Medical Xpress

SARS-CoV-2 encoded miRNA is a biomarker for stratification of severe patients

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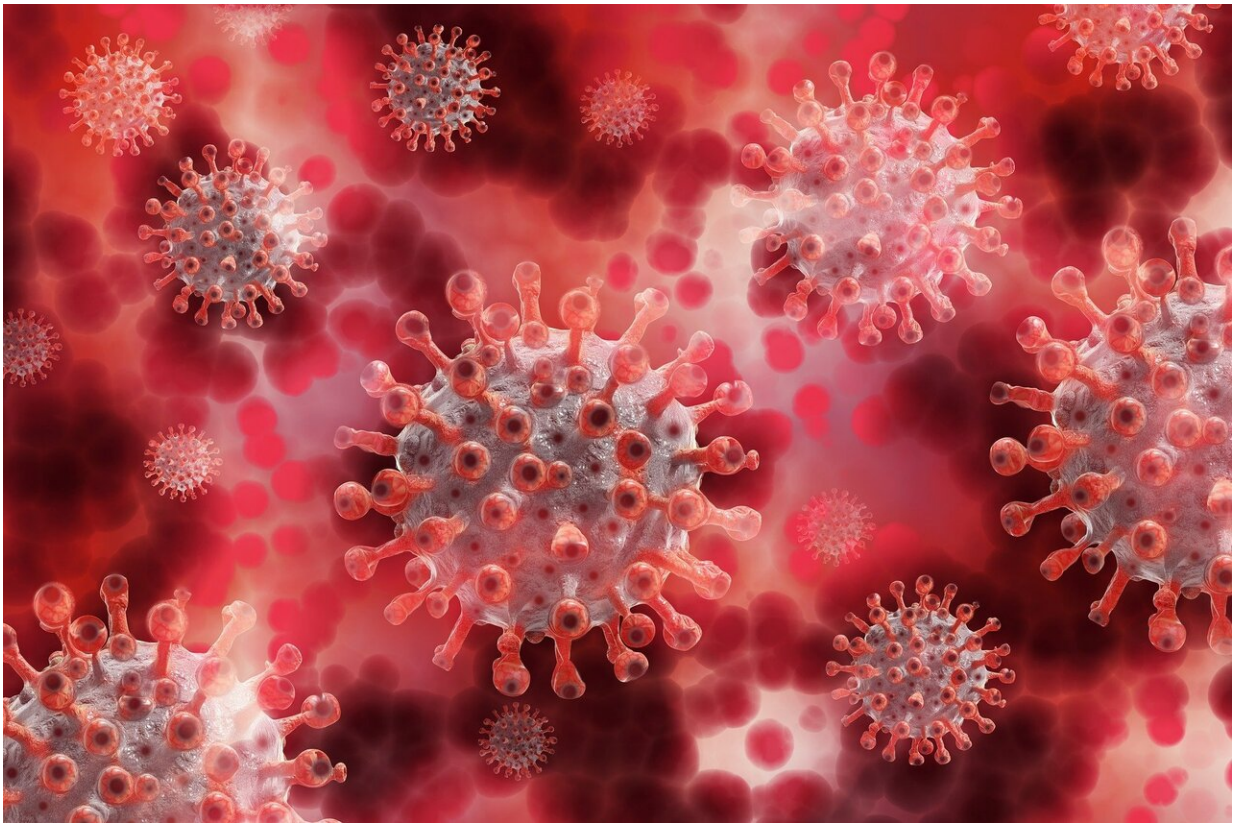

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In a retrospective, multi-center cohort study, a microRNA-like small RNA encoded by SARS-CoV-2 was identified in the serum of COVID-19 patients. This can be developed as a non-invasive biomarker

for stratification of severe patients from mild/moderate ones and for identification of high-risk individuals before clinical manifestation of severe symptoms. This biomarker ensures proper allocation of patients to different levels of medical facilities and allows more effective control of the pandemic and relief of social economic burdens.

COVID-19, caused by SARS-CoV-2, evolved into a global pandemic in 2020-2021. Although most COVID-19 cases are mild, some patients rapidly develop acute respiratory distress syndrome and other serious complications, leading to multiple organ failure and even death. Since medical facilities do not have reliable biomarkers to predict likelihood of disease progression and identify high-risk patients that require immediate medical attention, patients can only be treated after the appearance of severe symptoms, thereby missing the best treatment window. Furthermore, because patients cannot be stratified at admission, they have to be quarantined and treated without screening, which often leads to high pressure on healthcare services. To improve treatment outcome, reduce the mortality rate and prevent a total failure of the overwhelmed health services, it is essential to prioritize the patients at higher risk of developing life-threatening COVID-19 disease.

This study provides just this, a reliable early prognostic biomarker for COVID-19 severity. This biomarker is a microRNA-like small RNA encoded by SARS-CoV-2 virus, named miR-nsp3-3p, which is exclusively present in the serum of severe patients but not in non-severe patients and healthy controls. MiR-nsp3-3p is superior to the conventional biochemical characteristics (e.g., D-dimer, CRP, LDH and PLC) for stratification of severe patients from mild/moderate ones. More importantly, miR-nsp3-3p can capture the risk of critical illness far ahead of clinical manifestation of severe symptoms, exhibiting a significantly higher prediction horizon (7.4 days in advance) and higher accuracy (97.1%) than conventional indexes.

The critical points of this study are highlighted below:

1. COVID-19 patients typically suffer from a sudden deterioration into a severe illness. Predicting whom amongst COVID-19 patients will progress towards this severe downturn will provide a significant advantage to prevent the overwhelm of the hospitals and to provide optimized treatment to patients. MiR-nsp3-3p is a consistent prognostic biomarker, more precise and reliable than D-dimer, CRP, LDH and PLC. Most importantly, miR-nsp3-3p identifies the risk of critical illness early on the evolution of the disease. Early detection of miR-nsp3-3p indicates the higher risk of the patient to develop a critical illness, enables prioritizing the patient for special care, and hence improves treatment outcome and reduces the mortality rate.
2. Although some researches have shown that multi-omics analyses (transcriptomics, proteomics and metabolomics) can be used to characterize severity status, these techniques are too complex for rapid and general application in the pandemic. Because miR-nsp3-3p exhibits comparable sensitivity, specificity and precision to that of multi-omics, and because the quantification protocol is simple requiring only a small amount of serum, this new biomarker can be readily applied in the current COVID-19 pandemic and expectedly provide a simple mean to conveniently monitor disease progression in COVID-19 patients.
3. SARS-CoV-2, as a RNA virus, is evolving fast and now more transmissible variants like delta variant are becoming dominant in many regions. Since miR-nsp3-3p is highly conserved among different SARS-CoV-2 strains, it can be applied in the current pandemic as a reliable biomarker regardless of the emergence of a new variant of SARS-CoV-2.
4. Being a reliable prognostic biomarker, miR-nsp3-3p can be used to support decision-making and logistical planning in healthcare systems and facilitate more precise prevention and control of the

epidemic, especially in deprived regions with shortages of medical resources.

More information: Zheng Fu et al, A virus-derived microRNA-like small RNA serves as a serum biomarker to prioritize the COVID-19 patients at high risk of developing severe disease, *Cell Discovery* (2021). DOI: 10.1038/s41421-021-00289-8

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