

DNA methylation changes associated with COVID-19

Disease classifiers based on DNA methylation patterns offer the potential to predict clinical outcomes.



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Introduction

Kathleen Barnes, PhD wants to “disentangle the genetic underpinnings that contribute to health disparities.” It was this focus that led her to the Colorado Center for Personalized Medicine (CCPM). One goal of the CCPM is to link extensive electronic medical records with multiomics information to accelerate discoveries that will improve human health and fundamentally change the way medicine is practiced. To this end, CCPM established a CLIA- and CAP-certified biobank in collaboration with UHealth. When COVID-19 took the world by surprise, this biobank placed Dr. Barnes and her colleagues in a unique position to continue their research efforts while looking for ways to battle the SARS-CoV-2 virus.

Moving towards methylation in infectious disease

Prior to the pandemic, the CCPM team had partnered with Illumina to explore options for introducing clinical methylation-based testing for tumor classification and diagnostics into the CCPM Biobank. The day of the shutdown, Dr. Barnes read an article about the epigenetics of COVID-19. She immediately shifted her research to methylation and infectious disease.

A mad scramble for biospecimens

One of the biggest challenges to this study was obtaining samples. “There was a mad scramble to access biospecimens from COVID patients,” states Dr. Barnes. With a biobank-fueled collaboration, the team theorized, “because it’s infectious disease, we should be able to use blood,” which turned out to be easier than capturing leftover nasal pharyngeal samples. They also had a reliable health data warehouse through which they could track whether the subjects that they received samples from were tested for COVID-19 and if they were positive or negative for the virus.

Overview

SARS-CoV-2 infection generates a specific, detectable epigenetic signature in the host

Challenge

PCR -based techniques for COVID-19 testing do not detect this signature

Solution

Customize the Infinium MethylationEPIC BeadChip to detect and classify differential host DNA methylation patterns that arise due to SARS-CoV-2 infection

Benefits

Understand the potential of measuring methylation signatures for detecting and predicting the course of viral infections

Using an Illumina solution

As experienced Illumina users, who had even contributed content to the Infinium™ Multi-Ethnic Global Array, Dr. Barnes' team began the COVID studies by customizing the Infinium MethylationEPIC BeadChip. "We added about 7800 CpGs representing genes that we thought would be relevant, not just for SARS-CoV-2 infection, but infectious disease in general, and we called this EPIC+."

The importance of the methylome

"Even though there's been a lot of work to study infectious disease, we felt like the methylome hadn't been fully exploited...and methylation quantification, using the EPIC+ BeadChip, is actually pretty affordable at scale. The relationship between methylation patterns, in the presence or absence of a disease, is potentially as informative as other diagnostics platforms and we imagined that this could be scaled to address the pandemic," states Dr. Barnes.

One of the major findings is that DNA methylation profiling, in conjunction with machine learning techniques, can identify a SARS-CoV-2 specific epigenetic signature. "We've been able to demonstrate high sensitivity and specificity in predicting an infection, and also in-hospital clinical deterioration," states Dr. Barnes. "Our findings suggest that measuring methylation signatures, during and after SARS-CoV-2 infection, can provide clinicians with the ability to detect viral infection, as well as predict that patient's clinical course."

Read the paper

Konigsberg IR, Barnes B, Campbell M, et al. Host methylation predicts SARS-CoV-2 infection and clinical outcome. Preprint at www.researchsquare.com/article/rs-334297/v1. Posted March 22, 2021. Accessed September 8, 2021.

Learn more

Infinium MethylationEPIC BeadChip, www.illumina.com/products/by-type/microarray-kits/infinium-methylation-epic.html

Dr. Barnes, CCPM, creating a BeadChip, and COVID, www.illumina.com/content/dam/illumina-marketing/documents/icommunity/methylation-covid-barnes-interview-m-gl-00158.pdf

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M-GL-00167 v1.0



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