

Thrombosis-related miR-16-5p predicts the disease severity in patients hospitalised for COVID-19

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Introduction: SARS-CoV-2 tropism for the ACE2 receptor, along with the multifaceted inflammatory reaction, is likely to drive the generalized hypercoagulable state seen in patients with COVID-19.

Methodology: Using the original bioinformatic workflow and network medicine approaches we reanalyzed four coronavirus-related expression datasets and performed co-expression analysis focused on thrombosis and ACE2 related genes. We identified microRNAs (miRNAs) which play role in ACE2-related thrombosis in coronavirus infection and further, we validated the expressions of those miRNAs in 79 hospitalized COVID-19 patients and 32 healthy volunteers by PCR and monitored miRNAs patterns during the acute phase of COVID-19, as well as the prognostic potential of these miRNAs as biomarkers.

Results: We identified EGFR, HSP90AA1, APP, TP53, PTEN, UBC, FN1, ELAVL1 and CALM1 as regulatory genes which could play a pivotal role in COVID-19 related thrombosis. We also found miR-16-5p, miR-27a-3p, Let-7b-5p and miR-155-5p as regulators in coagulation and thrombosis pro-

cess. We observed in separate cohort of COVID-19 patients and healthy controls that (i) expression of miR-16-5p, miR-27a-3p and miR-155-5p increased during observation, compared to the baseline measurement; (ii) a low baseline miR-16-5p expression presents predictive utility in assessment of the hospital length of stay or death in follow-up as a composite endpoint (AUC: 0.810, 95% CI, 0.71–0.91, $p < 0.0001$); (iii) low baseline expression of miR-16-5p and diabetes mellitus are independent predictors of increased length of stay or death according to a multivariate analysis (OR: 9.417; 95% CI, 2.647–33.506; $p = 0.0005$ and OR: 6.257; 95% CI, 1.049–37.316; $p = 0.044$, respectively).

Conclusion: This study enabled us to better characterize changes in gene expression and signaling pathways related to COVID-19 thrombosis. In this study we identified, characterized and validated miRNAs which could serve as novel, thrombosis-related biomarkers of the COVID-19, can be used for early stratification of patients and prediction of severity of infection development in an individual.

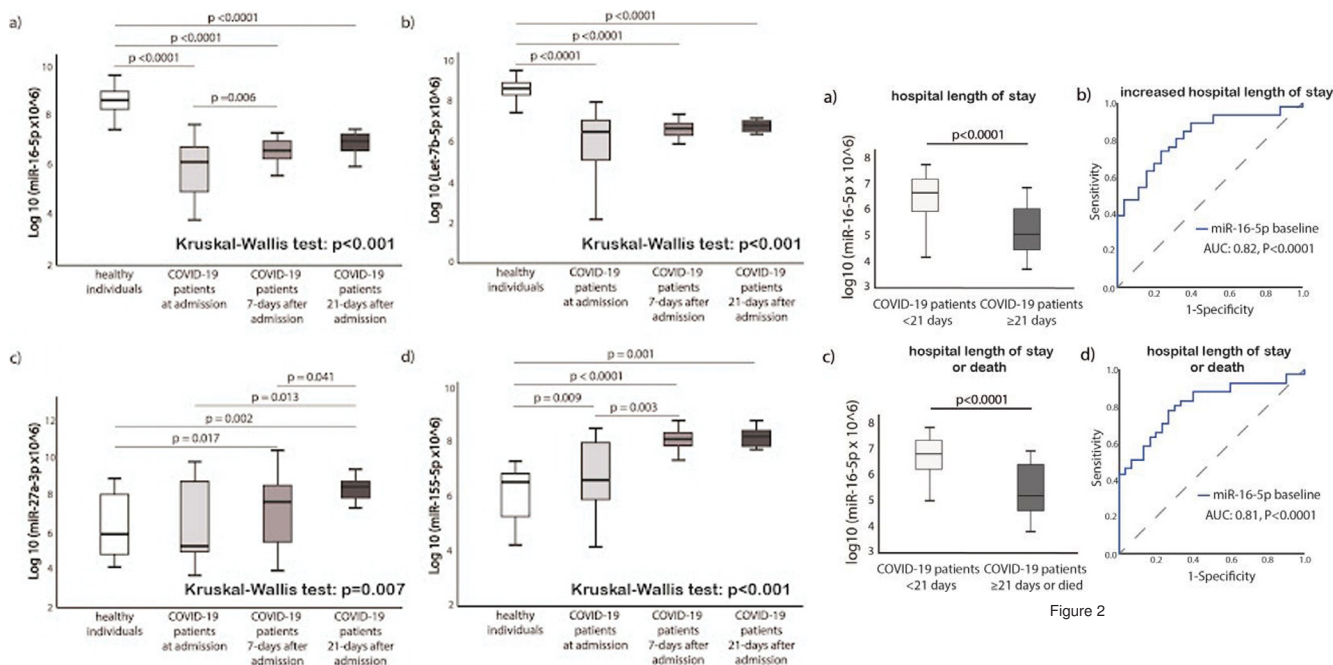


Figure 1

Figure 2