UT SOUTHWESTERN MEDICAL CENTER NEWS

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# UT Southwestern infection detectives use disease 'fingerprints' to track common infections in children

DALLAS – March 13, 2007 – Infectious disease specialists at UT Southwestern Medical Center have found a new method for identifying suspect viruses and bacteria that cause some of the most common acute infections in children.

Traditionally, researchers have looked for clues to an infection by tracking down the virus or bacteria causing it. But that doesn't always work because the bacteria or virus may not be present in the blood or other easily accessible area.

Researchers at UT Southwestern, Children's Medical Center Dallas and Baylor Institute for Immunology Research came up with a different approach – analyzing the telltale "fingerprints" a disease leaves behind on cells involved in the immune response, and using that information to get a composite sketch of the infectious agent.

"We are genetically programmed to respond differently to different infections. We have developed the tools to understand that," said Dr. Octavio Ramilo, professor of pediatrics at UT Southwestern and lead author of a study appearing in the March edition of the journal *Blood*.

"Infectious diseases are the No.1 cause of death in the world. So we hope this eventually can be used not only to diagnose, but also to understand the prognosis and how the body is responding to therapy," he said.

Different viruses and bacteria trigger the activation of very specific genes that code for proteins called receptors in leukocytes, the white blood cells that help the body fight infections. Researchers surmised that if they looked at the leukocytes, they could detect the specific pattern of receptors – similar to a disease "fingerprint" – and be able to identify which infection was present. The process to identify such biosignatures is called gene expression profiling, and it's done using microarray analysis.

Researchers extracted genetic material called RNA from a drop of blood and placed it on a special gene chip called a microarray, which contains probes for the whole human genome and measures which genes are turned on or off.

In this study, researchers analyzed gene expression patterns in leukocytes from 29 children at Children's known to have one of four common infections: flu (influenza A); staph (Staphylococcus aureus); strep (Streptococcus pneumoniae); or E. coli (Escherichia coli).

They analyzed 35 genes that help distinguish infections and identified infectious agents with better-than-average success rates. Doctors were able to distinguish between the influenza, E. coli and

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strep infections in 95 percent of cases. A different set of genes distinguished E. coli from staph infections with 85 percent accuracy. Further investigation demonstrated clear distinction between viral and bacterial pneumonias.

The next step will be to study whether the microarray analysis can be applied in a more challenging clinical setting, such as an emergency room.

"When a child comes in with a fever to the ER, we want to see if we can predict who just has a virus and can go home, and who has to be admitted and put into the intensive care unit and treated with antibiotics," said Dr. Ramilo. "This is just the first step. But it establishes a basis for us to do that."

While pediatricians couldn't perform the analysis in their offices, researchers are already thinking about a possible way they could send in the results from the chip and get the analysis back via the Internet, for example.

It could also prove useful for identifying previously unknown illnesses or biological weapons.

"Even if we don't know which pathogen it is, we still can tell which family or which group it's in, so if someone engineers a virus that has never been seen, we will have hints that it's close to something that is known," said Dr. Ramilo, who leads pediatric infectious disease research at UT Southwestern and Children's.

Further studies may eventually help doctors track the progression of disease and help assess risks of complications, Dr. Ramilo said.

Other UT Southwestern researchers involved are Drs. Asunción Mejías and Monica Ardura, postdoctoral clinicians in pediatric infectious diseases, and Dr. Wendy Chung, a former postdoctoral clinician in pediatric infectious diseases. Also involved are researchers from the Baylor Institute for Immunology Research and Rockefeller University in New York.

The study was supported by grants from the National Institutes of Health, Children's Medical Center Dallas Foundation, Baylor Health Care Systems Foundation, DANA Foundation and the Defense Advanced Research Planning Agency.

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UT Southwestern Medical Center, one of the premier medical centers in the nation, integrates pioneering biomedical research with exceptional clinical care and education. Its nearly 1,500 full-time faculty members – including four active Nobel Prize winners, more than any other medical school in the world – are responsible for groundbreaking medical advances and are committed to translating science-driven research to new clinical treatments. UT Southwestern physicians provide medical care in 40 specialties to about 92,000 hospitalized patients and oversee 1.7 million outpatient visits a year.

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