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: **2024-2025**	
Name of Working Group: **Airway Epithelial Cell Models for Theranostics**	Date of initial approval of working group: **23rd June 2023**

Title, name and email of coordinator, vice coordinator and assistant (if applicable):
Coordinator name: Isabelle Sermet
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ECFS Membership number: 4849

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Long term aims of the working group (maximum 100 words) including estimated achievement date:

Training and certification of ECFS CTN site staff in collection, cultivation and analysis of hNECs – this is ongoing and plans are in place for 2025 and into 2026 training as required by site staff.
Qualification of hNECs as a predictive biomarker to determine response of rare CFTR mutations to existing/novel CFTRm by preassessment in vitro – ongoing 2025 into 2026.

Outcomes already achieved (maximum 100 words):

1. In 2024 we published 3 new SOPs (shared via the ECFS Education Platform & CTN bimonthly newsletters to all site PIs and RCs), these were then promoted at our Steering Committee Meetings in Glasgow (June 2024) and Brussels (January 2025):
   - 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 completed training/certification (Koln & Prague CTN Centres in 2023-24). 7 further operators training upcoming summer 2025 (Essen, Warsaw, Koln, Istanbul, Hannover).
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, ongoing correspondence

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 the new central SOPs. 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 2024 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 CFTRm 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 successfully completed ECFS Glasgow June 2024
7. Online meetings: 12th January 2024; in person meeting ECFS Glasgow June 2024

Current number of members: n=28

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, USA (UAB, Alabama) and Montreal, Canada.

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 June 2025 – for planning of training workshops and wider discussion of techniques.

Tomati V, Capurro V, Pesce E, Pastorino C, Sondo E, Lena M, Borrelli A, Cresta F, Pantano S, Collini F, Ripani P, Terlizzi V, Fevola C, Costa S, Lucanto MC, Zara F, Bandiera T, Bocciardi R, Castellani C, Galietta LJV, Pedemonte

N. Pharmacological rescue of the G85E CFTR variant by preclinical and approved modulators. Front Pharmacol. 2024 Nov 18;15:1494327. doi: 10.3389/fphar.2024.1494327. PMID: 39624835; PMCID: PMC11608983.

Corrao F, Kelly-Aubert M, Sermet-Gaudelus I, Semeraro M. Unmet challenges in cystic fibrosis treatment with modulators. Expert Rev Respir Med. 2024 Mar-Apr;18(3-4):145-157. doi: 10.1080/17476348.2024.2357210. Epub 2024 May 21. PMID: 38755109.

Zajac M, Lepissier A, Dréano E, Chevalier B, Hatton A, Kelly-Aubert M, Guidone D, Planelles G, Edelman A, Girodon E, Hinzpeter A, Crambert G, Pranke I, Galietta LJV, Sermet-Gaudelus I. Putting bicarbonate on the spot: pharmacological insights for CFTR correction in the airway epithelium. Front Pharmacol. 2023 Dec 11;14:1293578. doi: 10.3389/fphar.2023.1293578. PMID: 38149052; PMCID: PMC10750368.

Pion A, Kavanagh E, Joynt AT, Raraigh KS, Vanscoy L, Langfelder-Schwind E, McNamara J, Moore B, Patel S, Merlo K, Temme R, Capurro V, Pesce E, Merlo C, Pedemonte N, Cutting GR, Sharma N. Investigation of CFTR Function in Human Nasal Epithelial Cells Informs Personalized Medicine. Am J Respir Cell Mol Biol. 2024 Nov;71(5):577-588. doi: 10.1165/rcmb.2023-0398OC. PMID: 39012815; PMCID: PMC11568479.

Guidone D, de Santis M, Pesce E, Capurro V, Pedemonte N, Galietta LJV. The apical mucus layer alters the pharmacological properties of the airway epitheliumy. J Physiol. 2025 Mar 6. doi: 10.1113/JP287891. Epub ahead of print. PMID: 40047394.

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, Languepin 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 & delivery of training 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

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)):

Balance remains at 10,000 Euros for 2024.

Budget amount requested for next year (please give the amount in Euros and the year):
10,000 euros 2024 (training approx 12 operators – travel to French and Italian training and accommodation plus basic subsistence)

The deadline for submission is 1st May 2025. Please email the report **and the excel spreadsheet of your members** to: **jess.matthews@ecfs.eu**

The report will then be presented to the board prior to the summer ECFS board meeting and then a decision will be made at the next board meeting for approval before being distributed.

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