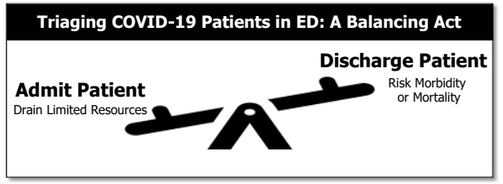
A 5-mRNA host response whole-blood classifier trained using patients with non-COVID-19 viral infections accurately predicts severity of COVID-19

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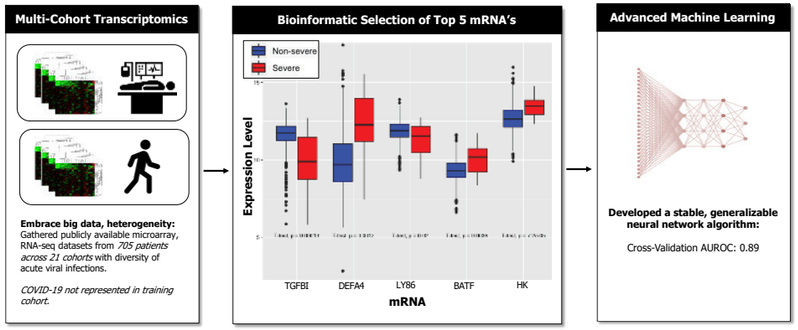
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Introduction



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-based 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



Design of prospective validation study

Enrollment

Enrolled n = 97 adults presenting with:
- Positive SARS-CoV-2 RT-PCR
- Lower resp. tract involvement by radiology
- Consent (by self or proxy)

Enrollment occurred during March to April 2020 at ATTIKON University Hospital (Athens, Greece). Whole blood drawn into PAXgene® Blood RNA tubes 24h of admission.

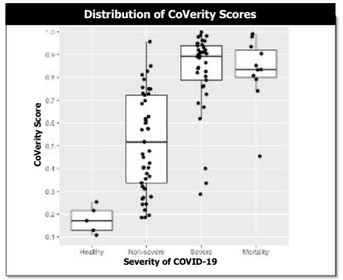
Patients were followed up daily for 30 days. Severe respiratory failure defined as PaO2/FiO2 ratio < 150 requiring mechanical ventilation.

Methods

- RNA extracted from whole blood
- mRNA quantified on NanoString nCounter™



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



Performance after applying cutoffs

Performance w/ Pre-Set Cutoffs	Performance with Locally-Derived Cutoffs
84% Sensitivity 74% Specificity for predicting severe respiratory failure using dichotomous cutoffs derived on training cohort.	90% Sensitivity 68% Specificity for predicting severe respiratory failure using dichotomous cutoffs derived on validation cohort.

Future Cutoffs Will Segment Results into 3 Interpretation Bands

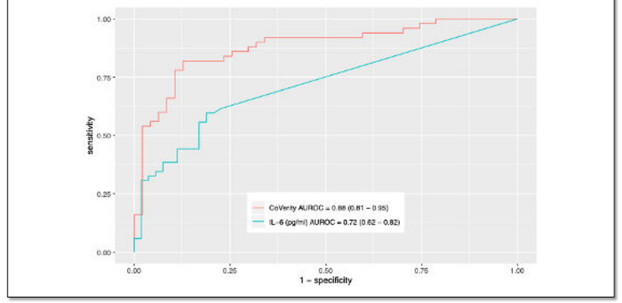


Future studies will inform the most optimal cutoffs to formally 'lock.'

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

(AUROC 0.88 vs. 0.72)

AUROC, Severe Respiratory Failure vs. No Severe Respiratory Failure



Currently translating CoVerity* into rapid LAMP assay

Short TAT will enable deployment into high acuity settings.



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, interventional 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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