

# **Report on the Activities of the ECFS Basic Science Working Group (BSWG)**

## **Annual Report – April 2019**

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### **1. Goals**

The renewal of ECFS Basic Science WG (BSWG) was approved in January 2018 with the following goals:

- 1) Widening the number of European scientists doing fundamental research on those areas of CF as ECFS members, in particular to attract, train and maintain younger investigators in the CF field;
- 2) Promote best practice procedures (through organization of workshops);
- 3) Develop a network (jointly with ECFS-TDN and Registry) for the creation of biobanks of CF patients' materials across Europe for the generation (e.g., primary cultures of epithelial cells, intestinal organoids, etc) and distribution of resources for CF research;
- 4) Production of consensus guidelines for standardization of research-derived laboratory techniques that can be applied to the clinic (e.g., novel biomarkers to be used in CF diagnosis or as "surrogate endpoints" for clinical trials, etc);
- 5) Prioritizing topics related to emergent needs in the field so as to create "task forces" (e.g., on assays to measure CFTR activity, drug discovery, etc);
- 6) Promotion of excellence in CF research by fostering European-scale research to avoid effort duplication at national level and fragmentation and to achieve competitiveness for EU consortia
- 7) Liaising with basic scientists in other societies (European Respiratory Society; United European Gastroenterology, UK Physiological Society) and patients associations (CFF-USA; Mukoviszidose e.V, CF Trust, Vaincre la Mucoviscidose, etc) to maximize and optimize efforts.

## 2. Activities

### 2.1. Meeting of the BSWG

The BSWG organized a session within the 16<sup>th</sup> ECFS Basic Science Conference in Dubrovnik, Croatia, 27 – 30 March 2019 on the topic "*Activating Alternative Chloride Channels to Treat CF: Friends or Foes?*", which took place on Thursday, 28 March (18:00 - 19:45).

The purpose of this session was to bring attention of participants in the ECFS BS Conference to chloride channels as good candidates for drug discovery in CF in the short/medium term, namely for individuals with CF who are not eligible for the approved CFTR modulator drugs. The session comprised two roundtables, the first on the topic "*Can we regulate TMEM16A independently of  $Ca^{2+}$ ? And TMEM16A /SLC26A9 independently of CFTR?*" moderated by Jeff Beekmann (NL) and Karl Kunzelmann (DE), the second on "TMEM16A and mucus" moderated by Margarida Amaral (PT) and Luis Galiotta (IT).

Abstracts submitted to the conference on these two topics (3 on the first topic and 4 on the second) were presented as very short talks (3 min each) to trigger discussion. Both round tables had a panel of invited discussants, selected among the invited speakers and participants in the Conference: 7 on the first topic and 4 on the second (see full programme in Annex 1).

A report on this symposium will be published in a special issue of JCF dedicated to the 2019 ECFS Basic Science Conference (to be submitted by 29 July).

### 2.2. BSWG Workshop

Still within the past year, the BSWG it organized a "3<sup>rd</sup> Hands-on Workshop on Epithelial Systems: Physiology and Pathophysiology" (ESP2018), which took place at the Faculty of Sciences of the University of Lisboa (FCUL), Portugal, between 23 – 27 July 2018 (see Programme in Annex 2).

This workshop aimed to elucidate researchers from the CF community on the theoretical aspects of basic CF science, as well as provide practical training in the new techniques underlying current and novel biomarkers based on CFTR activity and other molecular and cell biology parameters.

The Workshop was initially open to 12 participants, but given that it received 35 applicants, it was decided to accept 26 participants (see list of participants in Appendix 3): Brazil (1), Chile (1), Germany (6), Hungary (4), Portugal (9), UK (3), Italy (1), USA (1).

The Workshop counted with the support of National Patients Organizations in the form of travel grants for participants from the respective countries: Germany (6) and Italy (1).

Based on the very positive evaluations of the BSWG ESP 2018 Workshop (see evaluation by participants in Annex 4), it was decided to organize again at FCUL, Lisboa (Portugal) a 4<sup>th</sup> BSWG 2019 Workshop, now called "*2019 Summer School on Epithelial Systems: Physiology and Pathophysiology*" which will take place in Lisboa, 22 – 26 July 2019.

**Annex 1 – Programme of the Basic Science Working Group Symposium at the 16<sup>th</sup> ECFS Basic Science Conference, Dubrovnik Croatia (27 - 30 March 2019)**

**Activating Alternative Chloride Channels to Treat CF: Friends or Foes?**

Thursday 28 March 2019 (18:00 - 19:45)

18:00-18:05	Introduction	
18:05-18:50	<p><b>Round table 1: Can we regulate TMEM16A independently of Ca<sup>2+</sup>? And TMEM16A /SLC26A9 independently of CFTR?</b></p> <p><b>Moderators: Jeff Beekmann &amp; Karl Kunzelmann</b></p>	<p><b>Invited Discussants:</b> Raimund Dutzler; Yukiko Sato; Nicoletta Pedemonte; Martin Gosling; Renaud Beauwens; Michele Genovese; John Hanrahan</p>
18:05-18:10	Facts about ANO1	Karl Kunzelmann
18:10-18:19 (3 slides, 3 min each)	Abs 11 - EACT increases intracellular calcium levels by a TMEM16A-independent mechanism	Henry Danahay (United Kingdom)
	Abs 46 - Niclosamide repurposed for the treatment of inflammatory airway disease	Roberta Benedetto (DE)
	Abs 70 - Identification of novel ANO1/TMEM16A regulators as alternative therapeutic targets for cystic fibrosis	Madalena C. Pinto (PT)
18:09-18:50	Overall Discussion	
18:50-19:00	<i>Short Break</i>	
19:00-19:45	<p><b>Round table 2: TMEM16A and mucus</b></p> <p><b>Moderators: Margarida Amaral &amp; Luis Galietta</b></p>	<p><b>Invited Discussants:</b> Mike Gray; Mike Welsh; Pamela Millar-Büchner; Martial Delion</p>
19:00-19:12 (3 slides, 3 min each)	Abs 10 - TMEM16A channel function does not influence goblet cell numbers in the human airway epithelium	Henry Danahay (UK)
	Abs 52 - Cell Proliferation Upregulates ANO1 in Mucus Cell Hyperplasia	Filipa Simões (PT)
	Abs 81 - The attached stratified mucus in obstructive airway disease is detached by calcium removal	Dalia Fakihi (SE)
	Abs 144 - Physiological role and therapeutic importance of TMEM16A chloride channel in the airway epithelium	Arianna Venturini (IT)
19:12-19:45	Overall Discussion	

## Annex 2 – Programme of the "2018 Hands-on Workshop on Epithelial Systems: Physiology and Pathophysiology"



EPITHELIAL SYSTEMS: PHYSIOLOGY AND PATHOPHYSIOLOGY  
Lisboa, Faculty of Sciences, 23-27 July 2018



Time	Monday (23 Jul)	Tuesday (24 Jul)	Wednesday (25 Jul)	Thursday (26 Jul)	Friday (27 Jul)	Time
8.30-9.00						
9.00-9.30	Course Introduction	Physiology of the Epithelial Cells RT	Physiology of Intestinal Epithelial Cells KK	Measurement of transepithelial ion mov. With Ussing chamber MH	Functional diagnosis of Cystic Fibrosis by Ussing Chamber MH	9.00-9.30
9.30-10.00	Personalized Therapies for Cystic Fibrosis MDA	Coffee Break	Coffee Break	Coffee Break	Coffee Break	9.30-10.00
10.00-10.30	Culturing Respiratory Cells AK	New methodologies to implement clinical trials KB	Physiol. of Exocrine Pancreatic and Sweat Gland Epithelial Cells MG	Electrophysiology techniques MG	New aspects of epithelial physiology KK	10.00-10.30
10.30-11.00						10.30-11.00
11.00-11.30	Break	Break	Break	Break	Break	11.00-11.30
11.30-12.00	Research Seminar AK	Research Seminar RT	Research Seminar KB	Research Seminar KK	Research Seminar MG	11.30-12.00
12.00-12.30						12.00-12.30
12.30-13.00	Lunch Break	Lunch Break	Lunch Break	Lunch Break	Lunch Break	12.30-13.00
13.00-13.30						13.00-13.30
13.30-14.00	Lab 01 - Immuno MQ	Lab 03 - ASL RT	Lab 05 Swelling Assay IS	Lab 06 Ussing Chamber MH	Tutorial 01 - Organoids IS & HB	13.30-14.00
14.00-14.30						14.00-14.30
14.30-15.00	Lab 02 - Nasal cells AK	Lab 04 - Organoids IS				14.30-15.00
15.00-15.30						15.00-15.30
15.30-16.00						15.30-16.00
16.00-16.30					Coffee Break	16.00-16.30
16.30-17.00	Coffee Break	Coffee Break	Coffee Break	Coffee Break		16.30-17.00
17.00-17.30	Meet the Expert (Nasal Cells and Charact) - AK, MDA	Meet the Expert (Organoids and ASL) - RT, KB	Meet the Expert (Trans app of Uss Chamb Meas) - KK, MG	Meet the Expert (Alternative Channels) - MG	Tutorial 02 - Ussing Chamber MH & KK	17.00-17.30
17.30-18.00						17.30-18.00
18.00-18.30						18.00-18.30
18.30-19.00						18.30-19.00
19.00-19.30						19.00-19.30
19.30-20.00					Course Dinner	19.30-20.00

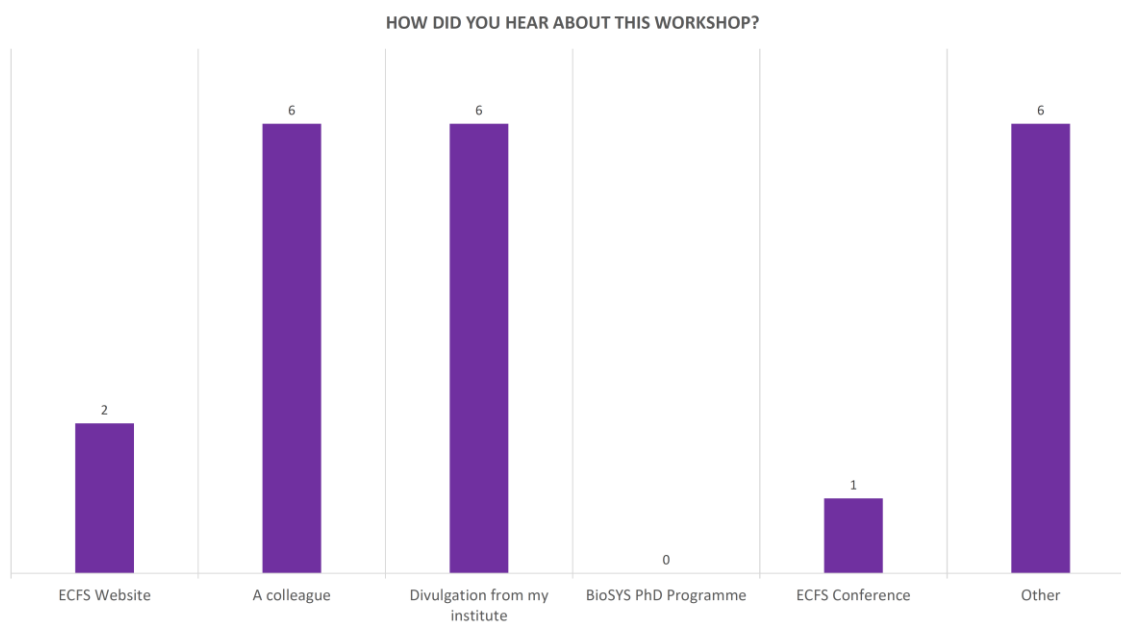
Detailed Programme				
Class	Title	Room	Faculty	Institution
Lecture 01	Personalized Therapies for Cystic Fibrosis: How to Rescue >2,000 Dysfunctional Channels?	Lecture room	Margarida Amaral	University of Lisboa (Portugal)
Lecture 02	Culturing Respiratory Cells	Lecture room	Anthony Kicic	University of Western Australia (Australia)
Lecture 03	Physiology of the Epithelial Cells	Lecture room	Rob Tarran	University of North Carolina (USA)
Lecture 04	New methodologies to implement clinical trials	Lecture room	Kris De Boeck	University of Leuven (Belgium)
Lecture 05	Physiology of Intestinal Epithelial Cells	Lecture room	Karl Kunzelmann	University of Regensburg (Germany)
Lecture 06	Physiology of Exocrine Pancreatic and Sweat Gland Epithelial Cells : focus on ion and fluid transport	Lecture room	Michael Gray	University of Newcastle (UK)
Lecture 07	Measurement of transepithelial ion movement with the Ussing chamber	Lecture room	Martin Hug	University of Freiburg (Germany)
Lecture 08	Electrophysiology techniques: from tissues to cells and single-molecules	Lecture room	Michael Gray	University of Newcastle (UK)
Lecture 09	Functional diagnosis of Cystic Fibrosis by Ussing Chamber	Lecture room	Martin Hug	University of Freiburg (Germany)
Lecture 10	New aspects of epithelial physiology	Lecture room	Karl Kunzelmann	University of Regensburg (Germany)
Lab 01	Immunofluorescence of Epithelial Cells & Tissues	Lab 8.1.71	Margarida Quaresma & Hugo Botelho	University of Lisboa (Portugal)
Lab 02	Processing Primary Nasal Epithelial Cells: Conditional reprogramming	Lab 8.1.74	Anthony Kicic & Luka Clarke	University of Western Australia (Australia); University of Lisboa (Portugal)
Lab 03	ASL Microscopy Measurements	Lab 8.1.71	Rob Tarran & Luis Marques	University of North Carolina (USA); University of Lisboa (Portugal)
Lab 04	Isolation of Intestinal Organoids from Murine biopsies	Lab 8.1.74	Íris Silva	University of Lisboa (Portugal)
Lab 05	Culture of Human Intestinal Organoids and Forskolin Induced Assay	Lab 8.1.74 / 79	Íris Silva	University of Lisboa (Portugal)
Lab 06	Ussing Chamber Analysis of Murine Native Tissues and Polarized Epithelial Cells	Lab 8.3.43	Martin Hug & Roberta Benedetto	University of Freiburg (Germany); University of Regensburg (Germany)
Tutorial 01	Analysis of Organoids Swelling Assay Data	Lecture room	Hugo Botelho & Íris Silva	University of Lisboa (Portugal)
Tutorial 02	Analysis of Ussing Chamber Data	Lecture room	Martin Hug & Karl Kunzelmann	University of Freiburg (Germany); University of Regensburg (Germany)

**Annex 3 – List of participants at the "2018 Hands-on Workshop on Epithelial Systems: Physiology and Pathophysiology"**

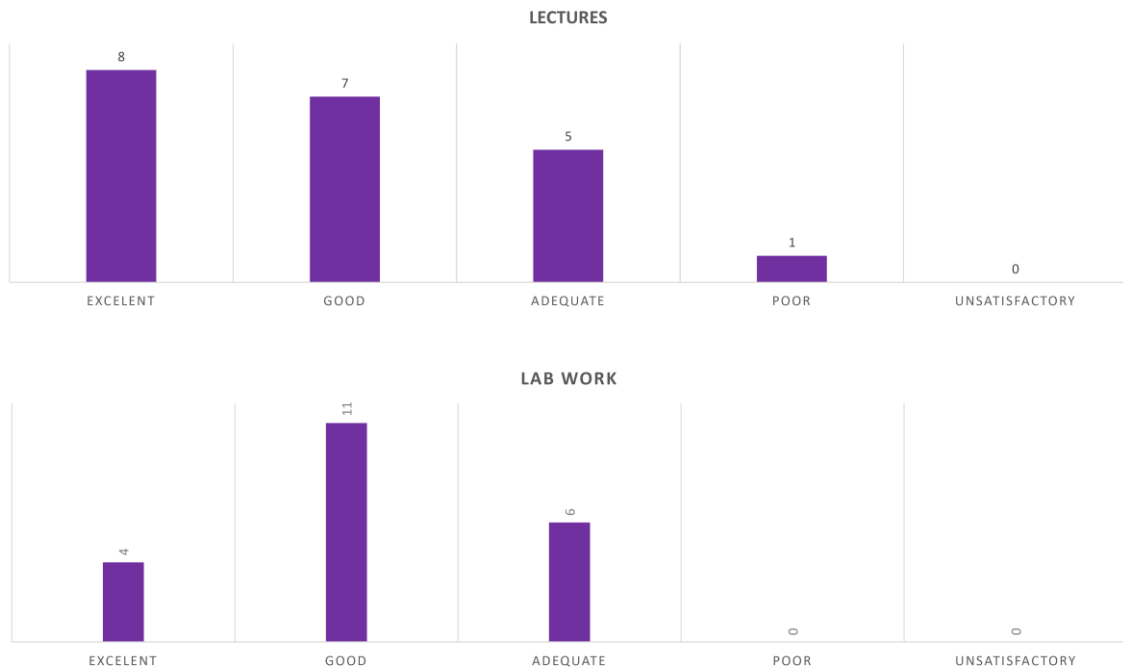
Anais Sahabian	Hannover Medical School	Germany
Anita Balazs	Charite Universitätsmedizin Berlin	Germany
Catarina Gouveia	BiolSI – University of Lisboa	Portugal
Christina Fey	University Hospital Würzburg	Germany
Claudia Rückes-Nilges	Pediatric CF-Centre, Giessen University	Germany
Eleonóra Gál	University of Szeged	Hungary
Emese Tóth	University of Szeged	Hungary
Fabiana Ciciriello	Bambino Gesù Hospital	Italy
Fernando Marson	State University of Campinas	Brazil
Genesis Hormazábal	Centro de Estudios Científicos	Chile
Guillem Santamaria	BiolSI – University of Lisboa	Portugal
Helena Santos	BiolSI – University of Lisboa	Portugal
Hendrik Beckert	University Medical Center Essen	Germany
James Reihill	Queens University Belfast	UK
Janina Treffon	University of Muenster	Germany
Juan Fernández	BiolSI – University of Lisboa	Portugal
Leyre Pernaute	BiolSI – University of Lisboa	Portugal
Lóránd Kiss	University of Szeged	Hungary
Margit Németh	University of Szeged	Hungary
Martin Attwood	UCL Great Ormond Street Institute of Child Health	UK
Ozge Bozkurt Beyazcicek	Cystic Fibrosis Center, UNC	USA
Rebeca André	BiolSI – University of Lisboa	Portugal
Ryan Kelsey	Ulster University	UK
Sofia Ramalho	BiolSI – University of Lisboa	Portugal
Tânia Marques	BiolSI – University of Lisboa	Portugal
Tiago Pedreira	BiolSI – University of Lisboa	Portugal

## Annex 4 – Evaluation by participants of the "2018 Hands-on Workshop on Epithelial Systems: Physiology and Pathophysiology"

### Information on the participants



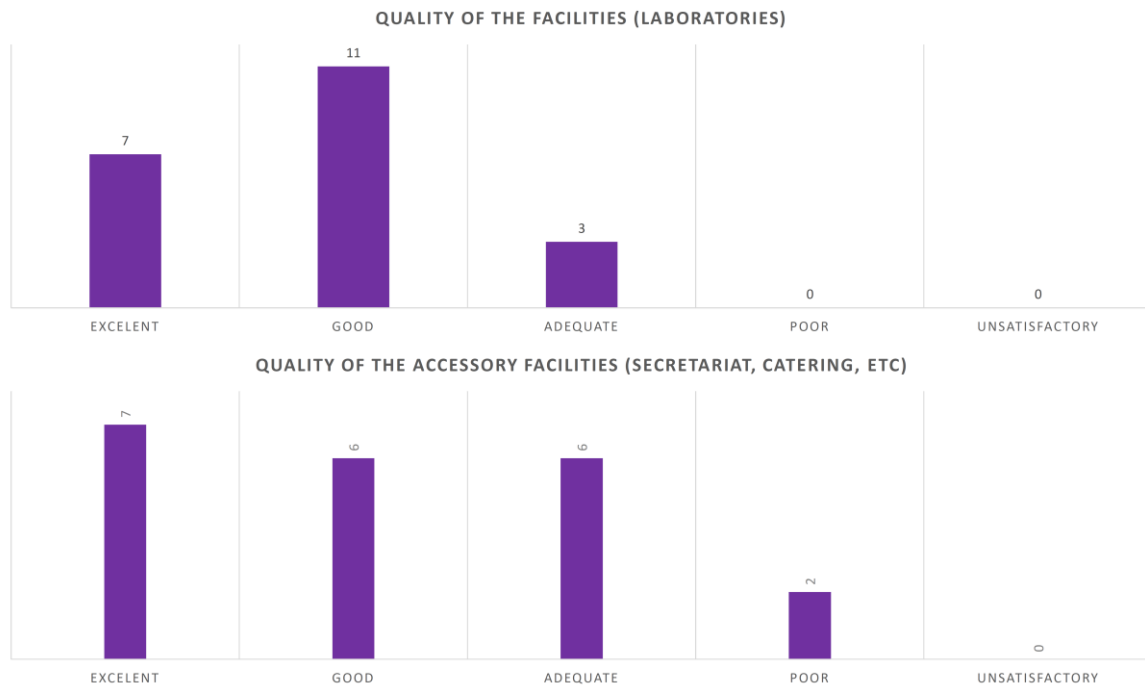
## Organization of Programme



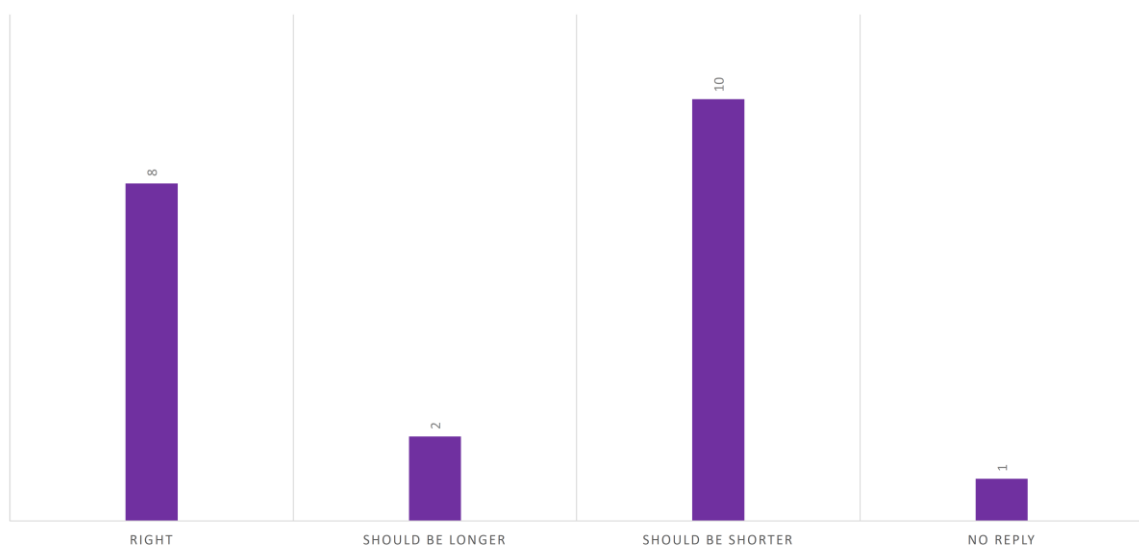
## Quality of the programme



## Quality of the programme



## Duration of the workshop





## Was there...

