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A machine-learning model to predict COVID-19 outcomes

EU-funded COVIRNA project publishes groundbreaking results

A collaborative effort led by the LIH and involving 15 institutions across Europe and Canada has resulted in the development of a machine-learning model to forecast in-hospital mortality following SARS-CoV-2 infection. This breakthrough, recently published in the prestigious international journal Nature Communications, could pave the way for personalised healthcare strategies, easing the burden of the disease on healthcare systems worldwide.

Back in March 2020, the COVIRNA project was launched with the goal of developing an RNA-based diagnostic test leveraging artificial intelligence (AI) to predict clinical outcomes after COVID-19 infection. "*Our rationale was to leverage the power of a specific type of RNA molecules, known as non-coding RNAs, which have emerged as new valuable candidate biomarkers and therapeutic targets for most pathologies*", explains Dr Yvan Devaux, leader of the Cardiovascular Research unit and leader of the study. Indeed, the consortium had previously identified a panel of 2,906 long non-coding RNAs (lncRNAs) associated with cardiovascular diseases which, together with an in-house developed bioinformatics algorithm, provided a new tool with the potential to help diagnosis and risk stratification for heart conditions. "*Since the panel contains many inflammation-related lncRNAs and inflammation is a hallmark of the body's response to infection by SARS-CoV-2, we thought we could "translate" our previous discovery and apply it to COVID-19, in order to identify predictors of its outcomes in individual patients*", says Dr Devaux.

The team analysed blood samples and clinical data from 1,286 COVID-19 patients across four cohorts from Luxembourg, Germany, the UK, and Canada, characterising a total of 2,906 long non-coding RNAs. Three cohorts with 804 patients were merged into a "discovery" cohort to be used in the selection of predictive features and choice of best performing machine learning (ML) models, while the fourth cohort of 482 patients was used for validation purposes.

"*From the discovery cohort, we were able to identify age and a specific long non-coding RNA, LEF1-AS1, as the two most clinically accurate predictors of in-hospital mortality in COVID-19 patients*", says Dr Devaux. In particular, higher levels of LEF1-AS1 were found to correlate with reduced mortality risk. Indeed, LEF1-AS1 is known to be involved in the proliferation of immune system B and T cells and in regulating inflammation, and the lower expression of LEF1-AS1 in severe patients can be associated with the observed decline in B cells following SARS-CoV-2 infection. Additionally, alveolar damage as observed following COVID-19 infection has been shown to be suppressed through the activation of the related LEF1 gene, thus hinting at a possible protective role of LEF1 following alveolar injury and SARS-CoV-2 infection. The present study therefore suggests a link between LEF1/LEF1-AS1, T and B cell proliferation, alveolar protection and COVID-19 severity.

"*By differentiating patients at high-risk of poor outcome or death from those with a high chance of survival, our predictive model has a promising translational potential to enhance patient management in clinical settings. Moreover, the identified long non-coding RNA could potentially act both as a biomarker and as a drug to help treat COVID-19*", he adds. "*In a follow-up study, we are also currently*

testing the model for its capacity to predict long COVID, notably in the Luxembourgish COVALUX cohort", he concludes.

The full study, published with the full title "Development of a long noncoding RNA-based machine learning model to predict COVID-19 in-hospital mortality", can be accessed [here](#).

Funding and collaborations

The COVIRNA Consortium, led by Dr Devaux and the LIH, is composed of 15 partners from 12 European countries. It was funded through the European Union's Horizon 2020 research and innovation programme under grant agreement No 101016072.

About the Luxembourg Institute of Health (LIH)

The Luxembourg Institute of Health (LIH) is a public biomedical research organisation focused on precision health and invested in becoming a leading reference in Europe for the translation of scientific excellence into meaningful benefits for patients.

The LIH places the patient at the heart of all its activities, driven by a collective obligation towards society to use knowledge and technology arising from research on patient derived data to have a direct impact on people's health. Its dedicated teams of multidisciplinary researchers strive for excellence, generating relevant knowledge linked to immune related diseases and cancer.

The institute embraces collaborations, disruptive technology and process innovation as unique opportunities to improve the application of diagnostics and therapeutics with the long-term goal of preventing disease.

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