Category :**Infections + antimicrobials**

A159 - *A breath-based in vitro diagnostic assay for the detection of lower respiratory tract infections*

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Introduction:

An accurate diagnosis is critical to reducing mortality in people with lower respiratory tract infections (LRTIs) which have been recognized as the fifth-leading cause of mortality globally.

Current microbiological culture is time-consuming, and nucleic acid amplification-based molecular technologies cannot distinguish between colonization and infection. Previously, we described the development of a sampling system for effectively capturing biomolecules from human breath, and identified a new class of proteoform markers of protease activation, termed proteolytic products of infection (PPI), for potentially detecting LRTIs [1].

Methods:

Here, we further present an in-vitro assay by designing a specific substrate-sensor to human neutrophil elastase (HNE), which is highly up-regulated in LRTIs. The sensor is an HNE substrate that is cleaved by the enzyme with higher sensitivity and specificity, yielding higher resolution.

We then applied this in-vitro assay to breath samples collected from both intubated patients and healthy volunteers (Fig A-B).

Results:

The findings revealed that the LRTI group demonstrated a significant mean differential, showing a 9.8-fold elevation in measured HNE as compared to the non-LRTI group, and a 9.2-fold compared to healthy volunteers (Fig 1C-D).

The in-vitro assay's diagnostic potential for LRTIs was assessed by constructing an ROC curve, resulting in an AUC value of 0.987 (Fig 1E). Using an optimal threshold for HNE at 0.2 pM, the sensitivity was determined to be 1.0 and the specificity to be 0.867. Further correlation analysis revealed a strong positive relationship between the measured HNE-activity and the protein concentration in the breath samples.

Conclusion:

Our results demonstrate that this breath-based, in-vitro assay provides high diagnostic performance for LRTIs, suggesting that the technology may be useful in the near term for the accurate diagnosis of LRTIs in critical care.

References:

Chen D, Bryden WA, McLoughlin MJ. *Breath Res*, 2000;*15:*16001.

Image :

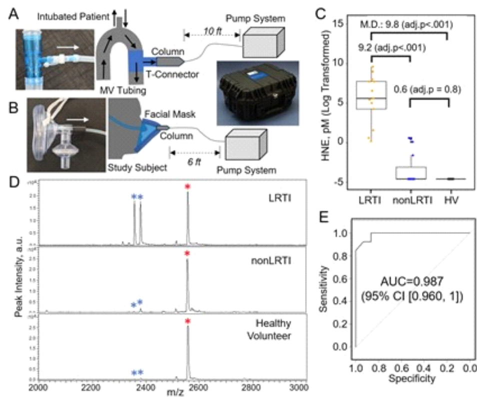

Fig. 1. (A&B) Schematic of breath collection from intubated patients on mechanical ventilation in ICU & from healthy volunteers using a facial mask. (C) Boxplot display of the distribution of natural-log-transformed HNE measurements. (D) Representative MALDI-TOF spectra of breath samples collected from different groups. (E) Receiver operating characteristic (ROC) curve analysis for the in-vitro assay performance.