Rapid Translation of a SARS-CoV-2 Targeted Peptide Immunoaffinity LC-MS Test from Research into Routine Clinical Use

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OBJECTIVES: During 2020, the Department of Health and Social Care (DHSC) of the United Kingdom established the Moonshot programme to fund various diagnostic approaches for the detection of SARS-CoV-2, the pathogen behind the COVID-19 pandemic. Mass spectrometry was one of the technologies proposed to increase testing capacity.

METHODS: Moonshot funded a multi-phase development programme, bringing together experts from academia, industry and the NHS to develop a state-of-the-art targeted protein assay utilising enrichment and liquid chromatography tandem mass spectrometry (LC-MS/MS) to capture and detect low levels of tryptic peptides derived from SARS-CoV-2 virus. The assay relies on detection of target peptides, ADETQALPQRK and AYNVTQAFGR, derived from the nucleocapsid protein of SARS-CoV-2, measurement of which allowed the specific, sensitive, and robust detection of the virus from nasopharyngeal (NP) swabs. The diagnostic sensitivity and specificity of LC-MS/MS was compared with reverse transcription quantitative real-time polymerase chain reaction (RT-qPCR) via a prospective study.

RESULTS: Analysis of NP swabs (n=361) with a median RT-qPCR quantification cycle (Cq) of 27 (range 16.7-39.1) demonstrated diagnostic sensitivity of 92.4% (87.4-95.5), specificity of 97.4% (94.0-98.9) and near total concordance with RT-qPCR (Cohen's Kappa 0.90). Excluding Cq>32 samples, sensitivity was 97.9% (94.1-99.3), specificity 97.4% (94.0-98.9) and Cohen's Kappa 0.95.

CONCLUSION: This unique collaboration between academia, industry and the NHS enabled development, translation, and validation of a SARS-CoV-2 method in NP swabs to be achieved in 5 months. This pilot provides a model and pipeline for future

accelerated development and implementation of LC-MS/MS protein/peptide assays into the routine clinical laboratory.

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