ECFS Diagnostic Network Working Group
Meeting Report

DNWG session during ECFS Digital Conference 2021

June 11th, 2021 - Webinar via Zoom

***Chair: Elke De Wachter** (Brussels, Belgium) **– Nick Simmonds** (London, UK)*

The virtual meeting started with welcome words by the coordinator of the ECFS Diagnostic Network Working Group, Elke De Wachter. She shared with us some news of the working group. New members were welcomed and encouarged (with a reminder that being an ECFS member is a pre-requisite).

The first presentation was given by **Bente Aalbers** (*Utrecht, The Netherlands*), in which she gave us more insight into her recent study: “Females with CF have a larger decrease in sweat chloride in response to lumacaftor/ivacaftor compared to males.” Furthermore, she explained the negative correlation of weight with the response in sweat chloride concentration after start of lumacaftor/ivacaftor. She also stressed the importance of further investigation into the difference between males and females in response to CFTR modulators.

Following, **Marco Salvatore** (*Rome, Italy*) gave an in-depth presentation on his recently published paper called "Does active participation in EQA improve quality of the sweat test?". In his study, an external quality assessment program for laboratories analyzing sweat test, was implemented and afterwards evaluated. The overall results obtained from the participating laboratories show that their performance improved significantly. The speaker concluded that EQA participation should become mandatory for laboratories as a requirement for accreditation.

Paola Melloti (*Verona, Italy*) gave an overview on the role of sweat ion ratios in diagnosing cystic fibrosis. The aim of her study was to define the most appropriate outcome of the sweat test. She started by comparing Cl^-, Cl^-/Na^+ ratio, Cl^-/K^+ ratio and $(Cl^-/Na^+)/ K^+$ ratio. She concluded that in the overall population all the ratios significantly discriminated CF from non-CF but Cl^-/Na^+ ratio showed the highest ability to distinguish CF.

Afterwards, **Senne Cuyx** (*Leuven, Belgium*), presented his work (as a recorded video) on the validation of rectal organoid morphology analysis (ROMA) as a new physiological CFTR assay for CF diagnosis. ROMA is a new physiological CFTR assay classifying organoid morphology using circularity index as a measure for roundness of organoids and intensity ratio to quantify whether a lumen is present or not.

Next, **Danya Muilwijk** (*Utrecht, The Netherlands*) informed us about her study called: "Forskolin-induced Swelling of Intestinal Organoids Predicts Long-term CF Disease Progression". In this study, they assessed the predictive value of forskolin-induced swelling of patient-derived organoids on long-term CF disease progression in multiple organs and compared FIS with the gold standard biomarker sweat chloride concentration.

The next speaker, **Marella Bouva** (*Bilthoven, The Netherlands*), talked about the NBS program in the Netherlands NBS. The screening program started in 2011 and used a four-step protocol: IRT, PAP, Inno-Lipa line blot and extended gene analysis. Due to an evaluation which reported a low sensitivity, changes in the protocol were implemented (PAP lower cut-off value, a new safety net was implemented and R117-7T/9T variants were considered as non-pathogenic). Her study showed that these changes improved the sensitivity significantly.

Silvia Gartner (*Barcelona, Spain*) was the last speaker of this session and talked about her study: "Inconclusive CFSPID: clinical outcomes". The aim of her study was to analyze sweat chloride values and the clinical characteristics of cases with CFSPID identified through the neonatal screening program for CF in Catalonia. Her study concluded that the rate of conversion from CFSPID designation to a CF diagnosis was lower than reported in literature. She provided us with a very important take home message that stated: "CFTR variants should be checked every year using CFTR 2 database as new CF causing variants are still being characterized".

Nicholas Simmonds, the vice-coordinator of the working group, closed the DNWG session during the ECFS conference and invited all the participants to the next DNWG meeting (10 - 12th February 2022) which will take place in Montpellier, France.

We would like to thank ECFS for this successful meeting. We thank all speakers and participants for their fantastic contribution and for making the meeting such a great success!

We are looking forward to seeing you at our next ECFS DNWG Meeting in Montpellier.

11th June 2021

Elke De Wachter – ECFS DNWG Coordinator

Nicholas Simmonds – ECFS DNWG Vice-coordinator

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