BEAT-PCD
BETTER EXPERIMENTAL APPROACHES TO TREAT PCD

cost
EUROPEAN COOPERATION IN SCIENCE AND TECHNOLOGY

NEWSLETTER

1st EDITION, AUGUST 2016

WELCOME

Welcome to the first issue of the BEAT-PCD e-newsletter. The aim of this publication is to keep you informed of all the events, outcomes, initiatives and updates concerning the BEAT-PCD Cost Action, and to encourage the building of rapport and networking amongst researchers working in this area. BEAT-PCD activities are supported by EU Framework Programme Horizon 2020 funded COST Action (BM1407). BEAT-PCD newsletters will be emailed twice yearly and will also be available on the BEAT-PCD website. We hope this will provide you with a valuable resource for collecting information relating to BEAT-PCD's objectives and progress.

The success of this newsletter depends on the support and contributions of its members, so we welcome your suggestions and feedback. Please send your comments and proposals via e-mail to Laura Behan (L.behan@soton.ac.uk) and/or Bruna Rubbo (B.Rubbo@soton.ac.uk).

Jane Lucas

Chair of BEAT-PCD

HIGHLIGHTS OF YEAR ONE

BEAT-PCD got off to an excellent start. By the end of our first year 213 individuals from 22 countries had signed up. Examples of activities in year 1 included:

BEAT-PCD First Meeting

5th May 2015, Brussels, Belgium

The First Management Meeting of the COST Action BM1407 "Translational research in primary ciliary dyskinesia - bench, bedside, and population perspectives (BEAT-PCD)" was held in Brussels, Belgium on 5th May 2015. The meeting was attended by 21 partners from 16 countries: Austria, Belgium, Cyprus, Denmark, France, Germany, Greece, Ireland, Israel, Italy, the Netherlands, Norway, Portugal, Spain, Switzerland, and the United Kingdom (UK).

The participants were welcomed by the COST representatives - *Dr Inga Dadeshidze*, Science Officer of the Action and *Ms Jeannette Nchung Oru,* Administrative Officer of the Action. *Dr Dadeshidze* chaired the first part of the meeting, including the election of the Action Chair, Vice Chair, and Grant Holder. *Professor Jane LUCAS (UK)* was elected as the Chair and *Professor Claudia KUEHNI (Switzerland)* as the Vice-Chair of BEATPCD.

HIGHLIGHTS OF YEAR ONE

The Action Chair presented the main objectives of the COST action under the umbrella of promoting basic research on PCD to underpin translational research leading to the development of new treatments and to improve diagnosis. More specifically, these aim to:

- Promote basic science that will translate into clinical care;
- Maintain epidemiological databases which will be used to understand the natural course of disease and influence of environment, management, etc;
- Improve clinical care for patients;
- Develop a plan for the conduct of clinical trials.

These objectives will be met through 4 highly integrated Working Groups and the Training School:

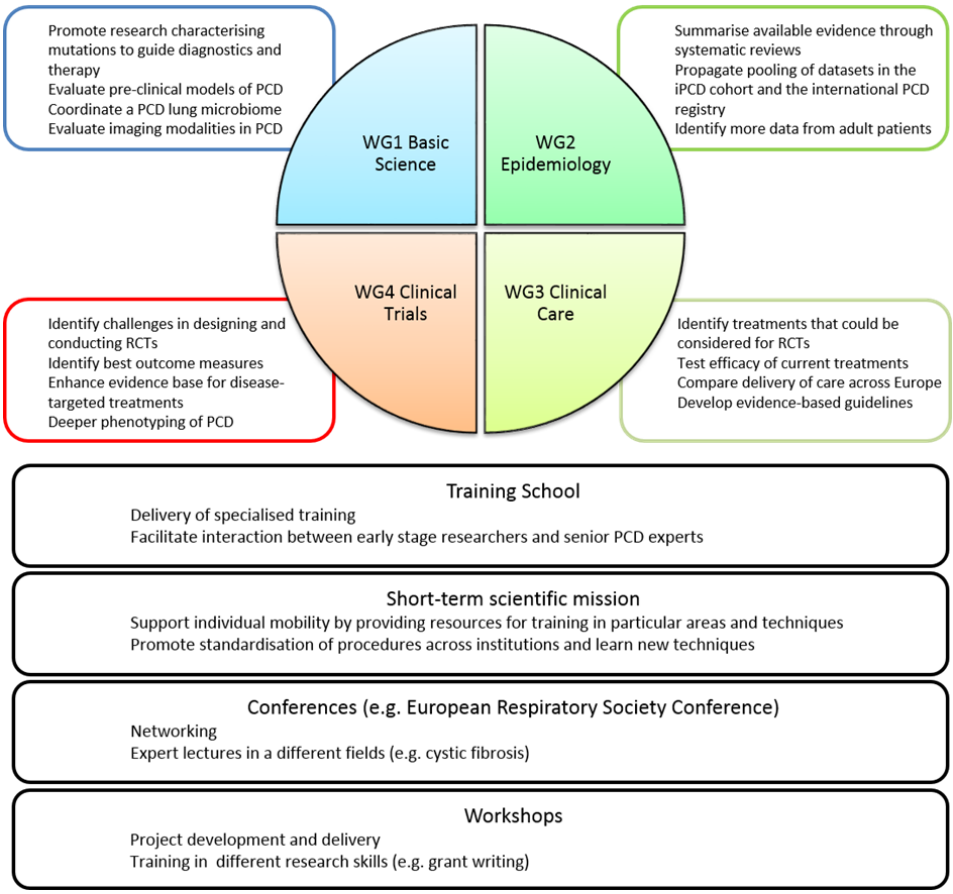
Work Group 1: Basic Science; Lead: Dominic Norris, Deputy: Mauro Pistello

Work Group 2: Epidemiology; Lead: Claudia Kuehni, Deputy: Jean-Francois Papon

Work Group 3: Clinical Care; Lead: Kim Nielsen, Deputy: Francesca Santamaria

Work Group 4: Clinical Outcomes; Lead: Philipp Latzin, Deputy: Nico Schwerk

Training School: Co-ordinator: Claire Hogg; Laura Behan and Myrona Goutaki are Early Stage Research Representatives (ESR).



HIGHLIGHTS OF YEAR ONE

PCD meeting at ERS Congress

26th September 2015, VU Medical Centre, Amsterdam

This meeting provided an excellent opportunity for BEAT-PCD to be introduced and discussed in the PCD research community. BEAT-PCD Chair Jane Lucas introduced the project and provided an overview of the project aims and objectives. This was followed by talks from each of the Work Group leaders. The audience were provided with information on how to join BEAT-PCD and sign up for the Work Groups through https://www.isurvey.soton.ac.uk/16640

The upcoming Inaugural Conference and Training School were advertised and discussed. Information was provided on how to register and submit an abstract.

SOCIAL MEDIA

FIND US ON TWITTER:

@beatpcd
https://twitter.com/beatpcd/

HIGHLIGHTS OF YEAR ONE

BEAT-PCD Inaugural Conference

7-9th December 2015, Southampton, UK

The Inaugural Conference of BEAT-PCD was held at Chilworth Manor near Southampton, UK in December 2015. The conference attracted 96 scientists, clinicians, allied health professionals, industrial partners and patient representatives from 20 countries including: Austria, Belgium, Cyprus, Czech Republic, Denmark, France, Germany, Greece, Ireland, Italy, Israel, the Netherlands, Norway, Palestine, Poland, Portugal, Spain, Switzerland, Turkey, and the UK. The BEAT-PCD Inaugural Conference successfully brought together clinical PCD specialists (paediatricians and adult pulmonologists, ENT, physiotherapists, specialist nurses) and scientists from varied backgrounds (genetics, imaging, cell biology, microbiology, bioinformatics). The multidisciplinary conference provided an interactive platform for research groups to exchange ideas through a programme of lectures, poster presentations, breakout sessions and workshops.

Rumman, Nisreen. BEAT-PCD Inaugural Conference Group Photograph. 2015, Chilworth, UK.

HIGHLIGHTS OF YEAR ONE

1st Training School of the COST Action and Second Young Researchers Meeting on Primary Ciliary Dyskinesia

27-29th April 2016, Paris, France

The Training School mission was to deliver teaching and intensive training and practical skills on novel and emerging aspects of basic and clinical science relevant to BEAT-PCD's objectives. A combination of lectures and workshops were held to familiarise and expose young researchers to expertise through an interactive approach, building on the programme developed at the Young Researchers Meeting in Bern in 2015. This second meeting brought together experts in the field to lead the programme alongside emerging young researchers gaining experience by chairing and organising sessions and workshops relevant to their areas of interest. It was also an opportunity for early stage researchers who had attended short term scientific missions to present their experiences and what they learned. This training school was well received by attendees, with the feedback survey reporting that 93% of participants found the conference overall to be good or very good. It also provided this growing group of international researchers an opportunity to drive forward collaboration in PCD translational research with 83% reporting they discussed new projects with members of other research groups during this time.

Bottier, Mathieu. BEAT-PCD Training School Group Photograph. 2016. Paris, France.

SAVE THE DATE!

Upcoming meetings sponsored by BEAT-PCD

- **PCD Meeting during ERS,** *Royal Brompton Hospital, London, Saturday 3rd September 2016 1300-1730hrs.* Agenda will be circulated separately. To register for the meeting please sign the Doodle Poll (limited to 100 participants) http://doodle.com/poll/3tygcv5snuxp6ffw
- **BEAT-PCD joint Conference and Training School,** *University of Valencia (Host: Francisco Dasí), 18th — 21st April 2017 (Tuesday to Friday).* A combined Conference and Training school will be held. This will allow trainees and seniors to meet and learn together; trainees will also have the opportunity to attend and take part in specialist lectures, workshops, networking activities and project meetings. A Management Committee meeting will take place during the conference.

Meetings of interest to BEAT-PCD

- **Cilia2016,** *Amsterdam 4-7th October 2016.* http://events.embo.org/16-cilia/
- **Gordon Research Conference,** *Galveston Texas, 12—17th February 2017.* Cilia, Mucus and Mucociliary Interactions https://www.grc.org/programs.aspx?id=13350
- **European Respiratory Society Congress,** *London, 3rd—7th September 2016.* http://erscongress.org/

EUROPEAN RESPIRATORY SOCIETY CONGRESS

London, 3rd -7th September 2016

The ERS promises to be an exciting conference for those of us interested in PCD. We have a PCD **symposium on Monday 5th September**. A PCD Poster Discussion session will also take place on this date. Presentations of PCD related abstracts are also included in a number of poster session. We have tabulated the sessions that might be of interest over the next few pages.

EUROPEAN RESPIRATORY SOCIETY CONGRESS

	Symposium
	Oral presentations
	Poster discussion
	Thematic poster

Day	Location	Title	Author (country)	8.30	10.30	10.45	12.45	12.50	14.40	14.45	16.45
Sunday	Room ICC Capital Suite 10	Lung growth in children and young adults with PCD: An iPCD cohort study	F. Halbeisen (Switzerland)								
		Sleep disordered breathing in children with PCD	E. Dehlink (UK)								
	Room ICC Capital Suite 12	Comparison of inspiratory muscle training and home-based rehabilitation approach in patients with PCD	H. Sonbahar Ulu (Turkey)								
		Presence of Kartagener syndrome reduces exercise capacity in PCD	D. Inal-Ince (Turkey)								
	Room A	Ciliary dysfunction	A. Bush (UK)				12.15				
	Room T-03	A pediatric case of *CCNO* associated congenital mucociliary disease – A novel entity in PCD	C. Happle (Germany)								
	Room T-05	Validation of a new health-related quality of life instrument specific to adults with pPCD: QOL-PCD	L. Behan (Ireland)								
	Room T-17	Is there a secondary defect in CFTR in the nasal epithelium of patients with PCD?	K. Harman (Australia)								
		PCD caused by loss-of-function *GAS8* mutations due to defects of the nexin-dynein regulatory complex	J. Raidt (Germany)								
	Room T-21	Cough detection in cystic fibrosis, primary ciliary dyskinesia and health	J. Grosse-Onnebrink (Germany)								
	Room T-31	Oxidative stress in ciliated nasal epithelial cells from patients with PCD	A. Reula (Spain)								
		Lung clearance index is stable in most PCD patients managed in a specialist centre: A pilot study	S. Irving (UK)								
	Room T-34	Success in eradication of upper and lower airway pathogens in children with PCD	G. Marsh (UK)								
	Room ICC Capital Suite 12	Objective videomicroscopy parameters correlate ciliary beating to ultrastructure in PCD	S. Blanchon (France)								
		Characteristics of adults with PCD in a bronchiectasis referral clinic	M. Shteinberg (Israel)								
		nNO measurement and a score of key clinical features for the screening of PCD in patients with non-CF bronchiectasis	J. Rademacher (Germany)								
	Room ICC Capital Suite 10	The effect of L-Arginine on cilia beat frequency in PCD patients, non-PCD referrals and healthy controls	P. Kouis (Cyprus)								
		Airway disease and inhaled corticosteroids (ICS) in children with PCD	E. Dehlink (UK)								
	Room G	Neurocognitive disorders and sleep in PCD children	T. Şişmanlar (Turkey)								16.00

EUROPEAN RESPIRATORY SOCIETY CONGRESS

	Symposium
	Oral presentations
	Poster discussion
	Thematic poster

Monday	Platinum Room 1+2	**Patients' perspectives on diagnostic testing**	**F. Copeland (UK)**								
		Barriers and solutions to accurate diagnoses	**C. Kuehni (Switzerland)**								
		Genetic mechanisms of PCD	**H. Omran (Germany)**								
		ERS PCD task force recommendations for diagnostic testing	**J. Lucas (UK)**								
	Room ICC Capital Suite 10	Mutational screening in Italian patients with PCD by next-generation sequencing	D. Snijders (Italy)								
		Effective patient selection for PCD diagnostics; the PICADAR score with nasal nitric oxide	S. Collins (UK)								
		Introducing immunofluorescence as a diagnostic tool for primary ciliary dyskinesia J. Coles	J. Coles (UK)								
		Prevalence of PCD among patients referred for specialized testing: A systematic review and meta-analysis	P. Kouis (Cyprus)								
		Changes in height and BMI in children and adolescents with PCD during the growth period: An iPCD cohort study	M. Goutaki (Switzerland)								
		Lung function and nutritional status in children with CF and PCD	W. Walker (UK)								
		Evaluating a method for diagnosing PCD in countries of limited resources; an ERS fellowship	N. Rumman (Palestine)								
		Presenting features in primary ciliary dyskinesia vary with age S. Collins	S. Collins (UK)								
		Knowledge of alpha-1 deficiency and primary ciliary dyskinesia by medical students and health professionals	M. Requena (Spain)								
Tuesday	Room ICC Capital Suite 11	nNO in paediatric PCD and in healthy children - On the lookout for optimal cut-off and reference range	M. Mikoś (Poland)								
	Room T-25	Lung function tests in patients with PCD	H. Özçelik (Turkey)								
	Room T-26	The development of translated, cross-cultural patient-reported outcome measures for patients with PCD	L.Behan (Ireland)								
		French translation and linguistic validation of the QOL-PCD, a quality of life questionnaire for patients with PCD	C. O'Neill (France)								
	Room T-18	Automated time-lapse analysis of ciliary function	C. Jackson (UK)								
Wed	Room ICC Capital Suite 12	Comparison of bronchodilator responsiveness in children with PCD and CF	V. Keenan (UK)								
	Room G	Limitations of nasal nitric oxide as a screening method of PCD in childhood	M. Romero Rubio (Spain)				12.15				

RESEARCH HIGHLIGHTS

Outcomes from the Inaugural Conference: December 2015

Work Group 1: Basic Science

Lead: Dr Dominic Norris

Work Group 1 aims to develop both a research network and an infrastructure to enable the sharing of samples, data and state-of-the-art knowledge between scientists studying cilia biology and PCD pathology. Major areas of interest for collaboration have been identified by WG1: characterization of PCD causing mutations; description of pre-clinical PCD models and how such models can be utilized in developing therapies; understanding the airway microbiome in PCD patients; and application of imaging technologies to facilitate PCD research and patient diagnostics. Imaging has become central to modern science and medicine, playing key roles in both the study of cilia biology and the diagnosis of PCD.

At this meeting the use of High-Speed Video Microscopy to analyse ciliary beating for diagnosis was discussed and a need for standardisation of methods and quantitative beat pattern analysis was identified since qualitative analysis is inherently subjective, even when performed by expert microscopists. The role of computer aided analysis was discussed; a number of talks and posters presented during the meeting providing evidence for these discussions. The group established a plan to share archived video data (from patient and control samples) for blind computational analysis; this can subsequently be compared to the original expert qualitative analysis. Lastly, during the inaugural conference, the concept of a database, that could incorporate genomic, phenotypic (ciliary motility and ultrastructural findings) and clinical data (respiratory and other systems) along with animal model data was debated.

Work Group 2: Epidemiology

Lead: Claudia Kuehni

As with other rare diseases, most epidemiological and clinical data on PCD to date have come from case reports or small clinical case series. Work Group 2 aims to make use of all existing data on PCD patients to gain essential knowledge on the clinical presentation and natural history of the disease and on predictors of disease progression. This will be a basis for planning future intervention studies but also for standardising and improving future prospective data collection.

In the framework of the EU-funded FP7 project BESTCILIA, existing datasets of PCD patients have been identified worldwide and put together into a

RESEARCH HIGHLIGHTS

retrospective cohort (international PCD Cohort- iPCD Cohort), the largest dataset ever assembled on PCD. WG2 aims to maintain, expand and enrich, clean and analyse the data of the iPCD Cohort. Some contributing groups are already adding new patients to their datasets or are adding repeated measurements (longitudinal data) to patients that have already been included. More groups have expressed an interest in contributing. In addition, BESTCILIA has funded the development of the international PCD registry, a valuable tool for prospective data collection and future research.

WG2 aims to include more countries into the registry and at the same time to establish a steering committee, responsible for managing the registry in the future. We aim to standardise and pool all these datasets together with additionally identified data from national and regional registries and clinical studies. We plan to engage in actively recruiting more adult physicians and include more adult patients' data. A secondary aim is to establish the approvals and agreements needed for international sharing of the data and identify how the datasets can be optimally used by the scientific community. At the inaugural conference planning of a series of scientific publications using these datasets was discussed. These consisted of clinical presentation and long-term prognosis of PCD, such as body growth, lung function growth and decline, development of chronic lung disease and respiratory insufficiency as well as clinical symptoms throughout lifetime. Participants agreed on the importance to apply for funding from national and international sources to support the exploitation of the collected data to answer important remaining questions.

Work Group 3: Clinical Care

Lead: Kim Nielsen

Current and future diagnosis, management and delivery of care in PCD across Europe and globally are the main focus areas of Work Group 3. The mission is to bring together clinicians from multi-disciplinary backgrounds to work with patient representatives to improve management strategies with a view to: identifying treatments that could be considered for clinical trials; identifying treatments already in use that might be suitable for efficacy testing (in *e.g.* use of antibiotics and sinus washes); investigating differences in delivery of care across Europe and identifying features associated with good clinical outcome; identifying priority areas for research through surveys and systematic literature reviews; and developing evidence based guidelines.

At this meeting, the need for a literature review on eradication studies of Pseudomonas Aeruginosa

RESEARCH HIGHLIGHTS

infection in PCD, cystic fibrosis (CF) and non-CF/PCD-bronchiectasis were discussed. This will facilitate the development of possible recommendations to be derived and form the basis for future randomized clinical trials among best-ranked methods or treatments for eradication of PsA infection in PCD. Meanwhile a European survey with the specific aim to aggregate knowledge on various existing treatment regimens regarding PsA infection in PCD is planned with a view to combining results of the review and the survey for intermediate guidelines to prevent or treat such infections. Other projects planned include an assessment of the risk of cross infection in PCD.

Participants also discussed the identification of the most efficacious treatment of sinus disease and hearing problems with the objective of identifying treatment modalities that can be the subject of clinical randomized trials. Another area discussed was the need for investigating the reasons for variations in disease severity and progression between patients diagnosed with PCD. It is likely that combinations of different factors are responsible for these variations, several of which are being investigated. Lastly, a survey investigating differences in delivery of care for PCD across Europe was discussed. Questionnaires and in-depth interviews with PCD specialists from different countries will provide data for the survey development, which will be circulated to all healthcare providers involved in PCD diagnostics and management.

Work Group 4: Clinical Outcomes

There is a clear need for clinically validated outcome measures for reporting in clinical trials and longitudinal studies, and the use of standardised methods to report them. This is particularly important for international collaborations and the expansion of ongoing research networks. Work Group 4 aim to identify and evaluate clinically relevant outcome measures for longitudinal monitoring of PCD patients in clinical care and future trials. Major areas of interest include: enhancing the evidence base for disease-targeted treatments; identifying challenges in designing and conducting clinical trials in PCD; and deeper phenotyping of PCD patients for better stratification in clinical trials.

Lead: Philipp Latzin

Discussions took place during the Inaugural Conference highlighting the necessity of identifying other possible outcome measures for monitoring lung disease progression and to serve as endpoints in clinical trials, such as multiple breath wash-outs (MBW), high-resolution computerised tomography and magnetic resonance imaging. Future applications of MBW and MRI in PCD need researching as a potential outcome measures in PCD. This will result in a series of

RESEARCH HIGHLIGHTS

which will identify and evaluate disease specific outcome measures to be recommended for future use. During the inaugural conference, participants heard from one a European consortium working on developing new statistical methods for rare diseases and small populations. Collaboration with these statistical networks will provide an additional toolbox from which BEAT-PCD members can draw expertise for new study designs tailored for rare diseases. It was also discussed that routinely collected data represent a rich and ample source for research but concerns over data standardisation across different countries should be fully addressed. An important step in this direction was the recent establishment of the European PCD registry.

SIGNING UP

BASECAMP

If you are interested in joining BEAT-PCD, please complete a short survey (via the link below) so that we can identify your area of expertise and contribution. From here you can be added to appropriate work groups, email lists etc. We will also then invite you to join Basecamp – where information about the action as a whole is available in addition to forums for the various work groups.

https://www.isurvey.soton.ac.uk/16640

For additional information about the project please also see the website:

http://www.beatpcd.org/

iPCD COHORT

The iPCD Cohort assembles available datasets with clinical and diagnostic data from PCD patients worldwide to answer pertinent questions on clinical phenotype, disease severity, prognosis and effect of treatments in patients with this rare multi-organ disease. Centres that wish to participate in the project and contribute data can contact the iPCD Cohort (pcd@ispm.unibe.ch) to sign a data delivery agreement. They will then receive a password to access the online software REDCap and they will be able to enter their data directly. They can also upload follow-up data or add additional patients at a later time point.

INTERNATIONAL PCD REGISTRY

The purpose of the International PCD Registry is to measure, examine and compare different aspects of the manifestation, course and treatment of PCD. It also aims to provide data for epidemiological research and to identify special patient groups suitable for multi-centre trials. If you are interested in signing up your institution as a registry centre, visit https://www.pcdregistry.eu for more information.

SHORT-TERM SCIENTIFIC MISSIONS

BEAT-PCD awards bursaries for STSM to enable clinicians and researchers to visit other European centres. For information about how to apply see the website or contact the Training School Coordinator, Claire Hogg. Here are two examples of recent STSMs:

Panayiotis Kouis, PhD candidate at the Cyprus University of Technology in Cyprus, spent 3 weeks at the Institute for Social and Preventive Medicine (ISPM), University of Bern in Switzerland.

The iPCD Cohort is a large international, multicentre cohort study containing baseline and longitudinal data on clinical characteristics, diagnostic testing and management therapies for patients diagnosed with PCD. The aim of the STSM was to learn techniques for data standardization, management, coding, and analysis from the research group that conducted the iPCD Cohort study.

Panayiotis said *"During my STSM at the ISPM, I had the opportunity to gain experience in study protocol development and meta-cohort data management, and to acquire new skills in the field of statistical analysis. Furthermore, this STSM provided an excellent platform for the initiation of an international and multicentre study on the frequency, determinants and impact of lobectomies in Primary Ciliary Dyskinesia patients, using the iPCD Cohort dataset."*

Amelia Shoemark, a PCD diagnostic scientist at The Royal Brompton Hospital in London, spent five days at Rikshospitalet in Oslo, Norway.

The host, Suzanne Crowley, is setting up a national competence centre to provide a diagnostic service for Norway which involves establishing a national register and biobank. The aim of the STSM was to establish a comprehensive and reliable method for the electron microscopic examination of cilia in Oslo. Activities included, conducting nasal brushings, teaching and assessing electron microscopy samples.

Amelia said *"This short term scientific mission has broadened my knowledge of PCD. In one week I was able to assess by electron microscopy a number of unusual and difficult samples from patients with probable PCD. The STSM really highlighted the need for standardisation of cilia electron microscopy methodology and reporting across Europe."*

SHORT REVIEW ON RECENT RESEARCH HIGHLIGHTS

Each BEAT-PCD edition will feature a short review from a work group on recent research highlights. This edition features an update from Work Group 1 from Hannah Farley and Dominic Norris who work at the UK Medical Research Council's MRC Harwell Institute, near to Oxford in the UK.

***Trp73* – the master regulator gene controlling motile ciliogenesis?**

The concept of a master regulator, a gene controlling the formation of specific cell lineages, was proposed by Susumu Ohno in 1979 as a "gene that occupies the very top of a regulatory hierarchy" [1]. For cells carrying multiple motile cilia, such as those of the respiratory tract, this role has been argued to be filled by the transcription factor FOXJ1. However, the fact that *FoxJ1* is expressed in some cell lineages that lack motile cilia [2], raises questions about this assignation.

Trp73 encodes the P73 protein, a member of the P53 family of transcription factors. As P53 knock-out mice exhibited spontaneous tumour development, it came as a surprise to many that P73 null-mutant mice do not form spontaneous tumours [3]. Two recent studies suggest that this is because its true function is as a master regulator of motile ciliogenesis [4, 5]. Indeed, careful phenotyping of *Trp73* knock-out mice reveals that they suffer from a range of PCD signs and symptoms.

Many of the *Trp73* phenotypes overlap those of published mouse models of PCD, including chronic sinusitis and rhinitis as well as otitis media. Both hydrocephalus and infertility were also reported. Uniquely, lower respiratory tract defects in the form of chronic bronchitis were evident, something never previously reported in a mouse model of PCD. However left-right patterning, which requires motile mono-ciliated rather than multi-ciliated cells, remained unaffected.

Analysis at the cellular level revealed that loss of P73 prevents the basal bodies from docking at the cell membrane, thus preventing ciliary assembly. The resulting absence of cilia was evident at a cellular level as demonstrated by histology, immunofluorescence and Scanning Electron Microscopy. While the *Trp73* null mouse does not model the classical PCD, it clearly removes the function of motile cilia.

The two studies, Marshall *et al* [4] and Nemajerova *et al* [5], both investigate the genes acting downstream of P73. Using chromatin immunoprecipitation sequencing (ChIP-seq) they identify areas of the genome where P73 binds. From this they identify candidate target genes – genes that map nearby. The genes identified include known cilia genes such as *Foxj1*, *Rfx3* and *Dnali1*, as well as loci known to cause PCD (e.g. *Ccdc39*, *Ccdc40*), demonstrating that this approach is valid: The gene targets include *Foxj1*, placing *P73* above *Foxj1*, at the top of a regulatory hierarchy. The resulting understanding of the genetic network controlling production of motile multiciliated cells is likely to feed

SHORT REVIEW ON RECENT RESEARCH HIGHLIGHTS

into our understanding of PCD on various levels. It will help us to identify new candidate PCD genes. It will help drive the development of hypothesis driven PCD research. And ultimately it should feed into the development and stratification of novel therapeutic approaches.

1. Ohno, S., *Major sex-determining genes.* . 1979, Berlin, Germany: Springer-Verlag.
2. Cruz, C., et al., *Foxj1 regulates floor plate cilia architecture and modifies the response of cells to sonic hedgehog signalling.* Development, 2010. **137**(24): p. 4271-82.
3. Yang, A., et al., *p73-deficient mice have neurological, pheromonal and inflammatory defects but lack spontaneous tumours.* Nature, 2000. **404**(6773): p. 99-103.
4. Marshall, C.B., et al., *p73 Is Required for Multiciliogenesis and Regulates the Foxj1-Associated Gene Network.* Cell Rep, 2016. **14** (10): p. 2289-300.
5. Nemajerova, A., et al., *TAp73 is a central transcriptional regulator of airway multiciliogenesis.* Genes Dev, 2016. **30**(11): p. 1300-12.