BRITISH COUNCIL
英国文化教育协会
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2018 Researcher Links Workshop on Childhood respiratory disease in UK and China
儿童呼吸道疾病中英双边论坛

October 2018
Chongqing, China
2018年10月
中国 重庆

Organised by:

Supported by:

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Speaker Name (Given+Family)	Organisation	Email	
Prof Enmei Liu	**Chongqing Medical University**	emliu186@126.com	

Biography

Prof EM Liu earned her M.D. and Ph.D. degrees from Chongqing Medical University and the University of Hong Kong, respectively. She is Professor and Chief Physician of Department of Respiratory Medicine, Vice President of Lijia Campus, Children's Hospital of Chongqing Medical University. Editorial Board member of Journal of Pediatric Pharmacy, Clinic J Pediatric, Chinese Journal of Practical Pediatrics, and Chinese Journal of Pediatrics.

Her interest is molecular epidemiology of respiratory viruses in children and pathogenesis of respiratory syncytial virus. Her works may contribute to the understanding of RSV evolution and to the potential development of a vaccine and treatment against RSV. She has published over 40 original papers and supervised over 75 graduate students. She received 8 programs from National Natural Science Foundation of China. She was awarded the "1st Prize of Scientific and Technical Progress" of Chongqing, for "Childhood respiratory viral infection", The "7th Yong Scientist Award" of Chongqing.

Speaker Name (Given+Family)	Organisation	Email	
Prof Rosalind Smyth	UCL Great Ormond Street Institute of Child Health	rosalind.smyth@ucl.ac.uk	

Biography

Rosalind Smyth is Director of The Great Ormond Street Institute of Child Health at University College London, Honorary Consultant Respiratory Paediatrician and non-executive director of Great Ormond Street Hospital NHS Foundation Trust. She graduated in medicine from Clare College, Cambridge and Westminster Medical School and trained in paediatrics in London, Cambridge and Liverpool. Until September 2012, she was Professor of Paediatric Medicine in at the University of Liverpool and, from 2005-2012, was Director of the NIHR Medicines for Children Research Network, which supports all clinical research with children in England. Her research interests include clinical studies of viral/host interactions in RSV bronchiolitis, clinical trials and systematic reviews of treatments for childhood respiratory disease.

She is a Fellow and previous Council member of the Academy of Medical Sciences (UK). She has been a panel member of numerous national and international research funding and assessment bodies and the UK's 2014 Research Evaluation Framework. She was a member of the Medicine and Healthcare Products Regulatory Agency's Commission on Human Medicines (2009-2013) and chaired its Paediatric Medicines Expert Advisory Group (2002-13). She was awarded a CBE in the Queen's New Year's Honours list in 2015 for services to drug regulation for children. She chairs the UK Medical Research Council's Clinical Careers and Training Committee, is a Governor of the Health Foundation and a Trustee of the UK's Cystic Fibrosis Trust.

Speaker Name (Given+Family)	Organisation	Email	
Prof Stephen Hart	UCL Great Ormond Street Institute of Child Health	s.hart@ucl.ac.uk	

Biography

Stephen Hart obtained his PhD from the University of Cape Town then undertook a postdoc at St. Mary's, London for three years before joining the Institute of Child Health (ICH) as a postdoc then Lecturer. He was promoted to professor in 2012 and is currently Deputy Head of the Genetics and Genomic Medicines programme at ICH. He has worked in the field of genetic therapies for more than 20 years with more than 100 publications to his name. His current research activities include the development of gene therapy, including gene editing strategies, for the treatment of cystic fibrosis, primary ciliary dyskinesias and neuroblastoma. His group have developed novel synthetic nanoparticles for the delivery of nucleic acid therapeutics including siRNA, messenger RNA and CRISPR/Cas9 formulations. This work has also led to being named inventor on nine patents concerning nanoparticle delivery formulations. He is the lead investigator on a Strategic Research Centre grant funded by the Cystic Fibrosis Trust, developing CRISPR gene editing therapies for cystic fibrosis. In 2017 Stephen was elected to the board of directors of the American Society of Gene and Cell Therapy. He is a Senior Editor for the journal *Annals of Human Genetics,* a member of the editorial board for the journal *Genes* and an assistant editor for *Nature Scientific Reports.* In 2011 he raised the financial investment to become the scientific founder of Nanogenic Solutions Ltd, a UCL spin-out company, commercialising nanoparticle delivery formulations for genetic therapies. He has acted as a consultant to biotech companies including Ryboquin Ltd and Glaxo SmithKline.

Speaker Name (Given+Family)	Organisation	Email	
Dr Hannah Mitchison	UCL Great Ormond Street Institute of Child Health	h.mitchison@ucl.ac.uk	

Biography

Dr Hannah Mitchison, B.Sc., Ph.D., is a GOSH Children's Charity Reader in Molecular and Medical Genetics at University College London, based at the UCL Great Ormond Street Institute of Child Health (UCL GOS-ICH). Her research is focussed on understanding the genetic basis of an expanding category of inherited disorders affecting cilia, which are termed 'cilopathies'. Since 2008, she has co-directed the Ciliopathy Disorders laboratory with Professor Phil Beales, located in the UCL GOS-ICH Newlife Birth Defects Research Centre. Using genomic and cell biology approaches, her group has characterised mutations in multiple genes causing a respiratory ciliopathy called primary ciliary dyskinesia (PCD) and skeletal ciliopathies. She is now working towards better understanding of the disease biology and development of novel gene-targeted therapies for cilia disorders. She is on the management group of the UK Cilia Network, the 'BEAT-PCD' EU COST Action and leads the Ciliopathies subdomain of the 100,000 Genomes project Paediatric Genomic England Clinical Interpretation Partnership (GeCIP). She is a founder of the Ciliopathy Alliance, since 2010. She is a scientific advisor to the PCD Family Support Group and Jeune Syndrome Foundation, for whom she is a trustee. Together with Prof Beales she launched the biennial 'CILIA' conferences which were adopted as an EMBO conference series in 2012 and are now the major ciliopathy conferences for Europe. She is a current co-Chair of the 2019 Gordon Research Conference on Cilia, Mucus and Mucociliary interactions. In her talk, Dr Mitchison will discuss the medical impact of cilia and respiratory cilia diseases and how these diseases are currently recognised and diagnosed. She will summarise the current state-of-the-art in our understanding, of the molecular genetic basis of the growing spectrum of cilia diseases.

Speaker Name (Given+Family)	Organisation	Email	
Prof Christopher O'Callaghan	UCL Great Ormond Street Institute of Child Health	c.ocallaghan@ucl.ac.uk	

Biography

Chris has a strong interest in translational research and leads on this for the UCL Great Ormond Street Biomedical Research Centre. He has major interests in the biology of the ciliated epithelium in both rare and common diseases of the respiratory tract and in biological aerosols and aerosol drug delivery. His Doctorate of Medicine was on 'Aerosol Delivery to Infants' and his PhD was on 'Brain Ependymal Cilia'. He defined the movement of brain and respiratory cilia leading to the development of diagnostic testing for primary ciliary dyskinesia that has been adopted internationally (PCD). He established the national diagnostic centres for PCD in the UK and his centre has diagnosed over 500 patients. His current epithelial research focuses on restoration of ciliary function in PCD, reducing epithelial inflammation and the earliest time points of viral and bacterial co infection of the respiratory epithelium. Work on aerosols is currently focusing on the development of two novel drug delivery devices and a system for the delivery of biological agents and drugs to ciliated cell cultures.

Chris also has a major interest in multimedia education acting as an advisor for the WHO in this area. He founded the not for profit organisation World Medical Education (www.worldmedicaleducation.org) and was recently awarded a 'Principal Fellowship of the Higher Education Academy' (PFHEA).

Speaker Name (Given+Family)	Organisation	Email	
Prof Jürgen Schwarze	University of Edinburgh	jurgen.schwarze@ed.ac.uk	

Biography

Prof Jürgen Schwarze is the Edward Clark Chair of Child Life and Health at the University of Edinburgh.

He is a paediatrician specialised in allergy and respiratory medicine and an internationally recognised expert on immune mechanisms of RSV bronchiolitis and associated airway allergy. His research tries to understand immune and inflammatory mechanisms of viral bronchiolitis in infants and of associated recurrent wheeze and asthma development, focussing on innate immune cells and mediators and their interface with adaptive immunity. To this end, his group uses small animal models, human cells in vitro and clinical observational studies.

Prof Schwarze has published over 90 scientific papers with over 6500 citations and an H-index of 36.

After qualifying in medicine from Freiburg University, Germany, and training in paediatrics, Prof Schwarze started to work on immune responses in RSV bronchiolitis and allergic airway disease as a post-doctoral fellow at National Jewish Medical and Research Centre in Denver, Colorado. He has continued his research in this field at Ruhr-University Bochum (Germany), as a Wellcome Trust Senior Clinical Fellow at Imperial College London, and since 2007 at MRC-Centre for Inflammation Research at the University of Edinburgh.

Speaker Name (Given+Family)	Organisation	Email	
Dr Claire Smith	UCL Great Ormond Street Institute of Child Health	c.m.smith@ucl.ac.uk	

Biography

Dr Claire Smith obtained her PhD from the University of Leicester studying the immunological behaviour of novel vaccines against *Streptococcus pneumoniae*. In 2007 she was appointed to a Research Associate position in Prof Chris O'Callaghan's respiratory group to study the effect of respiratory pathogens on differentiated airway epithelial cell models in healthy and disease. The success of this work led to a renewal in funding in 2010.

In January 2012 she moved to UCL GOS Institute of Child Health. Here she established and continues to run a research tissue bank that collects and supplies researchers with valuable human respiratory material from patients and healthy volunteers. This fantastic resource facilitates different projects focussed on respiratory diseases and infections across UCL and externally. Dr Smith was appointed as Lecturer in 2015 and working with Prof Rosalind Smyth she has expanded the airway epithelial cell model to explore the behaviour of the neutrophil during respiratory syncytial virus (RSV) and bacterial infection.

Her current research explores how RSV targets the airway ciliated epithelial cells, whether immune cells (neutrophils) contribute to damage caused to the airway and how this is exacerbated in bacterial and viral co-infections. She is currently funded by the Wellcome Trust and ESCMID to explore the impact of binding RSV on pneumococcal infection. She is funded by MedCity to test combination novel antiviral therapies against RSV using the ciliated air-liquid interface model.

For more info visit her group page http://www.ucl.ac.uk/ich/research/infection-immunity-inflammation/respiratory-critical-care-anaesthesia/respiratory-infection-epithelial-biology-research-group

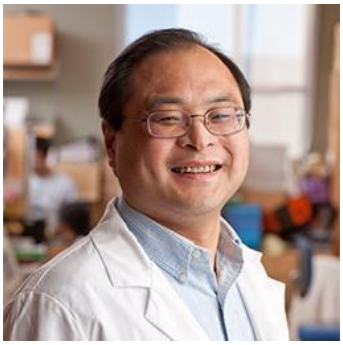
Speaker Name (Given+Family)	Organisation	Email	
Dr Colin Wallis	Great Ormond Street Hospital for Children NHS Trust	colin.wallis@gosh.nhs.uk	

Biography

Dr Colin Wallis is a Consultant Paediatrician in paediatric respiratory medicine at Great Ormond Street Hospital for Children (GOSH). He received his undergraduate training at the University of Cape Town and, after completing an MD degree, joined the paediatric registrar rotation at the Red Cross Children's Hospital in Cape Town. After additional jobs in the UK, and further experience in Canada, he joined the respiratory team at GOSH in 1993.

Dr Wallis has a specific interest in the care and management of children with chronic lung disease, in particular cystic fibrosis, and the child with long-term ventilatory needs, and is the respiratory representative on the GOSH NSCAG tracheal service. He is chairman of a UK working party looking at the needs of the chronically ventilated child and was awarded an NHS Health Technology Assessment grant to review the current status of paediatric long-term ventilation in the UK. He has also been awarded funding to evaluate the early changes in CF lung disease from the CF Trust together with researchers at the Institute of Child Health.

Dr Wallis is a senior examiner for the Royal College of Paediatrics and Child Health and past president of the British Paediatric Respiratory Society. He has published over 125 articles in peer-reviewed journals and is the author of several chapters in leading paediatric respiratory texts including the diagnostic aspects of cystic fibrosis. He is an associate editor for the Archives of Diseases in Childhood.

Speaker Name (Given+Family)	Organisation	Email	
Prof Wei Shi	Children's Hospital Los Angeles and Keck School of Medicine, USC	wshi@chla.usc.edu	

Biography

Wei Shi, MD, PhD, is a tenured Professor in the Developmental Biology and Regenerative Medicine Program at Children's Hospital Los Angeles and in the Department of Surgery at Keck School of Medicine, University of Southern California. Dr. Shi obtained his medical degree at Zhejiang Medical University in China and PhD degree at University of Tennessee, Memphis, US. He had his postdoctoral training on lung development and cell/molecular biology at Children's Hospital Los Angeles before he was appointed as the faculty member at University of Southern California. Dr. Shi has an international reputation as a thought leader in lung developmental biology and the related pulmonary diseases. He has been studying growth factor signaling in regulating lung development, injury repair and regeneration with the support of more than $9,000.000 from NIH and other funding agencies for over a decade. Dr. Shi has published more than 70 peer-reviewed articles in this field. In the past a few years, Dr. Shi's research focuses on lung mesenchymal progenitor cells in lung development and pulmonary diseases using different approaches including novel transgenic mouse models. In addition, Dr. Shi is also serving as academic editor and editorial board member for several journals including PLoS One, American Journal of Physiology-Lung Cellular and Molecular Physiology, and European Respiratory Journal.

Speaker Name (Given+Family)	Organisation	Email	
Prof Xiaodong Zhao	Chongqing Medical University	zhaoxd530@aliyun.com	

Biography

Dr. Xiaodong Zhao was graduated from the Department of Pediatrics, Chongqing Medical University in 1993 and received his doctorate degree from the same University in 1998 under the supervision of Prof. Xiqiang Yang. He finished his research postdoctoral training in University of Alabama at Birmingham from 2002 through 2004 in the field of Virology. Since returning to Chongqing in 2004, he has been focusing on primary immunodeficiency diseases. HIs team has established an advanced immune function assessment and PID molecular diagnostic platform to provide diagnostic and transplanting services for PID children from all over the country. He founded the PID summer school since 2011, and so far more than 300 pediatricians have been trained, and they are distributed in 30 provinces and cities in China to provide better clinical services for PID patients in the most populous country in the world . The main research interests of his team are pathogenesis of primary immunodeficiency diseases, especially immune cell differentiation and memory establishment in cytoskeleton related diseases such as Wiskott-Aldrich syndrome and DOCK8 deficiency; as the future directions, his team is also focusing on identifying novel genes in PIDs and developing new therapeutic strategies for PIDs. As the PI, he led the first large-scale research project on PID in mainland China. Through the unremitting efforts of nearly past four years from his entire team and colleagues from all over the country, the level of PID diagnosis, treatment and prevention in mainland China has been significantly improved. He published more than 60 articles in English journals including some of them in high impact journals such as Blood, J Allergy Clin Immunol, etc.

Participant Name (Given+Family)	Organisation	Email	
Linyan Ying	Chongqing Medical University	yinglinyan2013@163.com	

Abstract

Background Th2 and regulatory T cells (Tregs) have been postulated to have critical roles in the pathogenesis of allergic asthma. Cytotoxic T lymphocyte antigen 4 immunoglobulin (CTLA4Ig) gene-modified dendritic cells (DC-CTLA4Ig) have the potential to reduce Th2 cells and induce Tregs.

Methods In the present study, we evaluated the therapeutic effects and potential mechanisms of the adoptive transfer of DC-CTLA4Ig into mice in an experimental model of asthma. BALB/c mice were sensitised with ovalbumin (OVA) and challenged with aerosolised OVA for 7 days. Just prior to the first challenge, DC-CTLA4Ig, DCs or DCs transfected with AdGFP (DC-GFP) were injected intravenously into mice.

Results The administration of DC-CTLA4Ig reduced AHR, relieved asthmatic airway inflammation, and decreased the numbers of esosinophils in the BALF in OVA-sensitised/challenged mice compared to these mice without treating with DCs. In addition, DC-CTLA4Ig altered the balance of Th1/Th2 cytokine production in the lungs with increased IFN-γ levels and decreased IL-4 levels, decreased the percentage of Th2 and increased both the percentage of Th1and Tregs in the lungs.

Conclusion This research demonstrates that DC-CTL4Ig effectively reduces AHR and prevents airway inflammation in OVA-sensitised/challenged mice, which most likely due to attenuated secretion of Th2 cytokines and increased secretion of Th1 cytokines in local airway, and the correction of the pulmonary imbalance between Th1/Th2 cells and Th2/Tregs.

Participant Name (Given+Family)	Organisation	Email	
Qi Gao	Capital Medical University	doublelight1179@sina.com	

Abstract

Background Allergy march generally refers to progression of allergic diseases from infantile food allergy to the development of asthma and allergic rhinitis (AR). Effective measure to arrest the allergy march is promising while unclear yet. This study aimed to investigate allergy march in Chinese children with infantile food protein allergy (FPA) with a special focus on the effect of different formula interventions.

Methods From 2008 to 2010, 153 infants diagnosed with FPA were recruited in five tertiary hospitals across China. The patients were randomly treated with amino-acid-based formula or soy-protein-based formula for a period of 3 months. Long-term follow-up was performed when they reached early school age, using questionnaires, physical examinations, and serum-specific immunoglobulin E test to assess their allergy status.

Results The overall response rate was 73.20% at follow-up. In the patients' early school years, the prevalence of physician-diagnosed AR and asthma were 43.75% and 23.21%, respectively. Only 40% of the subjects remained positive for food sensitizations upon follow-up. Twenty-six subjects who received aeroallergen screening tests in infancy all proved negative, but upon follow-up, 65.57% were sensitized to aeroallergens ($P=0.005$). We found that persistent AD and familial history of allergic diseases were independent risk factors for developing airway allergies (OR 3.057 and 3.420, $P<0.05$). No significant differences between the effects of amino-acid-based formula and soy-protein-based formula were observed on children's allergy march.

Conclusion A high proportion (47.32%) of Chinese infants with early allergic symptoms developed respiratory allergies by their early school years. Most food-sensitized infants outgrew their condition several years later, but then aeroallergen sensitization often occurred. Early intervention with amino-acid-based formula showed no advantages over soy protein-based formula feeding with respect to arresting the allergy march at least till early school ages.

Participant Name (Given+Family)	Organisation	Email	
Zhen Qin	Shanghai Jiaotong University	sjtuqinzhen@foxmail.com	

Abstract

To assess the effectiveness and safety of clarithromycin in patients with chronic rhinosinusitis with or without nasal polyps (CRSwNP/CRSsNP).

Methods We searched all the published RCTs without limiting specific languages, regions or publication years in the following electronic database: The Cochrane Library, EMBASE, MEDLINE, PubMed, CBM, CNKI and Wanfang. We included studies with patients in which researchers reported on prespecified outcomes and had an intervention arm receiving any dosage or treatment duration of clarithromycin after diagnosed with chronic rhinosinusitis with or without nasal polyps (CRSwNP/CRSsNP). Only randomized controlled trials (RCTs) were included for efficacy. RCTs and nonRCTs were included for safety outcomes. Two reviewers extracted data. 34 studies with available data were included.

Results We found moderate-strength evidence that participants with CRSsNP received clarithromycin combined with other therapies had lower total VAS score of clinical symptoms than who did not received clarithromycin. There was moderate-strength evidence that participants received medium-term clarithromycin combined other therapies had lower Lund-Mackay score than other therapies alone. There was insufficient evidence on QoL. There was no statistical difference between the two compared groups on incidence of adverse events.

Conclusion In patients with chronic rhinosinusitis with or without nasal polyps (CRSwNP/CRSsNP), clarithromycin may reduce VAS score of clinical symptoms and Lund-Mackay score of endoscopic evaluation and CT scans. There is no significantly obvious adverse events when using clarithromycin.

Participant Name (Given+Family)	Organisation	Email	
Yiquan Xiong	Si Chuan University	xiongyq2018@126.com	

Abstract

A succession of studies has been published to show the association between HPV infection and adverse pregnancy outcomes with controversial results. The aim of this study was to estimate the impact of human papillomavirus (HPV) infection on spontaneous abortion, spontaneous preterm birth (sPTB), pregnancy rate of females undergoing assisted reproductive technologies (ART), and spontaneous abortion of ART pregnancy.

Methods

PubMed, Medline, Embase, and the Cochrane Library were searched until December 16, 2016. The OR or relative risk (RR) with its corresponding 95% CI were selected as effect size. Subgroup analysis of HPV genotype infection (high-risk HPV [HR-HPV] or indiscriminate genotype) was performed. Statistical analysis was conducted using STATA 12.0.

Results

Eighteen studies were included. Eight studies revealed no significant association between HPV infection and spontaneous abortion (OR 1.40, 95% CI 0.56-3.50). However, subgroup analysis showed indiscriminate genotype HPV infection increased the ratio of spontaneous abortion with OR of 2.24 (95% CI 1.37-3.65), while HR-HPV infection had no significant effect (OR 0.65, 95% CI 0.21-1.98). The results indicated that HR-HPV infection was a risk for sPTB with a pooled OR of 2.84 (95% CI 1.95-4.14). HPV infection was found to be independent of the ART-based clinical pregnancy rate (RR 1.04, 95% CI 0.64-1.70) and spontaneous abortion of ART pregnancy (RR 1.47, 95% CI 0.86-2.50).

Conclusion

Indiscriminate HPV genotype infection can increase the risk of spontaneous abortion and HR-HPV infection was a risk factor for sPTB. However, there was not enough evidence to indicate the association between HPV infection and pregnancy rate of ART, and spontaneous abortion of ART pregnancy. Different genotypes of HPV infection may play a discrepant role in adverse pregnancy outcomes.

Participant Name (Given+Family)	Organisation	Email	
Yanli Zhang	Capital Medical University	condi_zhangyl@qq.com	

Abstract

CFTR gene mutations have been suggested to be involved in Cystic fibrosis (CF),which is the most common reason for severe chronic lung disease in childhood. Our previous study indicates that the common mutations and phenotypes identified in Chinese CF patients are different from the Caucasians .The research of mechanisms and treatment for Chinese CF patients is rare.

Methods

In this project, we try to use peripheral blood of the pedigree with CFTR heterozygous mutation, the original generation of cultivating immortalized lymphocyte and the human small airway epithelial cells model of mutation, with the methods of RT-PCR, immunofluorescence, ion fluorescent probe and ELISA.

Results

The complex heterozygous mutation can affect the expression, cell surface localization and the ion channel function of CFTR and ENaC. (Not Completed)

Conclusion

The complex heterozygous mutation lead to CF lung disease.

Participant Name (Given+Family)	Organisation	Email	
Xiaohong Xie	Chongqing Medical University	68621472@qq.com	

Abstract

Bronchiolitis is a lower respiratory tract infection that occurs in infants with symptoms of wheezing, and respiratory syncytial virus (RSV) is the most common cause. Severe RSV infection in early life is an important risk factor for subsequent persistent wheezing and recurrent wheezing, and might associated with development of airway obstructive illness such as asthma and COPD. Glucocorticoids are potent inhibitors of inflammatory processes, however, steroids fail to relieve wheezing in children with RSV infection and the mechanisms are unknow.

Methods:

In our study, the anti-inflammatory effects of dexamethasone (DEX) were evaluated in RSV-infected BALB/C mice model. Results have shown that DEX failed to inhibit airway inflammation and airway hyperresponsiveness (AHR) induced by RSV, and similar results were observed when MAPK inhibitors were added. Series of experiments were designed to investigate the mechanisms of corticosteroid insensitivity in aspects of pathogen-host interaction and the results are shown as follows:

Results

(1) glucocorticoid receptor (GR) protein were down-regulated in nasopharyngeal aspirate of patients with RSV infection,lung tissue of RSV infected mice and RSV infected-A549 cells. Suppressed nuclear location and nuclear translocation of GR were found in lung tissue of RSV infected mice and RSV infected-A549 cells accompanied with down-regulation of anti-inflammatory gene, and Importin13 protein were down-regulated simultaneously. Quantity of GR nuclear translocation was increased by RSV NS1 specific siRNA interfering in RSV infected cells. NS1 of RSV, GR and importin 13 were found to be able to combined with each other by Co-IP and ST-pull down assay. The results suggest that defective of GR nuclear translocation is one of mechanisms of corticosteroid insensitivity of RSV induced inflammation, which is related to the competitive combination of RSV NS1 protein with importin13 protein. (2) TRIF protein was up-regulated during acute phase of RSV infection, which DEX failed to inhibit. RSV-induced airway inflammation and AHR during acute phase was TRIF dependent. TRIF protein maintained high level after 2 weeks of RSV infection, accompanied with no vital RSV action, and anti-inflammatory effect of DEX was blocked. With previous studies of our group that RSV induced airway inflammation and AHR during acute and chronic phase of RSV infection were suppressed by down-regulating TRIF when resveratrol was added, we presumed that TRIF-dependent inflammation is characterized by corticosteroid insensitivity, also is an independent factor involved in corticosteroid insensitivity.

Conclusion

The scientific significance of our study is to find out the differences of inflammation mechanism in RSV infection between acute and chronic course. RSV-NS1 protein and host-TRIF dependent signals are contributed to inflammation during acute course, and TRIF-dependent pathway is involved to inflammatory response in chronic course. These results might provide evidence for administrating individual therapeutic strategies to patients with RSV infection, as well as developing anti-inflammatory agent specific for TRIF-dependent pathway.

Participant Name (Given+Family)	Organisation	Email	
Li Lin	Wenzhou Medical University	linli97@126.com	

Abstract

Streptococcus pneumoniae is an important pathogen of pneumonia in human. Human alveolar epithelium acts as an effective barrier and is an active participant in host defense against invasion of bacterial by production of various mediators. Sirtuin 1 (SIRT1), the prototypic class III histone deacetylase, is involved in the molecular control of lifespans and immune responses. This study aimed to examine the role of SIRT1 in mediating S. pneumoniae-induced human β-defensin-2 (hBD2) and interleukin 8(IL-8) expression in the alveolar epithelial cell line A549 and the underlying mechanisms involved.

Methods

A549 cells were infected with S. pneumoniae for indicated times.

Results

Expose of A549 cells to S. pneumoniae increased the expression of SIRT1 protein, hBD2 and IL-8 mRNA and protein. The SIRT1 inducers resveratrol enhanced S. pneumoniae induced gene expression of hBD2 but decreased IL-8 mRNA levels. Blockade of SIRT1 activity by the SIRT1 inhibitors nicotinamide reduced S. pneumoniae induced hBD2 mRNA expression but increased its stimulatory effects on IL-8 mRNA. S. pneumoniae induced activation of extracellular signal-regulated kinase (ERK) and p38 mitogen-activated protein kinase (MAPK). SIRT1 expression was attenuated by selective inhibitors of ERK and p38 MAPK. The hBD2 mRNA production was decreased by pretreatment with p38 MAPK inhibitor but not with ERK inhibitor. Whereas the IL-8 mRNA expression was controlled by phosphorylation of ERK.

Conclusion

These results suggest that SIRT1 mediates the induction of hBD2 and IL-8 gene expression in A549 cell by S. pneumoniae. SIRT1 may play a key role in host immune and defense response in A549.

Participant Name (Given+Family)	Organisation	Email	
Li Hua	Shanghai Jiao Tong University	huali991229@163.com	

Abstract

IL13, IL4, IL4RA, FCER1B and ADRB2 are important inflammatory genes associated with immunoglobulin E levels. This study attempts to determine whether there are gene–gene interactions in the five genes among asthmatic children of Chinese Han nationality.

Methods

Nine single-nucleotide polymorphisms (SNPs) in the five genes were genotyped in 1000 asthmatic children and 1000 healthy controls using TaqMan real-time quantitative polymerase chain reaction. Multifactor-dimensionality reduction method was applied for the analysis.

Results

A four-way gene-gene interaction model consisting of IL13 rs20541, IL4 rs2243250, ADRB2 rs1042713 and FCER1B rs569108 was chosen as the optimal one for determining asthma susceptibility (testing balanced accuracy = 0.6089, cross-validation consistency = 10/10, P = 6.98E-05). Each of the four SNPs was identified to have an independent association with childhood asthma (G allele of rs20541, odds ratio (OR) = 1.24, P = 1.23E-03; T allele of rs2243250, OR = 1.25, P = 3.81E-03; A allele of rs1042713, OR = 1.29, P = 6.75E-05; G allele of rs569108, OR = 1.27, P = 3.86E-03). Individuals homozygous for the risk alleles at all the four loci (rs20541 GG, rs2243250 TT, rs1042713 AA and rs569108 GG) had a significantly higher risk of asthma compared with those without any risk homozygotes (OR = 13.55, P = 4.28E-03), and also greater than those with less than four risk homozygotes (OR = 10.09, P = 6.51E-03).

Conclusion

Our results suggest that IL13 rs20541, IL4 rs2243250, ADRB2 rs1042713 and FCER1B rs569108, four SNPs with significant sole effect on asthma, interact to confer a higher risk for the disease in Chinese Han children.

Participant Name (Given+Family)	Organisation	Email	
Hongmin Fu	Kunmin Medical University	510844660@qq.com	

Abstract

Hyperoxia therapy is a useful part of treatment for patients with acute and chronic cardiovascular and pulmonary diseases. However, prolonged exposure to hyperoxia could deteriorate ALI. Acute exposure to hyperoxia has been shown to induce lung inflammation and injury, leading to an impairment in respiratory function. It is been reported that the hyperoxia-induced injury is mediated by both accumulation of inflammatory factors and direct insult of reactive oxygen species.

Calcitonin gene-related peptide (CGRP) is a 37 amino acid neuropeptide, which is the predominant neuromediators to induce vasodilation and neurogenic inflammation. Recent study showed that CGRP also plays a role in anti-inflammatory actions and tissue repair, as it decreases interleukine-8 secretion, suppresses the formation of reactive oxygen species (ROS) and induces proliferation in epithelium. Whether CGRP has the same effects on hyperoxia-injured alveolar epithelial cell II (AEC II) is unknown. The present study was designed to evaluate the role of CGRP in a hyperoxic cell model (60% oxygen for 24 hours) in AEC II isolated from fetal rat at 19-20 d gestational age, and to investigate whether the mechanism involved in DNA damage repair.

Methods

AEC Ⅱ were isolated from 19d fetal rat lung and cultured for 12h to attach. Then AEC Ⅱ were randomly divided into four groups: air group, hyperoxia group, hyperoxia plus CGRP group, hyperoxia plus CGRP and CGRP8-37 group. AEC Ⅱ of air group and hyperoxia group were exposed to 21% or 60% oxygen respectively for 24h while hyperoxia plus CGRP group were added with CGRP and hyperoxia plus CGRP and CGRP8-37 group with CGRP and CGRP8-37(CGRP receptor antagonist) before placed into 60% oxygen. Concentrations of maleic dialdehyde(MDA), superoxide dismutase(SOD) and total antioxidant capacity (TAOC) in culture cells were detected by ultraviolet spectrophotometer. Reactive oxygen species (ROS) and apoptosis rate of AECII were analyzed by flow cytometry and the mRNA level of surfactant associated protein C (SPC) was measured by RT-PCR.

Results

The levels of MDA, ROS and apoptosis cell number were increased whereas TAOC, SOD and SPC mRNA expression declined in hyperoxia group compared with those in air group（$P<0.01$）. Reversely, MDA , ROS and apoptosis rate were significantly lower and levels of TAOC, SOD and SPC mRNA expression were significantly higher in group hyperoxia plus CGRP group than in hyperoxia group or hyperoxia plus CGRP and CGRP8-37 group.

Conclusion

Exposure to 60% oxygen for 24h could cause oxidative injury, induce apoptosis and decrease SPC mRNA level of AECII in vitro in premature rats, while CGRP may play a protective role against hyperoxic lung injury by antioxidant, inhibition of AEC apoptosis and promotion of the SPC mRNA expression.

Participant Name (Given+Family)	Organisation	Email	
Nan Yang	China Medical University	syyn719@163.com	

Abstract

Epigallocatechin gallate (EGCG) is a polyphenol that is found in green tea that has been shown to ameliorate airway inflammation in an ovalbumin-sensitized asthmatic mouse model. The purpose of this study was to investigate whether the immunomodulatory and anti-inflammatory effects of EGCG by enhancing the regulatory T cell (Treg) in this model.

Methods

Female BALB/c mice were sensitized and challenged with ovalbumin by intraperitoneal injection. EGCG was administered to asthmatic mice intraperitoneally one hour before each OVA challenge. Airway hyperresponsiveness (AHR) was measured, and lung inflammatory infiltrates were assessed by hematoxylin and eosin (HE) staining. Serum OVA-specific IgE level and Interleukin-10 (IL-10) levels in the bronchoalveolar lavage fluid (BALF), serum, and splenocyte culture supernatants were measures by ELISA. Flow cytometry was used to assess the effects of EGCG on the number of CD4+CD25+Foxp3+Treg cells in the splenocytes and real-time PCR was used to measure the expression of Forkhead box P3 (Foxp3) mRNA in the lung tissue.

Results

The results showed that administration of EGCG significantly decreased AHR and OVA specific IgE in the serum, increased IL-10 levels in the BALF, serum, and splenocyte culture supernatant, and the number of CD4+CD25+Foxp3+Treg cells in the splenocytes in asthmatic mice. Administration of EGCG also ameliorated airway inflammation and eosinophil infiltration in asthmatic mice.

Conclusion

These results suggested that EGCG likely ameliorated OVA-induced airway inflammation by increasing the production of IL-10, the number of CD4+CD25+Foxp3+Treg cells and expression of Foxp3 mRNA in the lung tissue, and it could be an effective agent for treating asthma

Participant Name (Given+Family)	Organisation	Email	
Yuqing Wang	Soochow University	wang_yu_qing@126.com	

Abstract

Protracted bacterial bronchitis (PBB) is the common cause of chronic cough in children worldwide, but its etiology has not been fully recognized in China.

Methods

We retrospectively investigated a total of 66 hospitalized infants under the age of three years with chronic wet cough enrolled in the Affiliated Children's Hospital of Soochow University from October 2010 to March 2014. All patients underwent bronchoscopy and broncho-alveolar lavage (BAL) samples were processed for microbiological and cytological analysis.

Results

Of 66 patients with wet cough, 50 (75.8%) were diagnosed with PBB. In the PBB group, wet cough was accompanied by wheezing (90%). Airway malacia were identified in 22 cases (44%). The clinical manifestations of PBB with airway malacia did not differ from those without malacia. Haemophilus influenzae (47.4%) and Streptococcus pneumoniae (36.8%) were the most commonly identified pathogens. Furthermore, CD3+ and CD3+CD4+ cells were significantly lower in the PBB group ($p < 0.01$), while CD19+, CD16+CD56+ and CD23+ cells were elevated ($p < 0.01$) in the PBB group.

Conclusion

Our study revealed PBB is an important cause of chronic wet cough in Chinese infants, and that changes of lymphocyte subsets are observed in children with PBB. Airway malacia frequently co-existed with PBB, but did not exacerbate the disease.

Participant Name (Given+Family)	Organisation	Email	
Yiheng Zan	West China Second University	yihenghx@163.com	

Abstract

To investigate the pathophysiological development of airway inflammation in different stages of asthma mouse model.

Methods

Female BALB／c mice were randomly divided into control group (group C) and asthma group (group A). Then divided by atomization time into 3-days groups, 7-days group, 3-weeks group, 5-weeks group, 6-weeks group and 10-weeks group. Each group had 8 mice, all 96 mice. Group C and group A sensitized twice by intraperitoneal injection on day 1 and day 14. From the day 21, the two groups were incubated with saline or 5% ovalbumin (OVA) solution respectively. The atomization frequency of 3-days group and 7-days group was 30 minutes daily, while the atomization frequency of other time groups was 30 minutes every other day. The pulmonary inflammation was analyzed by hematoxylin-eosin (HE) staining in lung tissue.

Results

Compared with group C, the peribronchial inflammation score and whole lung inflammation score of group A were significantly higher at 3-days to 6-weeks group ($P < 0.05$); there was no significant difference at 10-weeks ($P > 0.05$); the perivascular inflammation score of group A was significantly higher at all time groups($P < 0.05$). The score of the group A gradually reached the peak from 3-days to 3-weeks, and then decreased.

Conclusion

Inflammation started in the acute phase, gradually increased and reached the peak at 3 weeks, then decreased because of tolerance and it can't recover. The Infiltration of perivascular inflammation was higher than that of peribronchial infiltration.

Participant Name (Given+Family)	Organisation	Email	
Na Zang	Chongqing Medical University	zangna1214@126.com	

Abstract

Respiratory syncytial virus (RSV) infection is the major cause of respiratory tract infection in infants worldwide for which no vaccine or antiviral treatment is available. Previously we demonstrated that PCFs degeneration obviously increased IFN-α/β induction, STAT1 activation and reduced virus titer upon RSV infection, and correlated with alleviated inflammatory responses. In this study, we will investigate how PCFs affects type I interference responses.

Methods

Female PCF-degenerated mice and intact mice (6-8 weeks) were inoculated with 1.8 *107 PFU RSV (100 μl). IFN-α, IFN-β, SP, VIP and CGRP in BALF were tested by ELISA. RIG-I, TLR3, TLR4 and Mx1 mRNA expression were measured by Q-PCR. The levels of STAT1 and pSTAT1 were detected by Western blot. The virus titration in lung homogenation was determined by plaque assay.

Results

The study demonstrated that PCFs degeneration enhanced RSV-induced antiviral responses not only by inducing IFN-α/β production, STAT1 activation, but also upregulated Pattern recognition receptors (PRRs) and Interferon-stimulated genes (ISGs). Neuropeptides detection showed Vasoactive intestinal peptide (VIP) increased in PCF-degenerated mice. VIPhyb (a pan VIP receptors antagonist) treatment suppressed RSV-induced antiviral responses in PCF-degenerated mice and increased virus titers, while VIP and VPAC1 agonist treatment enhanced antiviral responses in intact mice and reduced virus titers.

Conclusion

We concluded that VIP involved in PCFs-mediated antiviral responses upon RSV infection through IFN-α/β-STAT1 signaling. The study suggested that targeting PCFs activation represents an alternative strategy for RSV infection, and the possibility that VIP promotes antiviral responses upon RSV infection potentiates new pharmaceutical applications of this neuropeptide.

Participant Name (Given+Family)	Organisation	Email	
Weihan Xu	Capital Medical University		

Abstract

Bronchiolitis obliterans (BO) is an uncommon disorder in children characterized by the persistence of continuous obstructive respiratory symptoms and an inflammatory process that obliterates the small airways, notably following severe lower respiratory tract infections. However, most previous study have been reported regarding post-transplant BO, not post-infectious BO. Accumulating evidence indicates that adaptive immunity plays important roles in the pathogenesis of BO, and different T cells subsets are identified in BO patients and animal models. Our project aims to analyse the cytokine profiles of CD4+T cells in patients with post-infectious BO, and explore associations between CD4+T cells subsets and clinical characteristics, thereby to provide new insight into the mechanisms of adaptive immunity in post-infectious BO.

Methods

Bronchoalveolar lavage (BAL) samples were obtained from 10 children with post-infectious BO and 6 children with foreign bodies in bronchi as controls. Blood samples were obtained from 8 children with post-infectious BO and 6 children with foreign bodies in bronchi as controls. The proportions of CD4+T cells subsets and neutrophil were evaluated using flow cytometry.

Results

In peripheral blood and BAL, a significantly increased proportion of Th17 and Th1 cells was demonstrated in post-infectious BO children, when compared with controls ($p<0.05$). Proportion of neutrophil was increased in children with post-infectious BO compared to controls, and correlated with percentage of Th17 cells ($r=0.463$; $p<0.05$). The proportion of circulating Treg showed no difference in post-infectious BO children and controls, even though there was a trend toward disturbed homeostasis among subsets of Tregs in post-infectious BO children.

Conclusion

Th17 and Th1 cells in BAL and blood are increased in post-infectious BO children, suggesting there are persistent airway inflammation and systemic inflammation, may play an important role in post-infectious BO progression.

Participant Name (Given+Family)	Organisation	Email	
Yuanyuan Zhang	Zhejiang University	17932846@qq.com	

Abstract

Excessive immune response against pathogens may play an important role in refracory Mycoplasma pneumoniae pneumonia (RMPP). The aim of this study was to elucidate the associations between cytokines and the prediction of RMPP in school-aged patients.

Methods

Retrospective analysis was performed on school-aged children with Mycoplasma pneumoniae pneumonia (MPP) hospitalized in our hospital between January 1, 2011 and December 31, 2015. The clinical charcteristics, including the cytokines in serum between the RMPP group and the general Mycoplasma pneumoniae pneumonia (GMPP) group were compared and the predictive values of RMPP were explored.

Results

Of total 180 patients, 115 patients were in the GMPP group, 65 were in the RMPP group. We found the levels of cytokines, including nterleukin (IL)-6, IL-10, interferon gamma (IFN-γ) in RMPP group were significantly higher than those in GMPP group ($P<0.01$). In ROC curve analysis, IL-10 and IFN-γ were useful for differentiating patients with RMPP from those with GMPP. Logistic regression analysis showed that the IL-10≥3.65 pg/ml and IFN-γ≥29.05 pg/ml were significant predictors regarding to RMPP. Additionally, a positive correlation between serum IL-10 and IFN-γ concentrations was observed.

Conclusion

IL-10 and IFN-γ could be used as the good predictors of RMPP in school-aged children.

Participant Name (Given+Family)	Organisation	Email	
Ting Wang	Chongqing Medical University	360412157@qq.com	

Abstract

Brahmarelated gene1 (Brg1), a key chromatin remodeling factor, is associated with cell proliferation and migration in kidney and heart cells, but few reports have examined its role in airway epithelial cell. Airway epithelial injury, which is involved in the entire pathological process of asthma, is an important cause of recurrent asthma. Here, we studied the function of Brg1 in an ovalbumin (OVA)induced asthma model (lungspecific conditional Brg1 (Brg1) knockdown mice) and human bronchial epithelial 16HBE cells stably expressing Brg1 shRNA.

Results

Our results showed that high expression of Brg1 was detected in asthmatic children and in mouse models. Brg1 mice showed improved airway hyperresponsiveness (AHR) and bronchial epithelial integrity, along with reduced inflammatory cell infiltration and airway mucus secretion, when challenged with OVA. Furthermore, cell proliferation, migration, and expression of Ecadherin increased in 16HBE cells in which Brg1 was silenced.

Conclusion

We further demonstrated that Brg1 bound to and inactivated a critical region (-86/+60 bp) within the Ecadherin promoter in bronchial epithelial cells. Thus, Brg1 might act as an important regulator of airway epithelial integrity in asthma progression and might be a novel therapeutic target.

Participant Name (Given+Family)	Organisation	Email	
Qingyuan Wu	Nanjing Medical University	827504565@qq.com	

Abstract

Background Pulmonary embolism is rare in children but does occur. Its clinical manifestations and risk factors are differs from those of adults.

Methods

Through the analysis of cases, to improve the cognition of clinicians on pulmonary embolism(PE) in children. The clinical information included clinical features, treatment and prognosis of 8 children with PE, who were admitted from July 2013 to June 2018 in Nanjing children's hospital Affiliated to Nanjing Medical University.

Results

In 8 cases, there were four male and four female, with an average age of 6.23±2.53 years old (3.83-11.75 years old). No significant difference was found between the two genders for incidence of PE ($P > 0.05$). Infection was the primary risk factor of PE. Among the 8 cases, 7 were confirmed with infection of mycoplasma pneumoniae, 1 with staphylococcus aureus. The 7 children infected by mycoplasma pneumoniae were all diagnosed for severe mycoplasma pneumonia. Sixty two point five percent children (5/8 cases) had typical PE symptoms including chest pain, chest tightness and dyspnea. These symptoms could be located accurately to the affected side of chest. The other 87.5% children (3/8 cases) had no characteristic symptom. In these patients, PE were diagnosed by enhanced chest computer tomography for a sustained increased level of D-Dimer and/or a unsatisfactory absorption of lung inflammation. Laboratory indicators as D-Dimer, lactate dehydrogenate, and erythrocyte increased obviously in these patients. Eighty seven point five percent embolization (7/8 cases) occurred in the right pulmonary artery, while one case (1/8 cases) occurred in the right pulmonary artery trunk, and the rest 6 cases (6/8 cases) occurred in the right lower pulmonary artery. Twelve point five percent embolization (1/8 cases) occurred in the left lower pulmonary artery.

Conclusion

Infection was the main risk factor for pulmonary embolism, especially in children with severe pneumoniae pneumonia. Embolization occurred in the right pulmonary artery more often than the left pulmonary artery. Most of the children have a ideal prognosis.

Participant Name (Given+Family)	Organisation	Email	
Jun Xie	Capital Medical University	cyxiejun@126.com	

Abstract

My long-term research objective is to elucidate relationship between clinical characteristics and immunological mechanisms of virus induced wheezing. I also investigate the role of RSV NS1 protein in HMGB1induced chronic inflammation, and glucocorticoids function in RSV induced acute and chronic airway inflammation. Furthermore my study try to clarify that insensitive of glucocorticoid in RSV induced airway inflammation, the role of neutrophil in RSV induced glucocorticoid insensitivity, and the role of protein NS1 in chronic inflammation

Participant Name (Given+Family)	Organisation	Email	
Sisi Chen	Capital Medical University	237758321@qq.com	

Abstract

The type 2 immune response, induced by infection of respiratory syncytial virus (RSV), has been linked to asthma development, but it remains unclear how the response is initiated. We reported that the high mobility group box-1 (HMGB1) protein promotes the type 2 response in the later stage of RSV infection. In mice, we found that type 2 cytokines were elevated in the later stages, which were strongly diminished after administration of anti-HMGB1 antibodies. Further investigation revealed that HMGB1 expression was localized to CC10+ club cells in the lung. In the clinic, levels of HMGB1 in nasopharyngeal aspirates (NPA) in hospitalized infants with RSV-bronchiolitis [median (interquartile range) 161.20 ng/ml (68.06–221.30)] were significantly higher than those without lower respiratory tract infections [21.94 ng/ml (12.12–59.82); $P<0.001$]. Moreover, higher levels of HMGB1 correlated with clinical severity. These results reveal a link between viral infection and the asthma-like type 2 responses that are associated with long-term consequences.

Participant Name (Given+Family)	Organisation	Email	
Leiqiong Gao	Capital Medical University	Gaoqiong2007220821@163.com	

Abstract

Human respiratory syncytial virus (RSV) is a leading cause of bronchiolitis in infants. RSV infection induced inflammatory is not responsive to glucocorticoids (GC) in nature. The specific mechanism still unclear. Reduction of GR is one of the important reason. However, there is still no study about how RSV infection reduce GR mRNA and protein expression. The miRNAs are critical for GR mRNA degradation. Here we first find that the miR29a is upregulated and both the GR mRNA and protein are downregulated in RSV-infected infants. In line with this data, we also found an enhancement of miR-29a and a dramatic depletion of GR during RSV infection in human epithelial A549 cells. Using gain or lost approaches we demonstrate that GR is the target of miR29a. Strikingly, silence viral NS1 expression could partially inhibit RSV infection induced miR-29a to disrupt GR degradation and interferes with the pathogen's anti-GC effect on host cells. We further suggest that NS1 downregulates GR in miR-29a manner. Thus, downregulation of GR is a key event in the RSV infection that reduce the sensitivity of GCs and this highlights the dependency of the viral NS1 protein on the induction of miR29a which could be a potential target to treat inflammation caused by RSV infection.

Participant Name (Given+Family)	Organisation	Email	
Malcolm Brodlie	Newcastle University	malcolm.brodlie@ncl.ac.uk	

Abstract

Investigating the pathogenesis of cystic fibrosis lung disease to inform the development of new treatment strategies is the major focus of my research. We aim to ask the most clinically meaningful questions possible and our approach to answer these involves combining innovative experimental techniques with clinical samples from children and people with cystic fibrosis.

Current cystic fibrosis projects include:

- The role of disordered sphingolipid metabolism in airway epithelial cells in inflammation and infection in the cystic fibrosis airway (MRC Clinician Scientist Fellowship)
- Abnormal airway surface liquid homeostasis including the role of non-CFTR transporters (Wellcome Trust Clinical Research Fellow, Dr Iram Haq; collaboration with Dr Mike Gray)
- Development of primary airway epithelial cell culture models as a model to study cystic fibrosis lung disease

Other areas of interest and active research include:

- Epidemiology of community-acquired pneumonia and empyema in children (Investigator-led study with Pfizer)
- Evaluation of Point of Care testing for respiratory viruses (NIHR DEC/MIC study with Roche Diagnostics)

Participant Name (Given+Family)	Organisation	Email	
Katy Pike	UCL Great Ormond Street Institute of Child Health	k.pike@ucl.ac.uk	

Abstract

I am a clinical academic with expertise in lung physiology and the epidemiology of paediatric respiratory disease. My clinical and research interests focus upon of children and young people with asthma. I am also clinical lead for infant respiratory function testing at GOSH and am developing translational research based upon the role of respiratory physiology testing in improving the health of children with diseases affecting respiratory function.

My most recent research proposals have addressed three themes:

Reducing asthma attacks or exacerbations
Improving engagement by children and young people with asthma in physical activity
Tailoring fitness to fly testing to better address the altered physiology of children and young people with type 2 respiratory failure in order to improve the recommendations made to those with for example neuromuscular disorders and their confidence in air travel

Participant Name (Given+Family)	Organisation	Email	
Anu Sironen	UCL Great Ormond Street Institute of Child Health	a.sironen@ucl.ac.uk	

Abstract

Ciliopathies and male infertility are genetic disorders associated with increased morbidity. My research aims to characterize the mechanisms involved in cilia and sperm tail formation and function, deficiency of which underlies a major disease burden. Ciliopathies cause a wide range of diseases including primary ciliary dyskinesia (PCD), which prevalence in Europe has been estimated around 1 in 10,000 individuals. PCD is characterised by recurrent infections of the respiratory tracts and inner ear starting soon after birth typically with neonatal respiratory distress, which without early intervention and symptomatic treatment will develop into severe respiratory disease progressing to permanent loss of lung function (bronchiectasis). Variable hydrocephalus, retinitis pigmentosa and infertility of both sexes are also features of PCD. The disease morbidity is high and is associated with early death in severe cases, though the negative impact on quality of life and psychosocial effects are better documented emphasising the importance of understanding the molecular mechanisms behind PCD. My current projects aim to identify the causative mutations for PCD and investigate their function in disease. Gene panel and exome sequencing are used for identification of mutations and cell and animal models to study the role of identified genes in cilia related mechanisms. The functionally similar microtubular core structure (‘axoneme’) of cilia and sperm tails means that compromised ciliary function is also a cause of male infertility and same mechanisms are required for both structures. Therefore, we also use spermatogenesis as a model to study mechanisms involved in cilia/flagella formation and motility. One line of research is the elucidation of the effect of PCD mutation on male fertility. Due to the similar structure of cilia and sperm tail, it can be expected that PCD mutations cause male infertility. Our studies of PCD associated genes during spermatogenesis and in mature sperm provide insights into the biological function of these genes and similarities/differences in cilia and sperm. The projects are designed to enhance the scientific knowledge of biological processes involved in cilia/flagella with a goal to advance the science towards the development of reliable diagnostics and novel therapeutics.

Participant Name (Given+Family)	Organisation	Email	
Gráinne McGill	Mackintosh Environmental Architecture Research Unit, Glasgow School of Art	g.mcgill@gsa.ac.uk	

Abstract

My research interests focus on the impact of indoor air quality on building users physical and psychological health and the role of architecture in the design of healthy buildings. I am particularly interested in multidisciplinary approaches to explore the relationship between architectural design, environmental exposure and childhood respiratory health.

My interest and involvement in this area stemmed from the outcomes of the HEMAC network, which was established to bring together researchers and practitioners from the fields of indoor air quality (IAQ), health and the built environment to identify shared research agendas and develop research questions and activity, with a particular focus on challenges concerning IAQ in modern UK dwellings. The steering committee (over 30 members) is made up of researchers from medicine (including participants from the Respiratory group, University of Aberdeen and Public Health England), indoor air science and ventilation, microbiology, engineering and architecture communities, mainly from the UK but also includes researchers from Ireland, the Netherlands, Denmark, Belgium and China. The network was established through funding received from the Arts and Humanities Research Council (AH/N006607/1) which supported a series of initial events (May 2016 - May 2017), including a symposium, a workshop and a sandpit (see www.hemacnetwork.com for more information). The activity of the network identified both the existing knowledge base and also significant research questions, including a strand of research concerned with children's health and the indoor built environment.

This theme was pursued through a HEMAC workshop and sandpit entitled *Cross sectional study on children's health and indoor environmental quality*, which resulted in a recently funded 12 month pilot study to explore the role of the home environment on the aetiology of asthma and allergies in Scottish children. The context of the proposed research is existing evidence of higher allergy levels in UK, Australia, and New Zealand; and a current impetus to address air pollution in the UK. This recently initiated study hopes to replicate a methodology used by Prof Jan Sundell (Tsinghua University) in previous studies in China.

In parallel to this, I am working on a research proposal that aims to compare bedroom ventilation rates and concomitant effects (moisture, temperature, air pollutants) with the frequency of asthma events and lung function of children (aged 5-11) with asthma living in modern homes. The proposed study is a joint collaboration between the Mackintosh Environmental Architecture Research Unit at the Glasgow School of Art and the Institute of Medical Sciences at the University of Aberdeen. We are currently working with Asthma UK Centre for Applied Research to organise a consultation with parents of asthmatic children (aged 5–11), to acquire knowledge to inform and strengthen the proposed research project, which has received support from Allergy UK, Asthma UK and the SPEAK Asthma Group for children and young people.

Participant Name (Given+Family)	Organisation	Email	
Daniela Cardinale	UCL Great Ormond Street Institute of Child Health	d.cardinale@ucl.ac.uk	

Abstract

Since I joined the Respiratory Infection and Epithelial Biology group at the ICH my research interest focused on diseases affecting respiratory epithelium in children and how overcome them.

My main research area focuses on Primary cilia diskynesia (PCD), a rare genetic condition affecting 1 in 10000 children that drastically reduces mucociliary clearance. Children, affected from birth, suffer chronic respiratory infections leading to progressive severe lung damage known as bronchiectasis. This condition involves mutations in more than 35 genes of which 30% are due to nonsense mutations. Those prevent proper formation of proteins involved leading to cilia defects.

We are growing primary respiratory cells from PCD patients and differentiate them in a multiciliated epithelium.

Our strategy is to restore cilia function in PCD by a combination of drugs that 'read-through' nonsense mutations and inhibitors of nonsense-mediated decay (NMD), a cell defense mechanism that degrade defective mRNAs.

We have exciting evidence that the read-through drugs gentamicin and Ataluren, promote production of the protein multicillin that is defective in a severe phenotype of PCD, 'Ciliary Aplasia' where all cilia are absent. Ataluren in particular restored basal body formation in patients' cells suggesting that cilia can regrow.

A major additional advantage of this research is that it could be applied to nonsense mutations causing other respiratory disease including the 30% of patients with primary ciliary dyskinesia (PCD) who have a causative nonsense mutation.

At the same time, we are developing a 96-transwell model of multiciliated respiratory epithelium that will enable the high-throughput screening of multiple drugs and drugs combination directly on patients' cells.

Participant Name (Given+Family)	Organisation	Email	
Luo Ren	UCL Great Ormond Street Institute of Child Health	luo.ren@ucl.ac.uk	

Abstract

Human respiratory syncytial virus (RSV) is the leading cause of acute lower respiratory tract infections, and also an important contributor to severe respiratory illness in infants and children under 5 years of age across the world. RSV can be divided into 2 subtypes, subtype A (RSV-A) and subtype B (RSV-B), based on sequencing and monoclonal antibody reactions. Both RSV subtypes can be further categorized into genotypes. It has been reported for some time that clinical RSV isolates are associated with greater pathogenicity than laboratory isolates.

We evaluated the genetic variability in the G protein gene of RSV viruses from clinical samples collected in Chongqing, southwestern China, from 2009 to 2017. Phylogenetic analysis was performed to establish the relationships between clinical isolates and previously described RSV genotypes deposited in Genbank. The molecular characterization of RSV amino acids and evolutionary rate were also further analyzed.

Our study revealed that the RSV ON1 genotype has rapidly disseminated across the world under selective pressures and ON1 circulated as predominant strain of RSV-A in Chongqing. As to RSV-B, a new genotype of GB named GB5 was observed. Patients infected with ON1 strains had a higher risk of respiratory failure than those infected with NA1 strains. G and F are the most important surface glycoproteins, responsible for RSV attachment and fusion, respectively. One hypothesis for the genotype mechanism of pathogenesis is that variation in G sequence leads higher F protein fusion activity, and higher fusion activity leads to more neutrophil migration and greater cytopathology in the airway epithelium. This study will develop a detailed understanding of how the RSV evolution affects diseases severity and host-pathogen interactions, to deepen the understanding of RSV pathogenesis

Participant Name (Given+Family)	Organisation	Email	
Stephanie Ascough	Imperial College	s.ascough@imperial.ac.uk	

Abstract
I am a senior academic immunologist in the Department of Infectious Diseases and Immunity, responsible for the laboratory aspects of clinical trials carried out within the group. Using clinical samples from trial participants, I investigate innate, humoral and cell-mediated immunity in respiratory viral infections, including influenza and respiratory syncytial virus (RSV). Specifically, I focus on defining novel correlates of protection that will enable us to design more effective treatments and vaccines against such pathogens.

Participant Name (Given+Family)	Organisation	Email	
Katie Bayfield	Manchester University NHS Foundation Trust	Katie.bayfield@mft.nhs.uk	

Abstract

Physiological outcome measures are our guide to diagnosis and treatment of those with respiratory diseases. As a physiologist I am fascinated by our ability to utilise these outcome measures in clinical trials in order to advance medicinal and clinical care. This is shown by my current role in coordination and management of a number of different phase clinical trials.

My main research interest lies in paediatric respiratory care of those with cystic fibrosis, specifically the lung function measure lung clearance index (LCI). My PhD allowed me to explore some of the more basic physiological properties of LCI testing and the utility and standardisation of LCI. In my current role I now have exposure to new equipment techniques and longitudinal studies involving LCI and different disease groups and ages.

In 2019, I hope to go on to complete post-doctoral research at The Westmead Children's hospital for the University of Sydney (supervisor Dr Paul Robinson) where I will be looking at LCI and other outcome measures such as Magnetic Resonance Imaging (MRI). I will look at large scale epidemiological data and other disease areas such as primary ciliary dyskinesia and asthma. The significance of which will be the identification of specific lung deterioration and advance the adoption of LCI into standard practice since the synergistic use of different outcome measures will help targeted treatment regimens and slow the progression of early lung disease.

Participant Name (Given+Family)	Organisation	Email	
Robert Hynds	University College London	rob.hynds@ucl.ac.uk	

Abstract

My research career to date has focused on understanding epithelial stem cell and cancer biology in the context of the human lung epithelium. My first key contribution during my PhD was to establish novel cell culture protocols for the long-term expansion of primary human airway epithelial cells that avoid both senescence and the requirement for transformation. In co-culture with murine 3T3-J2 fibroblast feeder cells and in RHO-associated protein kinase (ROCK) inhibitor-supplemented medium, epithelial cells proliferate rapidly for long culture periods and can differentiate into the major airway cell types. The main paper describing these results was published in the top respiratory journal, The American Journal of Respiratory and Critical Care Medicine, with an accompanying editorial commentary.

My second key contribution has been to use these protocols in translational studies. I have demonstrated the potential of cultured epithelial cells in future cell therapies (collaboration with Prof. Paolo De Coppi, Great Ormond Street Hospital, GOSH), in modelling primary ciliary dyskinesia, a genetic airway disease (collaboration with Prof. Chris O'Callaghan, GOSH) and in characterising novel stromal-epithelial signalling axes (collaboration with Dr. Cecilia Prêle, University of Western Australia). My data resulted in a seed funding award, a project grant from the Roy Castle Lung Cancer Foundation (PIs Hynds/Janes) and, to date, authorship of 10 primary articles, 5 reviews, editorial and 2 book chapters.

During my fellowship, as well as continuing work on the respiratory epithelium, I am now developing models to address the paucity of representative pre-clinical lung cancer models. I have derived multi-region patient-derived xenograft (PDX) tumours by subcutaneous injection of cancer cells in immune-compromised mice. With extensive genomic and immunological annotation of the tumour-of-origin and the availability of donor-matched immune cells, the technique represents a unique resource to interrogate open questions in lung cancer immunobiology.

Participant Name (Given+Family)	Organisation	Email	
Matthew Burgess	The Queens medical Research Institute	matthew.burgess@ed.ac.uk	

Abstract

Infant respiratory viral infections are a major cause of infant hospitalisation and a risk factor in the development of persistent wheeze, airway allergic responses and ultimately asthma. Ongoing infection in mice with the gut helminth Heligmosomoides polygyrus protects against respiratory syncytial virus (RSV) infection, reducing viral load, associated immunological changes and airway impairment. This protective effect is dependent upon the induction of type I interferons in the gut and/or the lung and the presence of normal gut microbiota. Intravenous serum transfer from mice 10 days after H polygyrus infection to naïve mice induced similar increases in interferon beta and interferon stimulated gene expression as seen in H polygyrus infection, and reduced peak viral load after subsequent RSV infection. Furthermore, infection with H Polygyrus also modulated the haematopoietic potential of the bone marrow with a persistent expansion of myelopoietic populations. This expansion facilitates an elevated number of circulatory monocytes and inflammatory monocytes in the lung. These bone marrow changes were also induced in serum transfer experiments. Together, these observations suggest that serum factors, e.g. translocated gut microbiota or gut produced interferons, are responsible for inducing antiviral changes directly in the lung and/or through the expansion of myeloid populations in the bone marrow, which could potentially exert antiviral effects after migrating to the lung.

Participant Name (Given+Family)	Organisation	Email	
Lisa Miyashita	Queen Mary University of London	l.miyashita@qmul.ac.uk	

Abstract

I currently work as a postdoctoral research scientist in Professor Jonathan Griggs's laboratory at the Centre for Genomics and Child Health. My two main projects are to investigate the effect of environmental toxins, E-cigarettes and air pollution derived particulate matter (PM) on susceptibility to respiratory infection. I have also been involved in other projects in our group that relate to paediatric respiratory health including the effect of PM on children with cystic fibrosis and asthma, and the use of cleaner-burning biomass stoves in Malawi to reduce pollution exposure. My two main areas of research are summarised below.

E-cigarette use and the risk of respiratory infection

A major concern currently in the UK is the rapid increase of E-cigarette (EC) use in the adolescent population. My current project investigates the effect of EC use on susceptibility to respiratory infection. We have a model of exposure in both the upper and lower airways and have evidence to suggest that EC use, in addition to the use of the latest EC technology on the market, heat-not-burn tobacco (iQOS), increases host expressed platelet-activating factor receptor (PAFR), which correlates to an increase in pneumococcal adherence and invasion of host cells. EC and iQOS are particularly popular in Asia and is of growing concern to respiratory health in the adult and adolescent population.

Air pollution derived particulate matter (PM) and PAFR expression

Air pollution is increasing worldwide and is of concern in children due to deleterious effects on the developing lung. We have previously reported that exposure to PM *in vitro* increases expression of PAFR. A receptor used commonly by respiratory pathogens to invade and infect host cells. We are currently investigating the use of this receptor as a biomarker to air pollution derived PM related infection. We are assessing nasal epithelial PAFR expression by flow cytometry, in individuals after exposure to high and low pollution in London, measured by a black carbon monitor. We have preliminary evidence to suggest that PAFR expression is increased *in vivo* subsequent to high levels of pollution exposure.

Participant Name (Given+Family)	Organisation	Email	
Claire Edmondson	Imperial College	c.edmondson@imperial.ac.uk	

Abstract

Despite the > 318,000 health apps available, the clinical status of CF children is still assessed at intermittent hospital visits irrespective of clinical severity; unlike for asthma, home monitoring is not routine. However, it is not clear how much monitoring CF children and families would be willing to undertake, or whether the additional focus on their health could have an adverse effect on their well-being. An additional benefit of monitoring could be the early recognition of pulmonary exacerbations (PEx) which are associated with a worse prognosis in CF. More sensitive diagnostic tools would allow prompt treatment and may improve outcomes. This project seeks to design a paediatric home monitoring app which is engaging for young people and parents and explores the feasibility of collecting a) data with this app ensuring no adverse effects on mood, anxiety and quality of life when compared with parents and patients receiving standard care and b) samples for PEx biomarker analysis.

METHODS: We designed a study-specific mobile phone app with integrated Bluetooth equipment and are collecting feasibility and clinical data from 8 sites across two countries (UK and Canada). Participants are asked to collect data either daily or twice a week for 6 months. In parallel, participants have the option of collecting a variety of samples at home weekly; these will be used for biomarker discovery. Parents and participants were also asked to complete depression, anxiety and quality of life measures during clinic visits. Data is also being collected in a parallel group of participants and parents at the Royal Brompton Hospital who are receiving normal standard of care.

RESULTS: Recruitment closed across the UK on the 31st March 2018 and in Canada on the 30th April 2018. Recruitment total was 149 out of a target of 160 undergoing home monitoring. All participants will conclude their 6 months enrollment by November 2018. Current recruitment to the routine standard of care group at the Royal Brompton Hospital is currently 91/100.

In parents of patients who have completed the study so far at RBH we have found no significant difference in levels of depression and anxiety in families using home monitoring when compared to standard clinical care only. We have found 6.6% moderate depression and 10.6% moderate anxiety levels in our parent cohort so far.

CONCLUSION

We have recruited 93% of our target within the allotted time. The feasibility data will be exported from a study-specific webpage for analysis after all participants have completed. From the early data levels of depression and anxiety appear similar when comparing those using home monitoring and normal clinical care, however further exploration of quality of life measures is ongoing. Feasibility of home sample collection is being explored and biomarker discovery is being targeted based on the results of this.

Participant Name (Given+Family)	Organisation	Email	
Maximillian Woodall	St. George's University London	mnjwoodall@gmail.com	

Abstract

I am part of a strategic research centre researching personalised genetic cures for cystic fibrosis. The accessibility of the lungs and monogenic nature of CF makes the disease an attractive candidate for gene editing. However, *in vivo*, the many technical barriers including inefficient vectors, mucus barriers and immune responses result in poor efficiency of treatment. Together our research aims include developing a CRISPR cas-9 technique to correct the mutation, an efficient delivery method into lung epithelial cells and a robust assessment of functional recovery in corrected cells.

Within my own dependent research I have been interested in developing a CFTR gene that delivers a protein with increased function. It has been suggested that ~10% CFTR expression in target cells *in vivo* is sufficient to prevent lung disease. However, WT CFTR is downregulated within the CF disease environment. Furthermore 10% of endogenous WT CFTR activity may not restore all essential functions critical in preventing CF disease progression.

However, over expression of CFTR has been shown to restore some functions in CF monolayers more efficiently than endogenous expression.

Therefore I have developed an enhanced CFTR gene for insertion downstream of the CFTR endogenous promoter. Codon optimisation, delivered increased protein expression and mutations K978C and K190C increased CFTR activity. I have prepared the gene for the recently developed Homology-Independent Targeted Integration (HITI) technique, allowing for precise insertion of a DNA sequence into the genome. It is my aim these features will be less sensitive to downregulation by the CF disease environment and allow restoration of healthy secretions in the lungs with a lower, achievable rate of genetic editing.

Participant Name (Given+Family)	Organisation	Email	
Norrice Liu	Blizard Institute, Queen Mary University of London, London	n.liu@qmul.ac.uk	

Abstract

My current research project investigates the effects of air pollution on children with Cystic Fibrosis (CF). My cells of interest are airway macrophages (AM). Purified populations of AM are obtained from children with CF and healthy controls by sputum induction. Personal exposure to air pollution (black carbon, nitrogen dioxide), along with AM functions *in vivo* and *in vitro* are compared between the two groups. *In vivo* phagocytic ability is analysed using our previously established method of measuring black carbon content within AM under light microscopy. *In vitro* function is tested by exposing purified populations of AM to diesel exhaust particles, while inflammatory markers /cytokines release is measured. Airway epithelial cells are also used to model the effect of pollutant exposure in the presence of CF vs healthy AM. The project explores the amount of pollutants our current generation of children in London are exposed to on a daily basis – identifying exposure peaks (during commutes and outdoor activities) and providing information and insights for the children and their family. Airway macrophages, being one of the key immune cells, play an important role in removing and protecting the airway from pollutants; their functionality therefore dictates how vulnerable the host is.

Participant Name (Given+Family)	Organisation	Email	
Kate Lewis	UCL Great Ormond Street Institute of Child Health	kate.lewis.14@ucl.ac.uk	

Abstract

I am broadly interested in the epidemiology of childhood respiratory conditions, with particular reference to the impact of socioeconomic deprivation. My PhD project is entitled 'the socioeconomic pathways to childhood respiratory conditions'. I am investigating the mechanisms that explain why children from socioeconomically deprived backgrounds are more vulnerable to respiratory conditions in early- and mid-childhood. I look at numerous risk factors including maternal smoking, being born prematurely and pollution. To do this work I am using national birth cohorts from England and Scotland constructed using routine health care data, but have previously worked with data from birth cohort studies. I have a lot of interest in data sources, linkage of data and in applying causal analysis to epidemiological research.

Participant Name (Given+Family)	Organisation	Email	
Elisabeth Robinson	UCL Great Ormond Street Institute of Child Health	elisabeth.robinson.17@ucl.ac.uk	

Abstract

Respiratory Syncytial Virus (RSV) is a ubiquitous virus, thought to infect all children before the age of 2. Most children develop a mild to moderate illness, whereas 3% of children develop a severe RSV bronchiolitis and require hospital admission. A significant proportion of these severely unwell children are otherwise healthy and have no known predisposition to disease. There is no licensed vaccine for RSV and treatment is limited to supportive care only. It has been shown from broncho-alveolar lavage samples of RSV babies that there is a massive infiltrate of neutrophils to the airway lumen during infection, with neutrophils comprising over 80% of all cells recovered. However, whether the summative effect of neutrophil infiltration is beneficial or detrimental to symptoms and recovery, remains unclear.

Our group has designed a new in vitro transepithelial migration model of airway epithelium, which we can use to model the disease state in RSV bronchiolitis and examine the effect on the neutrophils and the epithelium. To further understand the role of neutrophils in this interaction I have developed precision assays to assess neutrophil chemotaxis, apoptosis and phagocytosis as well as microscopy techniques to visualise interactions in real time. These methods have been optimised for validity using only a small number of neutrophils retrievable from an infant sample or our migration model.

I will use these methods to investigate the interaction between the neutrophil, RSV and the ciliated epithelium during in-vitro infection, and the result of these interactions on neutrophil morphology and function. I am currently completing a data set using healthy volunteer neutrophils and airway epithelium, and will next move into studies comparing cord blood neonatal neutrophils, and in the future examine neutrophils from babies with RSV.

Participant Name (Given+Family)	Organisation	Email	
Evelyn Robson	University College London Great Ormond street Institute of Child Health	evie.robson@nhs.net	

Abstract

Children and adults with chronic respiratory disease often develop permanent lung damage called bronchiectasis. In the best centres world-wide a diagnosis is only possible in approximately 50% for children and adults. Although airways obstruction and infection are associated with the development of bronchiectasis surprisingly little is known of the early stages of its development in patients with and without an identifiable cause. The project focuses on Primary Ciliary Dyskinesia (PCD), a major cause of bronchiectasis. Improving our understanding of the pathophysiology of PCD is important to develop appropriate treatment strategies. There have been very few studies in this area and no clinical trials to date.

In preparation for this work I have published a review of PCD and am currently writing two papers:

- Diagnostic testing of Primary ciliary dyskinesia: High speed video microscopy: Robson E & O'Callaghan C. This tested the hypothesis that high speed recognition of static or circularly moving cilia provided conclusive evidence of PCD.
- Ciliary Aplasia: A review of several patients with this rare and serious PCD phenotype. Robson E & O'Callaghan C.

This work markedly improved my background knowledge of PCD and helped me to contribute to the design of my MD. I have recently submitted ethical approval to undertake my project. My project has two strands:

1. Investigation of inflammation in PCD. I will test the hypothesis that PCD predisposes to airway inflammation. As underlying inflammation may cause inflammation my study will have two parts. Firstly, I will use SAM strips to collect epithelial airway fluid from the nose and induced sputum to provide samples from the lower airway. I will measure inflammatory cytokines and chemokines from these samples. To help determine if inflammation is present in the absence of infection I will investigate the inflammatory mediators in cell cultures from these patients. This hypothesis was generated based on preliminary research from Dr Smith and Prof O'Callaghan at UCL.

Investigation of cough: In children with bronchiectasis and cystic fibrosis exacerbation of cough is taken as a sign of underlying infection/inflammation. As PCD patients cough every day, there is need to determine if increased cough is associated with a respiratory exacerbation. To do this we will measure cough objectively using a cough recorder (Leicester cough recorder). Parents/patients will report when they suffer from a respiratory exacerbation allowing us to determine if this may be recognised by increasing cough counts.