

## Abstracts' Service

### The Cough Cylinder: A Tool to Study Measures Against Airborne Spread of (Myco-) Bacteria

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**Background.** 'Covering your cough' reduces droplet number, but its effect on airborne pathogen transmission is less clear. The World Health Organization specifically recommends cough etiquette to prevent the spread of *Mycobacterium tuberculosis*, but implementation is generally poor and evidence supporting its value is lacking.

**Methods.** We constructed a model to assess 'real life' transmission risk by counting viable pathogens from aerosols produced by coughing patients, thus allowing the assessment of outward protection measures in a standardised fashion. During the validation process, we focused on rod-shaped bacteria as surrogates for *M. tuberculosis*.

**Results.** The Cough Cylinder enabled us to sample *Pseudomonas aeruginosa*, *Escherichia coli* and mycobacteria from aerosols produced by patients with cystic fibrosis, primary ciliary dyskinesia and tuberculosis. Pathogens in droplets and in airborne particles could be sampled. Delayed air sampling allowed specific measurement of persistent airborne particles.

**Conclusion.** This novel experimental system allows measurement of aerosol pathogen spread in a highly standardised fashion. It also offers the possibility to assess the impact of different interventions to limit aerosol transmission.

### Updating and Curating Metabolic Pathways of TB

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The sequencing of complete genomes has accelerated biomedical research by providing information about the overall coding capacity of bacterial chromosomes. The original TB annotation resulted in putative functional assignment of ~60% of the genes to specific metabolic functions, however, the other 40% of the encoded ORFs were annotated as conserved hypothetical proteins, hypothetical proteins or encoding proteins of unknown function. The TB research community is now at the beginning of the next phases of post-genomics; namely reannotation and functional characterization by targeted experimentation. Arguably, this is the most significant time for basic microbiology in recent history. To foster basic TB research, the Tuberculosis Community Annotation Project (TBCAP) jamboree

exercise began the reannotation effort by providing additional information for previous annotations, and refining and substantiating the functional assignment of ORFs and genes within metabolic pathways. The overall goal of the TBCAP 2012 exercise was to gather and compile various data types and use this information with oversight from the scientific community to provide additional information to support the functional annotations of encoding genes. Another objective of this effort was to standardize the publicly accessible *Mycobacterium tuberculosis* reference sequence and its annotation. The greatest benefit of functional annotation information of genome sequence is that it fuels TB research for drug discovery, diagnostics, vaccine development and epidemiology.

## Single Nucleotide Polymorphisms in *Mycobacterium Tuberculosis* and the Need for a Curated Database

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Recent advances in DNA sequencing have led to the discovery of thousands of single nucleotide polymorphisms (SNPs) in clinical isolates of *Mycobacterium tuberculosis* complex (MTBC). This genetic variation has changed our understanding of the differences and phylogenetic relationships between strains. Many of these mutations can serve as phylogenetic markers for strain classification, while others cause drug resistance. Moreover, SNPs can affect the bacterial phenotype in various ways, which may have an impact on the outcome of tuberculosis (TB) infection and disease. Despite the

importance of SNPs for our understanding of the diversity of MTBC populations, the research community currently lacks a comprehensive, well-curated and user-friendly database dedicated to SNP data. First attempts to catalogue and annotate SNPs in MTBC have been made, but more work is needed. In this review, we discuss the biological and epidemiological relevance of SNPs in MTBC. We then review some of the analytical challenges involved in processing SNP data, and end with a list of features, which should be included in a new SNP database for MTBC.

## Of Flies, Mice and Men: A Systematic Approach to Understanding the Early Life Origins of Chronic Lung Disease

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Despite intensive research efforts, the aetiology of the majority of chronic lung diseases (CLD) in both, children and adults, remains elusive. Current therapeutic options are limited, providing only symptomatic relief, rather than treating the underlying condition, or preventing its development in the first place. Thus, there is a strong and unmet clinical need for the development of both, novel effective therapies and preventative strategies for CLD. Many studies suggest that modifications of prenatal and/or early postnatal lung development will have important implications for future lung function and risk of CLD throughout life. This view represents a fundamental change of current pathophysiological concepts and treatment paradigms, and holds the

potential to develop novel preventative and/or therapeutic strategies. However, for the successful development of such approaches, key questions, such as a clear understanding of underlying mechanisms of impaired lung development, the identification and validation of relevant preclinical models to facilitate translational research, and the development of concepts for correction of aberrant development, all need to be solved. Accordingly, a European Science Foundation Exploratory Workshop was held where clinical, translational and basic research scientists from different disciplines met to discuss potential mechanisms of developmental origins of CLD, and to identify major knowledge gaps in order to delineate a roadmap for future integrative research.

## The Relationship Between Maternal Adiposity and Infant Weight Gain, and Childhood Wheeze and Atopy

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**Background.** Obesity and asthma have increased in westernised countries. Maternal obesity may increase childhood asthma risk. If this relation is causal, it may be mediated through factors associated with maternal adiposity, such as fetal development, pregnancy complications or infant adiposity. We investigated the relationships of maternal body mass index (BMI) and fat mass with childhood wheeze, and examined the influences of infant weight gain and childhood obesity.

**Methods.** Maternal prepregnancy BMI and estimated fat mass (from skinfold thicknesses) were related to asthma, wheeze and atopy in 940 children. Transient or persistent/late wheeze was classified using questionnaire data collected at ages 6, 12, 24 and 36 months and 6 years. At 6 years, skin-prick testing was conducted and exhaled nitric oxide and spirometry measured. Infant adiposity gain was calculated from

skinfold thickness at birth and 6 months.

**Results.** Greater maternal BMI and fat mass were associated with increased childhood wheeze (relative risk (RR) 1.08 per 5 kg/m<sup>2</sup>,  $p=0.006$ ; RR 1.09 per 10 kg,  $p=0.003$ ); these reflected associations with transient wheeze (RR 1.11,  $p=0.003$ ; RR 1.13,  $p=0.002$ , respectively), but not with persistent wheeze or asthma. Infant adiposity gain was associated with persistent wheeze, but not significantly. Adjusting for infant adiposity gain or BMI at 3 or 6 years did not reduce the association between maternal adiposity and transient wheeze. Maternal adiposity was not associated with offspring atopy, exhaled nitric oxide, or spirometry.

**Discussion.** Greater maternal adiposity is associated with transient wheeze but not asthma or atopy, suggesting effects upon airway structure/function but not allergic predisposition.

## Research Resources for Tuberculosis at The National Institute of Allergy and Infectious Diseases

NIH, DMID TB programme

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Global control of tuberculosis (TB) requires the participation of multiple stakeholders that cross the spectrum of biomedical research, product development, and implementation and operational research. The National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health (NIH), plays a critical role in TB biomedical research and product development by directly supporting and leveraging other funding support strategies and providing research resources to

facilitate the translation of knowledge about TB into strategies and tools to more effectively combat disease. The primary mission of NIAID is to support high quality, peer reviewed, investigator initiated research that contributes to innovation in infectious disease research. It is also within the mission of NIAID to assure that research findings are translated into vaccines, diagnostics, and drugs to better prevent, diagnose, and treat this devastating disease.