AI-POWERED DIAGNOSTICS

Innate Immune Signatures Of Viral Exposure In Lung Epithelial Cells

Apoorv Shanker Los Alamos National Laboratory **Anna Matuszak** Los Alamos National Laboratory **Makaela Montoya** Los Alamos National Laboratory **Daniel Jacobsen** Los Alamos National Laboratory **Kaitlyn Martinez** Los Alamos National Laboratory **Kristen Wilding** Los Alamos National Laboratory **Carrie Manore** Los Alamos National Laboratory **Harshini Mukundan** Lawrence Berkeley National Laboratory **Jessica Kubicek-Sutherland** Los Alamos National Laboratory

Early and accurate determination of disease etiology is paramount to inform medical intervention on the battlefield. Despite previous studies identifying host response-based transcriptional signatures to individual viruses such as influenza and respiratory syncytial virus, generalizing these signatures across all viral infections remains a challenge. This limitation has hindered the implementation of machine learning models to determine viral and bacterial infections accurately. Since most viruses produce double-stranded RNA (dsRNA) during their replication cycle, we propose using synthetic dsRNA as a surrogate for viral infections to develop a generalizable dataset of transcriptional signatures of viral infection. However, synthetic dsRNA analogs such as poly(I:C) present challenges related to intracellular delivery and delineation of immune responses elicited by dsRNA and transfection agent-induced cellular toxicity.

Here, we present the development of in vitro cell assays to determine the transcriptional signatures of viral infections in lung epithelial cells. We first developed and characterized polyplexes by complexing poly(I:C) with a polycationic transfection agent, linear polyethyleneimine (LPEI). As a negative control, we also made bio-inactive polyplexes by combining poly(L-glutamic acid) (PLE) with LPEI. Our cell treatments included soluble poly(I:C), poly(I:C) and PLE polyplexes, and soluble LPEI. We then quantified gene expression levels of 84 cytokines and chemokines and cellular receptors of poly(I:C) to distinguish immune responses elicited by dsRNA from those induced by LPEI-induced cellular damage. Our findings highlighted the importance of selecting appropriate controls to account for cellular toxicity-induced immune activity when developing machine learning models of viral infections. We believe our approach offers a novel and effective way to create a generalizable dataset of transcriptional signatures of viral infections that could inform medical intervention and allocation of healthcare resources on the battleground.

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