Genomic signature in blood identifies underlying viral infection

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Scientists have identified a genomic "signature" in circulating blood that reveals exposure to common upper respiratory viruses, like the cold or flu, even before symptoms appear.

The tell-tale viral signature reflects a set of subtle but robust changes in genes that are activated as the body responds to infection. The signal from the signature is strong enough in symptomatic individuals to clearly reveal whether their infection is viral or bacterial. It can also discriminate between who has a viral infection and who does not - all from a single tube of blood.

"This work is still in a relatively early phase of discovery, but we are optimistic that these findings may lead to a whole new way of diagnosing infectious disease," says Geoffrey Ginsburg, M.D., Ph.D., director of Duke University's Center for Genomic Medicine in the Institute for Genome Sciences & Policy and the senior author of the study appearing in the journal *Cell Host & Microbe*.

Researchers say the discovery could lead to dramatic changes in the way doctors care for the millions of people who develop upper respiratory infections every year. Ginsburg says the symptoms of a cold, the flu or pneumonia can appear similar, but right now, doctors can't tell what the patient really has until laboratory tests are conducted, and that can take days.

"Until results are in, treatment is pretty much a best guess. Knowing

exactly which pathogen is involved is important because it affects the urgency of response and the type of treatment," says Ginsburg. "This approach could lead to more precise, informed and tailored therapy - essentially, personalized care for infectious disease. That's better for the patient and better for public health, in general."

Christopher Woods, M.D., an associate professor of medicine at Duke and the Chief of the Infectious Disease Section at the Durham Veterans Administration Medical Center, says a quick test to determine the real cause of disease has other benefits, too. "It could mean more appropriate use of antibiotics. Overuse of antibiotics can lead to the emergence of drug-resistant pathogens, and no one wants to see more of that."

The discovery is based upon the fact that the body's immune system starts responding very quickly and in a highly specific manner when exposed to a viral pathogen as opposed to a bacterial one. "A detailed reading of that response, using gene expression data, reveals what type of pathogen the person is reacting to," says Aimee Zaas, M.D., M.H.S., an infectious diseases physician at Duke and the lead author of the study.

Zaas and colleagues recruited 57 healthy volunteers who agreed to be inoculated with either a live cold virus (rhinovirus), the respiratory syncytial virus, or the influenza A virus. Researchers first took detailed baseline measures of genomic profiles in participants' blood, nasal fluid, breath and urine, and then inoculated the volunteers with one of the three viruses. They waited to see who became sick, and noted when symptoms first appeared, measuring markers of biological response at multiple time points after exposure. Volunteers were quarantined during the time they were infectious.

The research team studied changes in gene expression patterns in the participants' blood and identified 30 genes - many of which were already known to be active in the body's response to viral infections - whose

expression patterns changed only among those who became symptomatic.

Investigators tested this "acute respiratory viral signature" in an independently acquired data set of gene expression patterns among people infected with influenza A and found that the signature was able to clearly distinguish with 100 percent accuracy between individuals who were infected and those who were not.

"We believe there will be multiple applications for this discovery," says Ginsburg. "This is simply the first step. Right now we are replicating our results in additional studies and also trying to validate these expression patterns in additional studies. We want to be careful and not draw any conclusions too quickly. Even though the signature we identified appears to be an excellent diagnostic, there may be other genes that can make it even better."

The researchers say the acute viral response signature may be applicable only to people who have healthy immune systems. "We would need to show that this approach also works in patients with underlying immune deficiencies before we could offer it as a potential diagnostic tool for everyone," says Zaas.

Source: Duke University Medical Center (news : web)