LUNA PARK : Lung atlas from symbiosis to pneumonia dysbiosis: analysis of the respiratory kingdom

The lung microbiome is best understood as a low-biomass-flux ecosystem constrained by mucociliary and immune clearance, rather than as a stable resident community. In critical illness, this constrained symbiosis is rapidly reshaped by physiological stress and iatrogenic pressures such as antibiotics and immunomodulatory therapies, creating an ICU-associated perturbed state that can stabilise or progress to pneumonia. Pneumonia reflects specific breakdowns of immune constraints, yielding distinct dysbiotic regimes. Despite major advances in profiling bacteria, the lung metasystem also includes a virome dominated by bacteriophages whose dynamics can precede hospital-acquired pneumonia, yet current frameworks remain largely descriptive and do not formalise how host immunometabolism and microbial function reorganise during state transitions. We will address this gap by integrating bacterial and virome metagenomics and metatranscriptomics with lipidomic, proteomic, and metabolomic layers from respiratory samples. Aim 1 will define a multi-compartment reference state of healthy lung symbiosis using an existing healthy volunteer cohort. Aim 2 will generate longitudinal ICU multiomics at standardised day 1, day 3, and day 7 timepoints across three cohorts, IBIS, PrevHAP, and HAPDex, to characterise ICU perturbation and infection-associated dysbiosis and identify reproducible transition checkpoints. Aim 3 will apply Learning From Interpretation Transition (LFIT), a symbolic AI framework that infers interpretable state transition rules from heterogeneous dynamic data, to formalize three system states and their transitions, supported by robustness to partial observations, rule provenance, and clinician facing visualization. The project will deliver harmonised multiomics resources, transkingdom interaction maps, and an interpretable rule-based transition model linking microbial function, host metabolism, and immune regulation, enabling state-informed risk stratification and mechanistic hypotheses for prevention and treatment of ICU pneumonia.