Laboratory analysis workflows within the ASPIRE-ICU study

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* Advanced understanding of *Staphylococcus aureus* and *Pseudomonas aeruginosa* Infections in EuRopE – Intensive Care Units

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Facts & Figures

	COMBACTE-NET	-MAGNET
Start date:	01/01/2013	01/012015
End date:	28/02/2021	31/12/2021
Contributions		
IMI funding:	109 433 010 €	75 340 000 €
EFPIA in kind:	90 055 721 €	91 662 413 €
Other:	7 659 698 €	1 656 257 €
Total Cost:	207 148 429 €	168 658 670 €
Project website:	www.combacte.com	
Social media:	@combacte	

Challenge

The epidemiology and potential routes and reservoirs leading to the development of pneumonia by *Staphylococcus aureus* or *Pseudomonas aeruginosa* in mechanically ventilated patients are not well-elucidated. These data are, however, urgently needed to support the development of effective interventions[1,2].

Approach & Methodology

The objective of the ASPIRE-ICU study is to estimate the incidence of *S. aureus* and *P. aeruginosa* ICU pneumonia and to assess its association with patient-related and contextual risk factors, e.g., colonization status, serum antibody levels against *S. aureus* alpha toxin (AT) and the *P. aeruginosa* PcrV/Psl virulence factors and others.

The study is a prospective, observational, multi-centre cohort study nested within routine surveillance among ICU patients in Europe. Two thousand study cohort subjects are being enrolled (50% *S. aureus* colonized) from whom specimens and data are collected. Microbiological study samples (lower respiratory samples (LRS), nasal swabs (NS) and peri-anal swabs (PS) are being shipped to the central laboratory at the University of Antwerp to undergo uniform procedures (Figures 1 and 2).

Because of the centralised analysis, uniformly generated data will be obtained from around 4500 LRS, 2500 NS, 3500 PS, 2500 *S. aureus* isolates and 250 *P. aeruginosa* isolates by the end of ASPIRE-ICU.

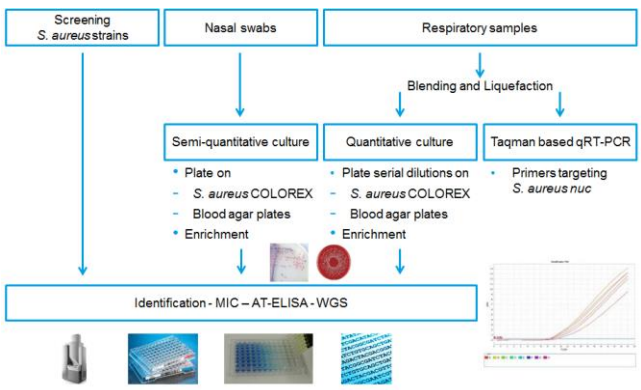

Figure 1: ASPIRE-ICU *S. aureus* workflow at the Central laboratory UAntwerp

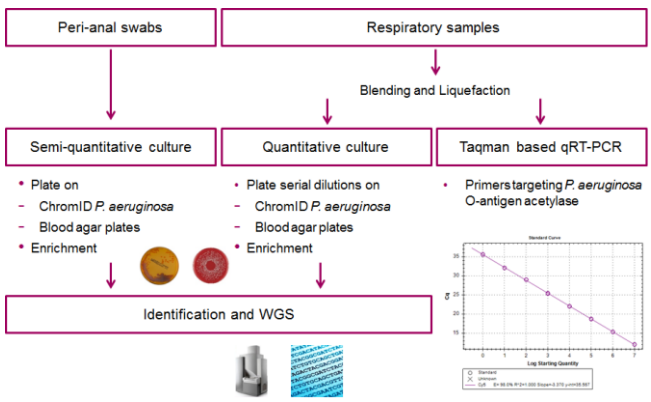

Figure 2: ASPIRE-ICU *P. aeruginosa* workflow at the Central laboratory UAntwerp

Results

To determine if the *S. aureus* and *P. aeruginosa* colonization loads in LRS are predictive of *S. aureus* and *P. aeruginosa* pneumonia development, these are measured and compared between patients developing and not developing infection. Also, the temporal evolution of the *S. aureus* and *P. aeruginosa* loads in LRS are investigated. In addition, the association of NS/LRS and PS/LRS colonization status at ICU admission with the incidence of ICU pneumonia caused by *S. aureus* or *P. aeruginosa,* respectively, is being determined. The spectrum of *S. aureus* / *P. aeruginosa* clonal types associated with colonization and infection is investigated. AT variants in *S. aureus* are identified and their expression characterized. The proportion of *P. aeruginosa* in which *pcrV* and the *psl* loci are present and expressed, along with variations in these and associated genes is assessed. Finally, antibiotic resistance profile of all strains is determined.

Value of IMI collaboration

IMI provides an unique framework to engage academic and industry experts in a mutually enriching collaboration, which along with fulfilling the primary goals of the project also allows capacity building. The provided framework also allows to run consecutive studies from observational to phase II and phase III trials where experiences and knowledge obtained from each study facilitates the subsequent trials.

Impact & take home message

By investigating one of the most deadly nosocomial infections, this epidemiological cohort study will provide new insights on predictors of *S. aureus* and *P. aeruginosa* ICU pneumonia. Outcomes of this observational study will also allow to refine the design of phase II and III follow-up trials on *S. aureus* and *P. aeruginosa* ICU pneumonia. Finally, the large expanse of clinical, bacteriological and immunological knowledge generated from a large number of patients in ASPIRE-ICU is also likely to facilitate further development of early diagnostic or prognostic disease markers and of therapeutic targets, possibly non-antibiotic based.

Abbreviations: AT: alpha toxin; LRS: Lower Respiratory Samples; NS: Nasal Swabs; PS: Peri-anal swabs

References:
[1] Paling et al. *Pseudomonas aeruginosa* colonization at ICU admission as a risk factor for developing *P. aeruginosa* ICU pneumonia, Antimicrob Resist Infect Control. 2017 Apr 20;6:38.
[2] Paling et al. *Staphylococcus aureus* colonization at ICU admission as a risk factor for developing *S. aureus* ICU pneumonia, Clin Microbiol Infect. 2017 Jan; 23(1).

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