**DOROTHY NELL MARZOL INNOVATION GRANT 2022**

Project Title: "Australian-wide surveillance for fungal infection: A national metagenomic analysis across 19 CF centres".

Grant Recipient: Steven Taylor

**Final Report**

Surveillance of emerging respiratory pathogens is imperative to facilitate effective and timely clinical management for people with CF. With increasing evidence of the emergence of fungi in the lungs of people with CF, the goal of this project was to better understand their prevalence and clinical importance. Specifically, this project aimed to:

- Establish an evidence base for the ongoing surveillance of fungi in the airways of people with CF across Australia.
- Identify risk factors associated with fungal composition.
- Investigate dynamics of fungal colonisation in relation to airway bacterial composition and airway inflammation.

To achieve this, we undertook fungal metagenomic and quantitative polymerase chain reaction (qPCR) analyses on 981 respiratory samples from a nation-wide cohort of people with CF. These methods allow not only detection of fungi but also enumeration. Overall, this analysis found fungal carriage was common, being detected in 39.4% of participants. The most common fungal genus was Aspergillus (27.6% of participants) followed by Candida (16.1% of participants). Detection of other pathogenic fungi (such as Scedosporium apiospermum and Exophiala dermatitidis) was rare (<1%). Reassuringly, no pathogenic fungi not previously reported in respiratory samples from persons with CF were detected in this cohort.

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We next assessed whether there is any concern around fungal detection in the airways. Reassuringly, we did not identify any clinical variables significantly associated with detection of any fungi. However, relationship between fungi and bacterial pathogens identified a negative relationship between P. aeruginosa (defined by detection at >30% relative abundance in metagenomic analysis) and Aspergillus detection. In contrast, a positive relationship was identified between nontuberculous mycobacterium (NTM) carriage (defined by any positive culture of NTM in the prior 12 months) and Aspergillus. The former

may represent P. aeruginosa eradication therapy increasing risk of Aspergillus, as previously reported.3 The later has not been previously reported but may inform infection risk of NTM.

We are now finalising this analysis, including multivariate regression to adjust for potentially confounding factors. We aim to publish these findings in relevant journals such as Journal of Cystic Fibrosis and Clinical Infectious Diseases, acknowledging the support of CF Australia.

**References**


1. Düesberg U, et al. Risk factors for respiratory Aspergillus fumigatus in German Cystic Fibrosis patients and impact on lung function. Sci Rep. 2020;10:18999.
2. Burns JL, et al. Effect of chronic intermittent administration of inhaled tobramycin on respiratory microbial flora in patients with cystic fibrosis. J Infect Dis. 1999;179:1190–6.
3. Harun SN, et al. Aspergillus and progression of lung disease in children with cystic fibrosis. Thorax. 2019;74(2):125-131.