New method predicts individual response to Ebola infection

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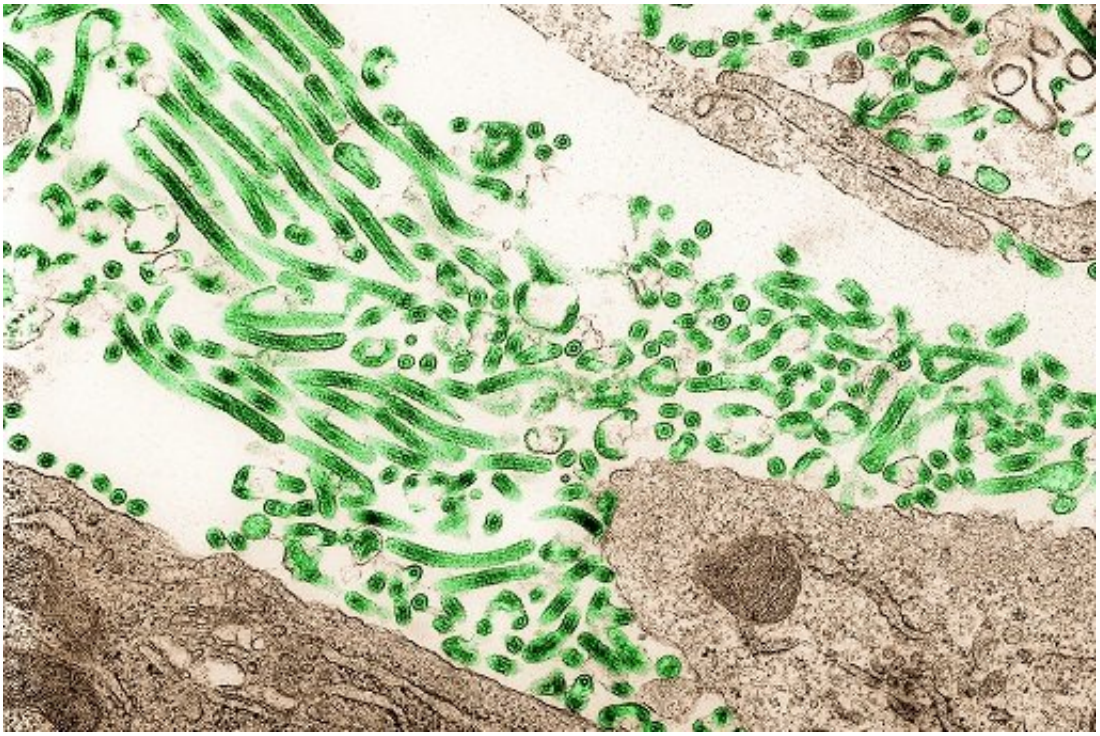

Ebola virus. Credit: NIAID

Not everyone who catches Ebola dies of the hemorrhagic virus infection. Some people mount a robust immune defense and recover fully. Yet risk factors for susceptibility to infection and disease severity remain poorly understood.

A team at the Center for Infection and Immunity (CII) at Columbia

University Mailman School of Public Health has used a specially bred population of laboratory mice that mimics human patterns of tolerance and susceptibility to the Ebola virus to identify human immune factors that predict outcomes among people infected with the disease.

In a new paper published by *Cell Reports*, the team describes how they identified differences in immune response among mice who recovered from Ebola and those who perished. Further analysis revealed differences in gene expression between the two groups that account for disparities in immune response. Using machine learning, the team created a model that accurately predicts human disease outcomes based on expression of a small subset of genes.

The researchers tested their model using a data set collected from Ebola patients in western Africa; the data set contains details on the presence of types of RNA associated with immune function in people's blood, as well as whether they lived or died after infection. The model predicted the patients' outcomes with 75 percent accuracy, confirming the factors identified as valid in the mouse model were also associated with outcomes among humans infected with Ebola.

While the work has not yet been translated into a clinically approved test for use among human patients, the findings could guide the development of new tools to triage patients in resource-poor countries, support immune function among those at higher risk of death, and boost vaccine response among those at greatest risk. "Since the current Ebola therapeutics being tested in the DRC [Democratic Republic of Congo] are most effective when given as early as possible in infection our model could be used to develop tests with a huge impact on clinical care and patient outcomes," says senior author Angela Rasmussen, Ph.D., an associate research scientist with the Center for Infection and Immunity.

Studies of Ebola infection and response among humans have historically

been limited by the difficulty of obtaining samples during an outbreak, says co-first author Adam Price, Ph.D., an analyst at Columbia Mailman's Center for Infection and Immunity. "The human data set we used to test our machine learning model is one of the only ones in existence that contains the information we needed on gene transcription among people infected with Ebola," Price explains.

"Human data collected during an outbreak rarely contains the combined breadth and specificity of information scientists need to perform detailed analyses of immune function," says co-first author Atsushi Okumura, Ph.D., DVM, an associate research scientist at CII. "Mouse models can help fill in the information gaps."

Rasmussen points out that by contrast to relying on patient data, the right mouse model can allow for comparatively expedited, low-cost studies to guide the study of human disease and the design of effective medications. "A common criticism of mouse models of Ebola is that they don't faithfully recapitulate human infection, and thus can't be used to develop diagnostic or prognostic tools," says Rasmussen. "Here we show that data generated in our mouse model can be applied to patient data to correctly predict outcomes."

Due to its size and low cost, the new mouse model removes research hurdles by making it easier for scientists to perform pre-clinical studies in maximum biocontainment, and with more robust statistical power than can be achieved with larger animal models. Using AI-driven approaches like machine learning to apply this to patients also overcomes the challenge of obtaining human samples.

The fidelity of the team's mouse model in replicating human responses to Ebola may prove helpful in understanding other viruses, such as the coronavirus outbreak that began in Wuhan, China. While much is still unknown about the new coronavirus, Rasmussen explains that the mouse

model may be a useful model in guiding further understanding of the disease.

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