Project Details	
Project Code	PHS27Br Hamilton
Title	Early-life infection exposure and risk of allergy and lung disease in adulthood
Research Theme	Infection, Immunity & Antimicrobial Resistance
Project Type	Other
Summary	Early-life respiratory infections influence long-term lung health, yet we do not understand why only some children later develop asthma, recurrent infections or reduced lung function. The Avon Longitudinal Study of Parents and Children (ALSPAC) in Bristol provides detailed respiratory data from birth to adulthood. Using PhIP-Seq antibody profiling and existing serology of ALSPAC samples, the student will identify how early pathogen exposure links to later lung outcomes. From these analyses the student will identify and nominate immune mechanisms for testing in preclinical models at Exeter, defining how early infections alter lung immunity.
Description	Early-life infections are increasingly recognised as critical modifiers of immunity and risk factors for subsequent disease. The clearest recent example is Epstein-Barr virus and multiple sclerosis, where longitudinal serology showed a marked rise in MS risk after EBV infection (Bjornevik et al., Science, 2022). Similar causal principles are established for HPV and cervical cancer and Helicobacter pylori and gastric cancer. The wider question is how the timing, sequence and immune context of common childhood infections shape later organ health, including the developing lung. This PhD will first address that question using the Avon Longitudinal Study of Parents and Children (ALSPAC), known to participants as Children of the 90s. ALSPAC is a world-leading birth cohort with repeated biological samples, detailed questionnaires, linked health records and exceptionally rich respiratory phenotyping. For this project, the student will define childhood lung health using asthma and wheeze trajectories, respiratory infection and medication data, linked GP/hospital information where available, and objective lung function measures including FEV1, FVC and FEV1/FVC from repeated spirometry (Objective 1). Next, the student will identify how serological readouts associate with childhood lung health. PhIP-Seq (Phage ImmunoPrecipitation Sequencing) uses phage-displayed peptide libraries and sequencing to provide a large-scale profile of antigens bound by the child's antibodies, generating an immune-history signature of antigen-specific exposure. Repeated PhIP-Seq profiles from birth through adolescence will be available for approximately 200 ALSPAC participants. VirScan data have also been generated for approximately 1,000 samples at around age 22, complemented by targeted infection serology at ages 5, 7, 11 and 15 (Mitchell et al., J Infect, 2026, Objective 2). The student will then use these data to identify putative mechanistic drivers of increased lung-disease risk (Objective 3).

	These findings will be used to test the key research question: what mechanisms link early-life infection timing and subsequent antibody profiles to health trajectories leading to asthma, wheeze and/or reduced lung function? In Objective 4, the student will undertake early-life infection studies using mice. Following infection, they will track immune development and test later-life susceptibility to lung disease, such as asthma, using established experimental infection and asthma models. They will then use molecular manipulation of immune targets identified in ALSPAC to test whether these pathways contribute to how early-life infection influences later lung health. In summary: Objective 1 will curate lung-health phenotypes in ALSPAC; Objective 2 will reconstruct infection and antibody histories using pathogen-agnostic clustering and prespecified respiratory pathogens; Objective 3 will prioritise one pathogen, antibody signature or infection-timing pattern for mechanistic follow-up; and Objective 4 will experimentally test the prioritised signal in the Horsnell laboratory. The student will own a coherent translational project from ALSPAC respiratory phenotyping, through computational serological omics and causal prioritisation, to focused experimental validation. The project will also be positioned for comparison with external respiratory birth cohorts, particularly COPSAC, where Klaus Bonnelykke and colleagues offer potential collaboration around childhood asthma phenotyping and related immune-profiling work.
Can be completed part time?	Yes
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