50-hour whole genome sequencing provides rapid diagnosis for children with genetic disorders

October 3 2012

Today investigators at Children's Mercy Hospitals and Clinics in Kansas City reported the first use of whole genome information for diagnosing critically ill infants. As reported in *Science Translational Medicine*, the team describes STAT-Seq, a whole genome sequencing approach - from blood sample to returning results to a physician - in about 50 hours. Currently, testing even a single gene takes six weeks or more.

Speed of diagnosis is most critical in acute care situations, as in a neonatal intensive care unit (NICU), where medical decision-making is made in hours not weeks. Using STAT-Seq, with consent from parents, the investigators diagnosed acutely ill infants from the hospital's NICU. By casting a broad net over the entire set of about 3,500 genetic diseases, STAT-Seq demonstrates for the first time the potential for genome sequencing to influence therapeutic decisions in the immediate needs of NICU patients.

"Up to one third of babies admitted to a NICU in the U.S. have genetic diseases," said Stephen Kingsmore, M.B. Ch.B., D.Sc., FRCPath, Director of the Center for Pediatric Genomic Medicine at Children's Mercy. "By obtaining an interpreted genome in about two days, physicians can make practical use of diagnostic results to tailor treatments to individual infants and children."

Genetic diseases affect about three percent of children and account for

15 percent of childhood hospitalizations. Treatments are currently available for more than 500 genetic diseases. In about 70 of these, such as infantile Pompe disease and Krabbe disease, initiation of therapy in newborns can help prevent disabilities and life-threatening illnesses.

STAT-Seq uses software that translates physician-entered clinical features in individual patients into a comprehensive set of relevant diseases. Developed at Children's Mercy, this software substantially automates identification of the DNA variations that can explain the child's condition. The team uses Illumina's HiSeq 2500 system, which sequences an entire genome at high coverage in about 25 hours.

Although further research is needed, STAT-Seq also has the potential to offer cost-saving benefits. "By shortening the time-to-diagnosis, we may markedly reduce the number of other tests performed and reduce delays to a diagnosis," said Kingsmore. "Reaching an accurate diagnosis quickly can help to shorten hospitalization and reduce costs and stress for families."

Provided by Children's Mercy Hospital