A 5-mRNA host response whole-blood classifier trained using patients with non-COVID-19 viral infections accurately predicts severity of COVID-19

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Introduction

While major progress has been made to establish diagnostic tools for the diagnosis of SARS-CoV-2 infection, determining the severity of COVID-19 remains an unmet medical need. With limited hospital resources, gauging severity would allow for some patients to safely recover in home quarantine while ensuring sicker patients get needed care. We derived CoVerity™, a 5-host mRNA classifier for the severity of influenza and other acute viral infections. We then prospectively validated CoVerity® for predicting severe respiratory failure in COVID-19 patients from Greece.

Derivation of 5-host mRNA classifier

Bioinformatics Selection of Top 5 mRNA

Methods

Enrolled n = 97 adults presenting with: • Positive SARS-CoV-2 RT-PCR • Lower resp. tract involvement by radiology or (by self or proxy) • Enrollment occurred during March to April 2020 at ATIONC University Hospital (Athens, Greece), White blood drawn into PaGEmix blood RNA tubes 24 h of admission.

Patients were followed up daily for 30 days. Severe respiratory failure defined as PaO2/FiO2 ratio < 150 requiring mechanical ventilation.

CoVerity® distinguishes non-severe from severe patients in prospective validation

• Performance after applying cutoffs

• Performance with Locally-Derived Cutoffs

CoVerity® outperforms IL-6 in Head-to-Head Comparison

AUCROC, Severe Respiratory Failure vs. Non Severe Respiratory Failure

Discussion

• Findings: We derived a 5-host mRNA classifier, CoVerity®, for predicting severity using a training cohort of non-COVID-19 viral infection patients. CoVerity® demonstrated very high accuracy for predicting severe respiratory failure in prospective validation and outperformed IL-6, the only FDA-approved prognostic biomarker for COVID-19

• Limitations: CoVerity®’s improvement over IL-6 requires larger cohorts to confirm statistical significance. CoVerity® is only intended for use in patients with confirmed viral infection. Finally, intervention trials are needed to assess the clinical utility of CoVerity®.

• Clinical Implications: When translated into a rapid LAMP assay, CoVerity® has potential to rule in severe patients (improving outcomes) and rule out non-severe patients (saving limited hospital resources). CoVerity® was designed to hold up across all acute infections as a conserved host immune response. Thus, the assay may be useful for any viral pandemic, from COVID-19 to influenza to ‘Disease X’.

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