From: Fauci, Anthony (NIH/NIAID) [E]
Sent: Mon, 9 Mar 2020 01:32:52 +0000
To: Cassetti, Cristina (NIH/NIAID) [E]
Subject: FW: can you use a miRNA-seq assay to detect covid-19 in blood samples?
Attachments: GSE81852 MERS vs Mock control PCA p=2.1e-8 q=7.79e-7 2 variables 8March2020.tif, GSE81852 MERS vs Mock control Hierarchical clustering heatmap p=2.1e-8 q=7.79e-7 2 variables 8March2020.tif, GSE81852 MERS vs Mock control PCA p=6.4e-7 q=4.2e-5 10 variables 8March2020.tif, GSE81852 MERS vs Mock control Hierarchical clustering heatmap p=6.4e-7 q=4.2e-5 10 variables 8March2020.tif

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From: Hellmich, Helen < (b) (6)
Sent: Sunday, March 8, 2020 5:52 PM
To: Fauci, Anthony (NIH/NIAID) [E] (b) (6)>
Subject: can you use a miRNA-seq assay to detect covid-19 in blood samples?

Dr. Fauci, how are you sir?

Long ago, in the early 90's, I was a post-doctoral fellow in the Laboratory of Viral and Molecular Pathogenesis at NIH. I don't know if the same lab is still there. Now I work on brain injury and Alzheimer's but my interest in viruses and mechanisms of viral pathogenesis has not waned and the recent covid-19 outbreak prompted me to do a little investigation on my own.

My studies of blood microRNA changes after TBI and AD suggest that principal component analysis of distinct changes in circulating miRNAs can identify the patient population. MicroRNA alterations can be measured by real-time PCR which I presume is the basis of the test that is developed for this disease but I am analyzing blood miRNA-seq expression profiles and now it is possible to quickly sequence blood samples in a few hours and get accurate results. Blood gene expression in my studies was more variable (lots of RNases in blood) so I found that microRNAs are much more stable in blood and serum samples.

I attach an example of a PCA/hierarchical clustering heatmap analysis of a GEO dataset for MERs-coV from 2016 https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE81852
I performed the PCA and heatmap analyses at two different stringencies and you can see that the patients can be unequivocably distinguished from the controls at very significant p and FDR values.

Just a thought but many clinical centers, hospitals, academic institutions can quickly perform transcriptome-wide sequencing. Blood RNA can be isolated in 1-2 hrs, sequencing libraries made in a few hres and one miRNA sequencing run can handle up to 48 samples and the data can be quickly analyzed.

Just my two cents on how NIH could accelerate the analysis of new blood samples for this new strain of coronanvirus. You could mobilize hundreds of sequencing centers to help in the analysis.

Regards