapidly identifies resistance mutations, enabling personalized treatments to improve patient outcomes. Now recommended by the WHO, tNGS is beginning to be implemented within national TB programs worldwide, bridging innovation with practical application and becoming a cornerstone for precision medicine and large-scale antimicrobial resistance surveillance. Its scalability and adaptability allow for the integration of new targets as knowledge evolves, ensuring its long-term relevance. Beyond tuberculosis, tNGS offers a versatile solution for antimicrobial resistance across other diseases, reinforcing its global importance.



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## **Session #4 - Prevention, inner air pollution and environmental aspects**

**Advanced immunocompetent in vitro primary human lung models for toxicity evaluation of airborne fibers and nanomaterials**

**Samuel CONSTANT, Epithelix**

The main function of the human airway epithelium is to generate sterile atmosphere for the alveolar region where the gas exchange occurs. As first line of defence against airborne pathogens or xenobiotics, the airway epithelium acts not only as key physical barrier endowed with mucociliary clearance and innate host defence mechanisms, but also as an important immunoregulator through production of key messengers and physical interactions with immune cells especially macrophages.

We will describe the development and characterization, as well as the use of fully primary human cell based co-culture models made of nasal, tracheal, bronchial, small-airways and alveolar epithelia (MucilAir™, SmallAir™ and AlveolAir™) and alveolar macrophages.

Impact of Man-Made Vitreous Fibres (MMVF) and nanomaterials on these advanced immunocompetent ALI models will be discussed via evaluation of: (i) local tolerance; (ii) pro-inflammation; (iii) macrophage activity; (iv) ciliopathic effect.





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## **Session #4 - Prevention, inner air pollution and environmental aspects**

### **Prevention of viral respiratory infections**

**Didier LECOINTE, Université Caen Normandie**

Viral respiratory infections are caused by several viruses, and can be seasonal or not, both in the community and in healthcare institutions. Preventive measures are proposed, in the goal to avoid viruses' acquisition and transmission, to prevent their spread in the general population and nosocomial cases in immunocompromised patients. The mode of transmission is associated with a continuum of respiratory infectious particles within a turbulent cloud, which increases the range by a factor of over 200 for particles smaller than 10 microns. This leads us to systematically distinguish between a near field and a far field of exposure.

In the community, prevention is based on universal hygiene measures, vaccination and prophylactic treatment. Universal hygiene measures have been described in 2022 by the Haut Conseil de la Santé Publique (HCSP), which adapted the five priority actions of the Ottawa Charter: developing sound public policy, create healthy environments, strengthen community action, acquire individual skills and reorienting health services. The main vaccinations recommended are those against COVID, influenza and bronchiolitis, and cannot dispense with the strict application of universal hygiene measures. A prophylactic treatment based on monoclonal antibodies is also available for bronchiolitis.

In healthcare institutions, the measures to be implemented were described by the HCSP in 2023, in a reference document describing five decision-making matrices based on professionals, patients and care situations. This guideline was supplemented in 2024 by another, published by the Société Française d'Hygiène Hospitalière, on the prevention of respiratory transmission.



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Early detection and quantification of human pathogens in the environment

Franz DURANDET, IAGE (Ingénierie et Analyse Génétique Environnementale)  
Montpellier

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### **Sanitary warnings to the population and medical care professionals in case of atmospheric pollution episodes**

**Frédéric MAUNY, CHRU Besançon**

Le Haut Conseil de la santé publique (HCSP) recommande une actualisation des messages sanitaires à diffuser en cas d'épisodes de pollution.

Pour prendre en compte les facteurs de co-exposition, le HCSP recommande de moduler les conditions de déclenchement de la procédure d'alerte lorsque le territoire concerné fait déjà l'objet d'un niveau du plan canicule orange ou rouge, à l'instar des situations de persistance d'un épisode de pollution pour les particules et l'ozone.

Le HCSP recommande l'anticipation des conditions d'accentuation ou de prolongation des épisodes de pollution, le développement d'une information adaptée aux différentes populations et l'évaluation de l'efficacité et de la pertinence des messages, la mise en place d'un numéro vert et le recours élargi à des moyens d'information diversifiés. Le HCSP insiste sur la nécessité d'adapter, voire de reporter les compétitions lors d'épisodes de pollution dépassant les seuils d'alerte.

Le HCSP recommande aussi une meilleure prise en compte des populations exposées grâce aux outils cartographiques, la promotion de partenariats pour améliorer la surveillance et la prévision des niveaux de pollution, ainsi que la coordination et l'ajustement des alertes au niveau local.

Enfin, le HCSP ne recommande pas la diffusion de message préconisant le port de masque FFP1 ou FFP2 en cas de dépassement des seuils.



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**Session #4 - Prevention, inner air pollution and environmental aspects**

**Strategy of ventilation and aeration of facilities in case of exceptional epidemic situation**

**Evelyne GÉHIN, Université Paris-Est Créteil**

La récente crise du Covid19 a démontré l'importance de la prise en compte de la transmission par voie aérienne des maladies respiratoires et a mis en évidence le rôle essentiel de la ventilation pour réduire les risques de contamination. Les modèles de type « Wells-Riley » permettent d'estimer la probabilité d'infection liée à une exposition en champ lointain (au-delà de 2 m de la personne infectée) en fonction du débit de ventilation dans une pièce. Ces modèles ont été utilisés par l'ASHRAE (American Society of Heating, Refrigerating and Air-Conditioning Engineers) et le REHVA (Federation of European Heating, Ventilation and Air Conditioning Associations) pour proposer des débits de ventilations à utiliser en période d'épidémie. Ces débits sont comparés aux débits préconisés par le Code du Travail (CT), le Règlement Sanitaire Départemental Type (RSDT) et à ceux proposés par le Haut Conseil de la Santé Publique (HCSP) dans son avis du 12/10/2023.



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## **Session #4 - Prevention, inner air pollution and environmental aspects**

### **Workplace respiratory risks management**

**Philippe DUQUENNE, INRS**

L'exposition professionnelle aux agents biologiques par voie d'inhalation a été objectivée dans nombreux secteurs d'activités professionnelles. Elle peut avoir des effets délétères sur la santé des travailleurs et la mise en place de mesures de prévention adaptées s'avère nécessaire pour les situations de travail problématiques. L'exposé vis à faire le point des connaissances sur l'exposition professionnelle aux agents biologiques aéroportés pour des situations de travail présentant un contexte de poly-exposition (agents biologiques /substances chimiques) et sur les problématiques de prévention associées.

Après avoir rappelé les fondamentaux de la prévention, la présentation aborde des exemples de secteurs d'activités pour lesquelles des expositions à des agents biologiques et chimiques ont pu être mises en évidence, ainsi que les approches de prévention qui peuvent être proposées. Pour chaque exemple, l'exposé s'attarde sur la problématique de santé au travail concernée, les connaissances sur les expositions, les mesures de prévention utilisables ainsi que les perspectives d'études.

Un premier exemple fait le point sur l'exposition des travailleurs dans les centres de tri des déchets ménagers recyclables. L'exposé précise les niveaux d'expositions ainsi que les microorganismes et composés microbiens concernés et qui ont été mis en évidence lors de campagnes de mesure effectuées dans différents centres. L'accent est mis sur les perspectives d'évolution de la filière Française et, notamment, l'extension des consignes de tri qui imposent la modernisation des centres qui doivent être adaptés aux nouveaux emballages à trier.

Un autre exemple détaille des données d'exposition acquises à l'occasion de campagnes de mesure effectuées dans des caves d'affinage de fromages. Dans ces environnements, des symptômes de type allergique ont été observés chez certains travailleurs. Les données mettent en évidence les expositions aux bactéries et aux moisissures émises dans l'air, particulièrement importantes lors d'opérations comme le brossage des fromages. De plus, des expositions à des composés chimiques produits par les communautés microbiennes des fromages (CO<sub>2</sub>, NH<sub>3</sub>, etc.) sont également observées. La poly-exposition mise en évidence rend délicate la mise en œuvre des mesures de prévention qui doivent à la fois traiter les nuisances chimiques et biologiques sans perturber le bon déroulement de l'affinage des produits.