BEAT-PCD
BETTER EXPERIMENTAL APPROACHES TO TREAT PCD

cost
EUROPEAN COOPERATION IN SCIENCE AND TECHNOLOGY

NEWSLETTER

2nd EDITION, JULY 2017

INTRODUCTION

Jane Lucas

Chair of BEATPCD

Welcome to the second edition of the BEAT-PCD e-newsletter. In this edition we highlight the excellent work by BEAT-PCD members, displaying the breadth and depth of current PCD research. The section entitled 'Selected publications' summarises three high-impact papers; past events are briefly reviewed on the 'Highlights of year 2' section; achievements and awards received by trainees and senior members are outlined in the 'Achievements' section. We also presented a feedback from our trainees from Short Term Scientific Missions founded by BEAT-PCD.

I look forward to seeing you all at our BEAT-PCD meetings in Milan (9th September 2017) and in Lisbon (6-9th February 2017).

We hope you enjoy this e-newsletter!

SAVE THE DATE—IMPORTANT PCD EVENTS

- Pre-ERS PCD Meeting, **9th September 2017** from 13:00 to 17:00 at the Aula Magna of Mangiagalli Clinic, University of Milan
- ERS International Congress 2017, **9th-13th September 2017**, Milan, Italy
- BEAT-PCD Conference & 4th Training School**, 6th-9th February 2018**, Lisbon, Portugal

PUBLICATIONS FROM BEAT-PCD NETWORK

1. In preparation for our 24-month report to the COST office, the national representatives contributed details of PCD publications since 2014. We have all been very busy, with over 60 publications! (http://www.beatpcd.org/publications/)

2. Many of the publications did not acknowledge BEAT-PCD; please include the following wording when submitting papers so that we can report your manuscripts to COST: *XX, YY and ZZ are members of EU-funded COST Action BEAT-PCD (BM1407).*

3. To encourage dissemination in high impact journals BEAT-PCD will contribute 500 Euros for Open Access fees, in the following cases:

- Authors from at least two BEAT-PCD countries.
- The first author should usually be a BEAT-PCD trainee.
- The journal should NOT usually be exclusively open access. The subsidy is for fees to high impact journals where open access fees are optional.

To apply for funding send the draft manuscript and covering letter to L.E.Reeves@soton.ac.uk

SELECTED PUBLICATIONS

Olcese et al. X-linked primary ciliary dyskinesia due to mutations in the cytoplasmic axonemal dynein assembly factor PIH1D3. *Nat Commun.* 2017 Feb 8;8:14279.

PIH1D3 gene mutations cause a previously unrecognised X-linked form of PCD resulting in dynein arm loss in affected males. 3D tomography cilia imaging revealed certain patients lose only specific components of in the inner dynein arm. PIH1D3 is a cytoplasmic protein that appears to act within an HSP90 co-chaperone complex that pre-assembles dynein arms for import into the cilia.
https://www.ncbi.nlm.nih.gov/pubmed/28176794

Goutaki et al. The international primary ciliary dyskinesia cohort (iPCD Cohort): methods and first results. *Eur Respir J.* 2017 Jan 4;49(1). pii: 1601181.

This article describes the aims and methods of the iPCD Cohort and outlines how the data can be accessed for future research. The iPCD Cohort is a valuable resource for epidemiological studies in PCD and it can be further enriched and used in the framework of the BEAT-PCD EU COST Action. This dataset is now available to be further exploited and offers a unique opportunity to study PCD in a large international patient-based cohort with sufficient statistical power. Results will help to improve survival, care and quality of life of PCD patients.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5298195/

Kobbernagel et al. Study protocol, rationale and recruitment in a European multi-centre randomized controlled trial to determine the efficacy and safety of azithromycin maintenance therapy for 6 months in primary ciliary dyskinesia. *BMC Pulm Med.* 2016 Jul 22;16(1):104.

This article presents the study protocol of an ongoing RCT evaluating for the first time the efficacy and safety of a pharmacotherapeutic treatment for patients with PCD. The RCT evaluates azithromycin maintenance therapy, a drug already commonly prescribed in other chronic respiratory disorders. The publication details the background, the study's rationale, inclusion and exclusion criteria, as well as methods used in connection with the primary and secondary outcomes. In addition, the obstacles affecting planning and approval of the study due to many different ethical and legal instances across all sites of this international multicenter study and the recruitment aspects that have hampered the conduction of the study at the planned pace are discussed.
https://www.ncbi.nlm.nih.gov/pubmed/27450411

HIGHLIGHTS OF BEAT-PCD, YEAR 2

European Respiratory Society International Congress, London 3rd – 7th September 2016

BEAT-PCD held an ERS meeting at the Royal Brompton Hospital on 3rd September, attended by more than 100 people working in PCD. Four state-of-the-art presentations on two selected topics were followed by a series of short presentations and discussions on collaborative projects led by BEAT-PCD members. The 2016 ERS Congress displayed the breadth and depth of PCD research: 7 oral presentations and over 30 posters emphasised the high volume of quality work by BEAT-PCD members. In Addition, PCD was featured at one of the ERS symposiums, which outlined the latest developments in PCD research, with a particular focus on the recently published (link below) ERS PCD task force recommendations for diagnostic testing. http://erj.ersjournals.com/content/early/2016/11/11/13993003.01090-2016.article-info

BEAT-PCD ERS Meeting 2016, Royal Brompton Hospital, UK.

2nd BEAT-PCD Conference & 3rd PCD Training School, 18th-21st April 2017, Valencia, Spain.

The conference goal was to meet PCD experts and people in training from a wide range of disciplines, including: clinicians, physiotherapists, respiratory nurses, diagnostic technicians, basic scientists, methodologists, physiologists, patient representatives and industry. This meeting was attended by more than 120 attendees from 20 different countries. It was highly interactive, including state of the art lectures, poster sessions, short oral presentations, workshops, small group discussions and interactive plenary sessions. It was an opportunity to increase the knowledge in the PCD field, to establish new collaborations and studies, as well as to learn from people who had undertaken Short Term Scientific missions.

BEAT-PCD Conference and Training School 2017, Valencia, Spain.

ACHIEVEMENTS

Achievements by BEAT-PCD trainees: PhD studies

Myrofora Goutaki, University of Bern (Switzerland)

"I defended my PhD thesis on 'Epidemiology of Primary Ciliary Dyskinesia (PCD)' on September 2016, at the Institute of Social and Preventive Medicine, University of Bern. I completed my PhD studies working on different PCD epidemiological projects and collaborating in a variety of PCD and other paediatric respiratory epidemiological and clinical studies. The main focus of my work was the development of the international PCD (iPCD) Cohort, in the framework of the EU funded project BESTCILIA, under the supervision of Prof. Claudia Kuehni."

Mathieu Bottier, Université Paris-Est (France)

Mathieu Bottier

"I obtained my PhD 'Characterization of ciliary beating mechanisms under the normal and pathological mucociliary clearance' in November 2016 in the team of Bruno Louis and Marcel Filoche (Inserm U955, CNRS ERL 7240, Université Paris-Est, Creteil, France). Two articles from this PhD work entitle 'A New Index for Characterizing Micro-Bead Motion in a Flow Induced by Ciliary Beating: Part I, Experimental Analysis & Part II, Modeling' will be published soon.

I am now Postdoctoral Research Associate in the Philip Bayly lab at Washington University in St Louis, MO, USA since January 2017. I work on the and modelling of flagella motion. I am using the model of Chlamydomonas in collaboration with Susan Dutcher. As a member of the Washington University cilia group (Susan Dutcher, Steven Brody and Moe Mahjoub labs), I still keep an interest in PCD."

Sam Collins, University of Southampton (UK)

Sam Collins

"I completed my PhD at the University of Southampton from 2014-2017 studying the role of bacterial biofilms in PCD and healthy epithelium. My research allowed me to identify potential differences in the response of PCD epithelium to colonising bacteria and showed that nitric oxide could potentially be used as an adjunct to treat these bacterial infections. As well as learning a number of cutting-edge research techniques, I gained exposure to the PCD clinical service in Southampton; it was great to see the patients that may eventually benefit from my lab research. The work also provides excellent opportunities to get involved in European collaborations within the ERS and BEAT-PCD."

Mikkel Alanin, University of Copenhagen (Denmark)

Mikkel Alanin

"In my PhD project entitled 'Bacteriology and treatment of infections in the upper and lower airways of patients with primary ciliary dyskinesia' I identified the paranasal sinuses as a potential reservoir for bacteria which could lead to lung colonization and infection. Subsequently, we investigated the potential for sinus surgery and found that sinus surgery with adjuvant therapy can reduce infections and improve patient health and quality of life. "

Mari Lehti, University of Turku (Finland)

My PhD studies entitled 'Microtubule-mediated protein transport mechanisms during spermiogenesis' has given me strong knowledge on male fertility, sperm tail and cilia formation, in

addition to specific laboratory skills required for studies with male germ cells. During this project I have generated two male germ cell-specific knockout mouse models for Kif3A and Spef2 to characterize their role during sperm tail development and specifically their role in microtubule related processes.

Mari Lehti

Laura Behan, University of Southampton/University College Cork (UK/Ireland)

"I graduated with a PhD in Social Sciences in February this year. Supervised by Professor Jane Lucas (University of Southampton) and Dr Audrey Dunn Galvin (University College Cork), my thesis entitled 'Primary ciliary dyskinesia: A Biopsychosocial Approach' aimed to provide an overview of the PCD patient's perspective and experience of living with PCD, to address some of the complexities in referring and diagnosing PCD patients, and to provide age specific, PCD-specific validated health-related quality of life (HRQoL) measures to monitor patient outcomes and measure effectiveness of interventions. The development, validation and translation of QOL-PCD has provided the first disease specific patient-reported outcome measure to allow for the assessment of new and existing treatments. Findings from the international survey and interviews has allowed the voice of the PCD patient to contribute and advise on ERS Task Force guidelines for diagnosing PCD. The development of a clinical predictive tool 'PICADAR' will hopefully lead to earlier referral of patients and improved awareness among medical practitioner of the signs and symptoms of PCD."

Laura Behan

Achievements by BEAT-PCD members: awards

North Rhine Westphalian Academy of Sciences, Humanities and the Arts (2016)

In May 2016 **Heymut Omran** was elected as full member of the North Rhine-Westphalian Academy of Sciences, Humanities and the Arts, an association of leading scientists in NRW. One of the tasks of the Academy is to advise the state government on research funding and to stimulate scientific research, but also to offer scientifically supported arguments and decision-making aids in socially relevant questions.

Care-for-Rare Science Award 2016 (2016)

In November 2016, the Care-for-Rare Science Award 2016 was awarded to **Heymut Omran**. The overall aim of this project is to accelerate diagnosis of PCD and thus to improve clinical care – finally through the development of adequate therapies. Crucial ingredients into the combined efforts of Omran's team around PCD are international clinical trials, networking between clinical and research centers and awareness raising.

Manes-Kartagener prize 2017

In March 2017, the Manes-Kartagener Prize was awarded to **Myrofora Goutaki** for her publication "The international primary ciliary dyskinesia cohort (iPCD Cohort): methods and first results". The award was handed over by representative of the German-Swiss PCD patient organization during the 39th annual meeting of the Gesellschaft für Pädiatrische Pneumologie.

Myrofora Goutaki award

Founder`s Award of the US Primary Ciliary Dyskinesia Foundation

Awarded to **Heymut Omran** by Michele Manion, the Founder of the US PCD foundation.

BEAT-PCD Conference awards:

Best Poster Presentations:

Clinical - sponsored by Vertex, awarded to **Bruna Rubbo**

Scientific - sponsored by Circassia, awarded to **Panayiotis Kouis**

Best Oral Presentation:

sponsored by Vertex, awarded to **Mahmoud Fassad**

Outstanding Contributions to BEAT-PCD:

sponsored by Vertex, awarded to **Myrofora Goutaki & Laura Behan**

YEAR 2 SHORT-TERM SCIENTIFIC MISSIONS

Myrofora Goutaki from the University of Bern, hosted by the Kremlin-Bicetre hospital in France

"During my STSM in March 2017, I visited the ENT clinic of the Kremlin-Bicetre hospital in Paris, under the supervision of my host Prof. Papon. I was introduced to the diagnostic, follow-up and management protocol of PCD patients at the clinic, observed interviews, clinical examinations and nasal functional measurements and got an overview of the existing databases. This allowed me to identify important questions of clinical relevance for the ENT management and follow-up of PCD patients and discuss possible collaborative epidemiological projects with the host. In addition, I had a series of meetings and discussions with many members of the French multidisciplinary PCD team focusing on ongoing projects (iPCD cohort, development of follow-up PCD proforma) but also development of future collaborative projects (e.g. data linkage with the newly developed PCD Rare Disease Cohort -PCD RaDiCo)."

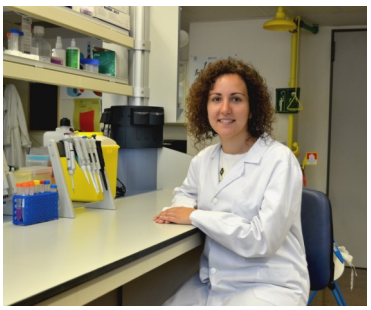
Pierrick Le Borgne from Paris Saclay/UVSQ University, hosted by ICH/UCL in the UK

"I enjoyed the STSM in Hannah Mitchison's lab (University College London, Institute of Child Health) as much for the scientific discussion with the team as for the techniques I acquired. The results I had helped me a lot to progress in my project. This mission offered me some new perspectives for my work. Today I'm still in touch with the team to discuss about future experiment for our collaboration."

Pierrick Le Borgne

Ana Reula from the University of Valencia, hosted by the University of Southampton in the UK

"I carried out my STSM from the beginning of September 2016 to the 17th of December 2016 in the Faculty of Medicine of the University of Southampton, under Prof. Jane Lucas supervision. I was introduced to the Southampton diagnostic pathway, having the of sample yield/quality checking and the preparation



Ana Reula

of the samples for diagnostic tests: High Speed Video Microscopy, Transmission Electron Microscopy, Immunofluorescence and ALI-culture. I gained experience with ciliary beat pattern and frequency analysis by HSVM. I also learnt to process and analyse diagnostic samples by EM. I processed samples by IF and observed them on the confocal microscope. Moreover, I learnt ALI culture of healthy samples, and to observe sample preparation and analysis by HSVM from ciliated ALI-cultures. In addition, I attended diagnostic reviews of cases at multidisciplinary meetings, and PCD research meetings. Additionally, I had the opportunity to visit the Royal Brompton Hospital in London to observe the diagnostic pathway another UK service."

Raquel Jacinto from CEDOC at Nova Medical School (Lisbon), hosted by the University of Pisa in Italy

Raquel Jacinto

"During my STSM I visited the University of Pisa, the lab of Dr Mauro Pistello. It was a very good experience, both from the professional and personal point of view. I brought the expertise of cell transfection to our lab and are now working on building new mutants to further study PCD. It was a fruitful collaboration and we expect to extend it even further."

CALL FOR PUBLICATIONS, EVENTS, AWARDS & ACTIVITIES

Please send us new publications, achievements, events or activities you would like to see featured on the next e-newsletter edition at b.rubbo@soton.ac.uk. The BEAT-PCD newsletter team will be delighted to receive your updates!

Please remember to follow BEAT-PCD on Twitter (@beatpcd) and keep up-to-date with the latest developments in PCD research on the BEAT-PCD official website (http://www.beatpcd.org/).

BEAT-PCD Newsletter team

Bruna Rubbo, Myrona Goutaki, Ana Reula, Panayiotis Kouis, Maciej Dabrowski, and Regan Doherty

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