2021-2022 STUDENT PROJECT OPPORTUNITIES

Tackling polymicrobial respiratory infections

HONOURS | MASTERS | PhD

menzies
school of health research

Course Name: Master by Research (IAS) CRICOS Course Code: 053295G | Course Name: Doctor of Philosophy (IAS) CRICOS Course Code: 053291A
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Early life microbiome, immune development and susceptibility to acute respiratory infection

CHILD HEALTH | **MASTER BY RESEARCH** | **PhD**

We are recruiting for a Masters/PhD student project within part of a research program that aims to achieve sustainable improvements in the respiratory health of Aboriginal children.

Background: Indigenous children have a high burden of early infectious disease. A growing body of research shows the early life gut microbiome shapes future immune function and health. Exposure to antibiotics, preterm birth, C-section, and bottle feeding are shown to influence the composition of the infant gut microbiota increasing the risk of ARI. Understanding the relationship between the gut microbiome and infant susceptibility to infectious disease is an essential stepping stone toward larger studies and clinical trials of microbiome modifying factors such as probiotics. These simple interventions could have profound benefits for Indigenous child health.

Hypothesis: Early life events can alter the neonatal gut microbiome, impacting immune development and the risk of acute respiratory infection (ARI) in the first year of life.

The aims of this pilot study are to describe associations between the neonatal gut microbiome and:

1. Upstream drivers: Antibiotic exposure, gestation at birth, mode of delivery and mode of feeding
2. Downstream outcomes: Oral and nasopharyngeal (NP) IL-22 levels, NP pneumococcal carriage, ARIs

Project outline: We propose a pilot microbiome study among a cohort of NT Indigenous infants. Nested within the D-Kids RCT (NHMRC 1138604; HREC 2018-3160) the clinical team are collecting faecal samples from consented infants at both birth and 4 months of age. Following stool DNA extraction, shotgun metagenomic sequencing will be conducted at the Australian Genome Research Facility. Microbiota (MetaPhlAn2, Kraken2) and functional (KEGG) profiles will be produced using established pipelines.7 Non-stool sampling, microbiology, systemic immunology assays and clinical data generated by the funded D-Kids trial and will contribute to the analysis.

Dr Michael Binks
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What is the role of Moraxella catarrhalis in chronic lung disease in children?

CHILD HEALTH | HONOURS | MASTER BY RESEARCH | PhD

Chronic suppurative lung disease (CSLD) is responsible for a high burden of paediatric disease and for some children, reduced life expectancy. Moraxella catarrhalis is one of the three major respiratory bacterial pathogens, yet its role in paediatric CSLD has received little attention. We are looking for Honours, Masters and PhD students who are interested in a program of work incorporating a selection of the following projects:

a. Perform systematic reviews

b. Use whole genome sequence data to improve M. catarrhalis diagnostics

   1. Determine reliability of commonly used phenotypic methods for identifying M. catarrhalis
   2. Develop a sensitive and specific diagnostic PCR target for M. catarrhalis

c. Use whole genome sequence data to study M. catarrhalis global epidemiology

   1. Assess the population structure of M. catarrhalis global genomes using phylogenetics with Bayesian analysis
   2. Develop a core genome MLST scheme for enhanced typing and surveillance of M. catarrhalis

d. Use whole genome sequence data to investigate the virulence and antimicrobial resistance determinants in M. catarrhalis

   1. Perform GWAS on M. catarrhalis isolates from asymptomatic carriage and paediatric CSLD to identify disease correlates
   2. Analyse antimicrobial resistance determinants in M. catarrhalis

e. Use microbiomic data from lower respiratory specimens and in vitro assays to investigate the role of M. catarrhalis in polymicrobial CLSD

   1. Investigate the relative prevalences of M. catarrhalis, other Moraxellaceae, and closely related genera in carriage versus CSLD-associated lower respiratory specimens, and across different disease states
   2. Perform interaction assays to identify the potential role of M. catarrhalis and other Moraxellaceae in modulating growth and virulence of other respiratory species in polymicrobial infections

Significance: This program of work will develop accurate M. catarrhalis diagnostic tests; facilitate epidemiological studies and surveillance for M. catarrhalis carriage, disease and antimicrobial resistance; improve understanding of M. catarrhalis pathogenesis and potential vaccine targets; improve understanding of polymicrobial CSLD, and potentially elucidate alternative therapies for testing.

Assoc Prof Heidi Smith-Vaughan
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Characterising Ornithobacterium hominis interactions with respiratory bacteria and host responses

CHILD HEALTH | MASTER BY RESEARCH | PhD

Background: The microbiome of the upper airways is a critical determinant of respiratory and hearing health. Earlier microbiome studies characterised the complex bacterial communities that reside in the upper airways of children and revealed the presence of a new bacterial species called Ornithobacterium hominis. In 2019, researchers at Menzies were the first in the world to culture this new bacterium.

O. hominis is one of only two Ornithobacterium species to have been discovered. The second species, O. rhinotracheale, is found in the upper airways of birds and is associated with pneumonia in poultry. It is not yet known whether O. hominis contributes to respiratory infections in humans; however, microbiota studies have shown O. hominis carriage can be both prevalent and persistent in paediatric populations with high rates of pneumonia. Further evidence is emerging from our 2020 pilot study which has shown O. hominis interacts with other bacteria present in the human respiratory microbiome. No studies to date have examined interactions between O. hominis and human cells.

Project outline: The overarching objective of our work is to determine whether O. hominis may directly or indirectly affect diseases processes that result in middle ear and/or lower airway infections in children. The specific aims of this study are to: i) characterise mechanisms underlying interactions between O. hominis and other members of the respiratory microbiome; ii) determine whether O. hominis adheres to respiratory epithelial cells; and iii) determine whether O. hominis can induce an inflammatory response.

Dr Robyn Marsh
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The role of human microbiome in paediatric respiratory disease: Using -omics technologies to identify new ways to diagnose airway infections in young children

CHILD HEALTH | MASTER BY RESEARCH | PhD

Respiratory infections in children are believed to occur across a disease continuum that extends from acute lower respiratory infections such as pneumonia or bronchiolitis, through to protracted bacterial bronchitis (PBB) and subsequent bronchiectasis. This continuum is believed to be driven by repeated cycles of lower airway infection and inflammation which eventually result in irreversible tissue damage and progressive loss of lung function. Antibiotics are used to treat acute symptoms and to prevent exacerbations; however, infections in a subset of children are recalcitrant to standard therapies. Long courses (up to two years) of continuous antibiotic therapy are used to prevent acute exacerbations among children with bronchiectasis. Although important to bronchiectasis clinical management, prolonged antibiotic treatment risks emergent antibiotic resistance.

Achieving better prevention and clinical management of acute and persistent respiratory infections requires deeper understanding of the pathobiological drivers of the disease, including microbial, inflammatory and immune processes. Our multi-disciplinary team is working together to translate the findings of clinical studies (including randomised controlled trials) and basic science research into new ways to prevent, diagnose and treat respiratory infections in children.

In this laboratory and bioinformatics-based study, -omics technologies and machine learning techniques will be used to identify biomarkers that can distinguish bacterial profiles associated with endobronchial infection in PBB. The student will also determine whether airway biomarker profiles could be used to identify children at risk of persistent respiratory infections and/or progression to more severe disease. The study will be based in Darwin, with potential opportunities for some components to be undertaken at the laboratories of our international collaborators.

Dr Robyn Marsh
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Eligibility: The successful applicant will meet the eligibility criteria for admission to a Master by Research or Doctor of Philosophy degree at Charles Darwin University.

Scholarship Provisions:

Candidates will be encouraged to seek Research Training Program (RTP) scholarship funding through Charles Darwin University. Further information about RTP scholarship application process, eligibility criteria and key dates can be found on this CDU webpage

A successful candidate who is a recipient of a primary scholarship such as RTP will be eligible to apply for a Menzies top-up scholarship to the value of $10,000 per annum for up to 3.5 years. Successful candidates will receive $3,500 per annum for up to 3.5 years to cover direct costs of the research.

Application Process

Applicants should submit the following:

- Brief summary of why they want to complete the project
- Current CV
- Copies of certified academic transcripts
- Proof of Residency (not required for Australian citizens)

For further information, please email the contact listed for each project by 30th September 2021.