

TEMPLATE FOR ECFS WORKING GROUP REPORTS

Please use this template for your annual working group report. Please use black ink, Calibri font size 11. For more information, please read the ECFS working group Terms of Reference document

Year of report:
2023-2024

Name of Working Group:
Airway Epithelial Cell Models for Theranostics

Date of initial approval of working group:
23rd June 2023

Contact details of coordinator, vice coordinator and assistant (if applicable) including ECFS membership numbers:

Coordinator name: Isabelle Sermet
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ECFS Membership number: 278

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ECFS Membership number: 4849

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ECFS Membership number: 5388

Outcomes already achieved (maximum 100 words):

1. Developed 3 new SOPs for culture of hNECs, Ussing Chamber and Certification of operators:
 - ECFS CTN 4.1/001/v2 Isolation, cultivation and application of primary epithelial cells obtained by nasal brushing SOP.
 - ECFS CTN 4.1/002 Transepithelial electrical measurements with the Ussing Chamber SOP.
 - ECFS CTN 4.1/003 SOP for Certification for Transepithelial electrical measurements with the Ussing Chamber.
2. Ongoing training: 2 operators have completed training/certification (Koln & Prague CTN Centres).
3. Contact with EMA to request qualification of hNECs as a predictive biomarker to determine response of rare CFTR mutations to existing/novel CFTRm by preassessment in vitro.

Report for this year (max 1000 words)

- short term goals for the year
- current number of members
- measures taken to encourage ECFS membership
- outcomes/achievements (e.g. meetings, activities, website development, awards, publications etc).

Short term goals for the year:

1. standardisation of primary airway (nasal and bronchial) epithelial cell sampling, culture, evaluation and biobanking: Standardisation is needed across our multiple CF centres as there is considerable heterogeneity despite a central SOP. There is variability in terms of technique, equipment and media used. Cell brushing, transport, media of cell expansion and re-differentiation, freezing media and coating of inserts all vary in practice. The purpose of the Working Group in 2023 was to facilitate sharing of best practice and harmonisation across centres to promote the applications of this timely technique and to facilitate access for patients to HEMT all over Europe.
2. Linking to the 1st goal above, our 2nd goal was completion of a revised SOP for isolation, cultivation, and application of hNECs through collaboration across centres. This was successfully completed.
3. Linked to the 2nd goal, was completion of a new SOP for the use of the Ussing Chamber: this was successfully achieved.
4. Testing of expansion and freezing media: ongoing in French and Italian labs.
5. To facilitate the acquisition of the technique to labs within ECFS and allied countries, based on workshops, staff exchanges and certification of laboratories (ECFS lab network) – this was initiated with the staff exchange/training in our Paris lab, of 2 staff from Prague and Koln CTN centres.
6. In-person meeting at ECFS to agree updated SOPs and plan training workshops (completed June 2023), and planned for ECFS Glasgow June 2024
7. Online meetings: 6th July 2023; 14th September 2023; 18th October 2023; 12th January 2024

Current number of members: n=24

Measures taken to encourage ECFS membership:

The group has sought to expand membership across CTN centres and beyond at international level, through shared practice across labs and centre teams, via ECFS Conference and NACFC, to facilitate sharing of best practice and harmonisation across centres to promote the applications of this timely technique. We have also linked with experts in Australia and the USA.

Outcomes/achievements (e.g. meetings, activities, website development, awards, publications etc):

The working group has successfully completed regular teleconference meetings, developing new SOPs for wider distribution across ECFS:

- ECFS CTN 4.1/001/v2 Isolation, cultivation and application of primary epithelial cells obtained by nasal brushing SOP.
- ECFS CTN 4.1/002 Transepithelial electrical measurements with the Ussing Chamber SOP.
- ECFS CTN 4.1/003 SOP for Certification for Transepithelial electrical measurements with the Ussing Chamber.

In-person meeting planned at ECFS 2024 – for planning of training workshops and wider discussion of techniques.

Dreano E, Burgel PR, Hatton A, Bouazza N, Chevalier B, Macey J, Leroy S, Durieu I, Weiss L, Grenet D, Stremler N, Ohlmann C, Reix P, Porzio M, Roux Claude P, Rémus N, Douvry B, Montcouquiol S, Cosson L, Mankikian J, Languépin J, Houdouin V, Le Clainche L, Guillaumot A, Pouradier D, Tissot A, Priou P, Mély L, Chedevergne F,

Lebourgeois M, Lebihan J, Martin C, Zavala F, Da Silva J, Lemonnier L, Kelly-Aubert M, Golec A, Foucaud P, Marguet C, Edelman A, Hinzpeter A, de Carli P, Girodon E, Sermet-Gaudelus I, Pranke I; French CF Reference Network study group. Theratyping cystic fibrosis patients to guide elexacaftor/tezacaftor/ivacaftor out-of-label prescription. *Eur Respir J.* 2023 Oct 19;62(4):2300110. doi: 10.1183/13993003.00110-2023. PMID: 37696564.

Terlizzi V, Pesce E, Capurro V, Tomati V, Lena M, Pastorino C, Bocciardi R, Zara F, Centrone C, Taccetti G, Castellani C and Pedemonte N. Clinical Consequences and Functional Impact of the Rare S737F CFTR Variant and Its Responsiveness to CFTR Modulators. *International Journal of Molecular Sciences.* 2023; 24(7):6576. <https://doi.org/10.3390/ijms24076576>

Aims for the coming year (please state year) (max 50 words):

1. Widen training/certification
2. Organization of 2 workshops
3. Dissemination of SOP/technique: conference abstracts/publication
4. Continuation of certification
5. Quality control: Inter-lab sharing of samples
6. Evaluation of samples of rare genotypes in certified laboratories
7. Biobank list for sharing of results
8. Encouragement of young investigators
9. International collaboration with research partners: TDN/CanACT

Summary (maximum 100 words):

Using ALI-culture models such as those outlined in the hNEC SOP, the wider application of theratyping in reference laboratories could extend analysis of CFTR response to patients with rare and ultrarare mutants who cannot access HEMT all over Europe. Given the breadth of scope of this application, there is an urgent need to standardise and certify operators in the techniques of cell sampling, cell amplification, differentiation, and analysis of hNE cells. Furthermore, the relative accessibility of patient-derived nasal epithelial cells and the use of their cultures for pre-clinical studies is an idea welcomed by the patient community.

Breakdown of expenses (please include total amount received as well as expenditure and, if applicable, the outstanding balance (Euros)):

Funding for 2023 requested and confirmed to be carried forward to next fiscal year – 2024 to provide on-site workshop training at INSERM laboratory (Paris) – carried over due to excessive cost of Paris accommodation in 2023 (due to Olympic games).
Balance remains at 10,000 Euros for 2023.

Budget amount requested for next year (please give the amount in Euros and the year):

10,000 euros 2023 (training approx 12 operators – travel to Paris lab and accommodation plus basic subsistence)
10,000 euros 2024 (training approx 12 operators – travel to Paris lab and accommodation plus basic subsistence)

Please provide us with a list of all current members (name, professional title, email address and ECFS membership number):

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For ECFS board use only:

Report received in Office on:

Number of years of working group

Report accepted / rejected

Follow-up action to be taken by ECFS