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Drugs in the Lungs Network: Recent and future symposiums

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On behalf of the APS Drugs in the Lungs Network

It has been a busy time for the Academy of Pharmaceutical Scientists (APS) Drugs in the Lungs Network.

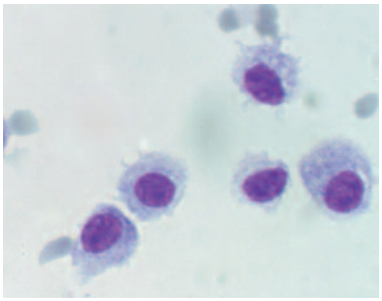
A symposium on induced alveolar macrophage responses

A two-day symposium entitled Challenges for Inhaled Drug Discovery and Development: Induced Alveolar Macrophage Responses, co-organized with the Health and Environmental Science Institute, was held in October 2012 on the topic of induced macrophage responses to inhaled pharmaceuticals. This issue was identified as a priority area for the major developers of inhaled medicines. It is relevant to all inhaled pharmaceuticals, from simple to advanced delivery systems, because many projects do not progress to the clinic on the basis of "difficult-to-interpret" pre-clinical findings. During the symposium, a multi-sector, multidisciplinary approach was applied to this modern drug delivery problem. Industry and academic experts considered the biological and physicochemical principles underlying the induction of macrophage/inflammatory response. They also provided examples and suggestions for new approaches to understanding the biology of responses, i.e., distinguishing physiological adaptive responses from adverse findings. The meeting also included a current regulatory perspective.

Presentations at the meeting and a summary of the breakout sessions and panel discussion are freely available at the Drugs in the Lungs website (www.apsgb.org/drugsinthelungs/). Figure 1 shows alveolar macrophages.

Figure 1

Understanding alveolar macrophage response to inhaled pharmaceuticals was identified as a priority for the developers of inhaled medicines; magnification 40x.



The symposium began with a review of the problem. The induction of macrophages is a common cause of attrition during the development of inhaled medicines due to safety concerns in late stage development. This makes the interpretation of macrophage responses and inflammatory markers arising during inhaled drug toxicology studies a major scientific challenge in the development and registration of new inhaled therapies. Avoidance, identification and quantification of adverse findings during pre-clinical and clinical development, along with discrimination of adaptive lung responses from adverse events, require a modern scientific understanding of alveolar macrophage responses to inhaled pharmaceuticals. During the symposium, the complex biology of alveolar macrophages and current concepts of macrophage "sub-types" with different roles in health and disease were explained. The mechanism and timescale of induction and resolution of macrophage responses to inhaled particles were also discussed. Experimental evidence for factors known or suspected to induce alveolar macrophage-mediated adverse events was considered with reference to material properties, dosimetry and relevance to inhaled medicines. Current practices for measuring and interpreting induced alveolar macrophage responses in pre-clinical development were defined along with the interpretation of such data. In addition, the consistency of pathology measurement and reporting, new and improved assays, the utility of toxicokinetics and the requirement for biomarkers were discussed. The risk assessment for pre-clinical toxicology findings and the translation to clinical pathology in man were also explored.

There was clearly an imperative to improve understanding of alveolar macrophage responses to inhaled materials, thereby providing better evidence upon which to evaluate the risk of taking inhaled investigational products into human trials when primary adaptive lung responses (i.e. non-adverse, reversible responses) are observed pre-clinically. Recommendations were made for (i)

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better industry-academia-regulatory cooperation, (ii) sharing of existing pre-competitive data and (iii) priority topics for collaborative research to address gaps in knowledge.

Drug Delivery to the Lungs 23: Mini-symposium

The Network was delighted to be invited to hold a pre-conference session at the Aerosol Society's DDL23 Conference in Edinburgh, UK in December 2012. This followed the precedent established by the European Pharmaceutical Aerosols Group (EPAG) in 2010 and the International Society for Aerosol Medicine (ISAM) in 2011. The meeting provided an opportunity to disseminate the findings of earlier activities with Lea Ann Dailey (King's College London) providing an update on lung imaging in inhaled product development and Jan Klapwijk (GSK) providing a report on the induced macrophage responses symposium described above. With a view to gauging interest on future topics, Darragh Murnane (University of Hertfordshire) presented a case study on an understanding of the kinetic growth of hygroscopic aerosols in the respiratory tract and Mark Gumbleton (University of Cardiff) discussed the impact of lung transporters on inhaled drug pharmacokinetics. An up-date on the work of the Network in supporting industrial and academic consortia in open innovation initiatives was also presented. The presentations from this workshop are also available on the Drugs in the Lungs website.

UK PharmSci 2013: A session on airway mucus

This year, the Drugs in the Lungs Network will organize a session of the Academy of Pharmaceutical Sciences annual conference. The session, to be held on Wednesday, September 4, will address airway mucus and its influence on drug delivery via the respiratory tract. The session will include talks on the biology and chemistry of airway mucus, drug-mucus interactions and a panel discussion.

Future meetings

Proposals under consideration as topics for future meetings include drug solubility and dissolution in lung lining fluid and the pharmacokinetics/pharmacodynamics of inhaled medicines.

The Drugs in the Lungs Network is happy to receive all other suggestions, collaborate in the organization of symposia or facilitate initiatives for open innovation in the area of inhalation biopharmaceutics. Please contact Ben Forbes (ben.forbes@kcl.ac.uk) for further information.