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MULTI-OMICS SURVEILLANCE OF COVID-19 ALLOWS THE IDENTIFICATION OF CLINICALLY RELEVANT LINEAGES AND HOST TRANSCRIPTIONAL SIGNATURES

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Genomic surveillance of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is the only approach to rapidly monitor and tackle emerging variants of concern (VOC) of the COVID-19 pandemic. Such scrutiny is crucial to limit the spread of VOC that might escape the immune protection conferred by vaccination strategies. It is also becoming clear now that efficient genomic surveillance would require monitoring of the host gene expression to identify prognostic biomarkers of treatments efficacy and disease progression. Here we applied an integrated workflow for RNA extracted from nasal swabs to obtain in parallel the full genome of SARS-CoV-2 and transcriptome of host respiratory epithelium, altogether representing the majority of Italian processed genomic samples. We have matured and applied novel proof-of-principle approaches to prioritize possible gain-of-function mutations by leveraging patients' metadata and isolated patient-specific signatures of SARS-CoV-2 infection. The aforementioned goals have all been achieved in a cost-effective manner that does not require automation, in an effort to allow any lab with a benchtop sequencer and a limited budget to perform integrated genomic surveillance on premises. Our approach extends the scope of SARS-CoV-2 genomic surveillance, as it allows for the examination of in-vivo samples characterized by the predominance of degraded RNA molecules. This competence enables overcoming the limitation of in-vitro and single-cell studies, such as model-specific variations and a small number of samples limit, respectively. Gene expression data from COVID-19 patients might have a pivotal role as a bridge between genomic data and translational medicine. On one hand, finding a gene signature that describes and defines the patient status after SARS-CoV-2 infection might support new variants surveillance and address their pathogenic effect on the host. On the other hand, it might be used to evaluate the efficacy of new treatments, especially non vaccine-based.

Department

TIGEM

Primary author(s) : Mr. GRIMALDI, Antonio (Tigem); Dr. CACCHIARELLI, Davide (TIGEM); Mr. PANARIELLO FRANCESCO (TIGEM); Mrs. ANNUNZIATA, Patrizia; Prof. BALLABIO, Andrea

Co-author(s) : Dr. SALVI, Marcello; Dr. COLANTUONO, Chiara

Presenter(s) : Dr. SALVI, Marcello