Study demonstrates potential of rapid whole-genome sequencing in critically ill infants

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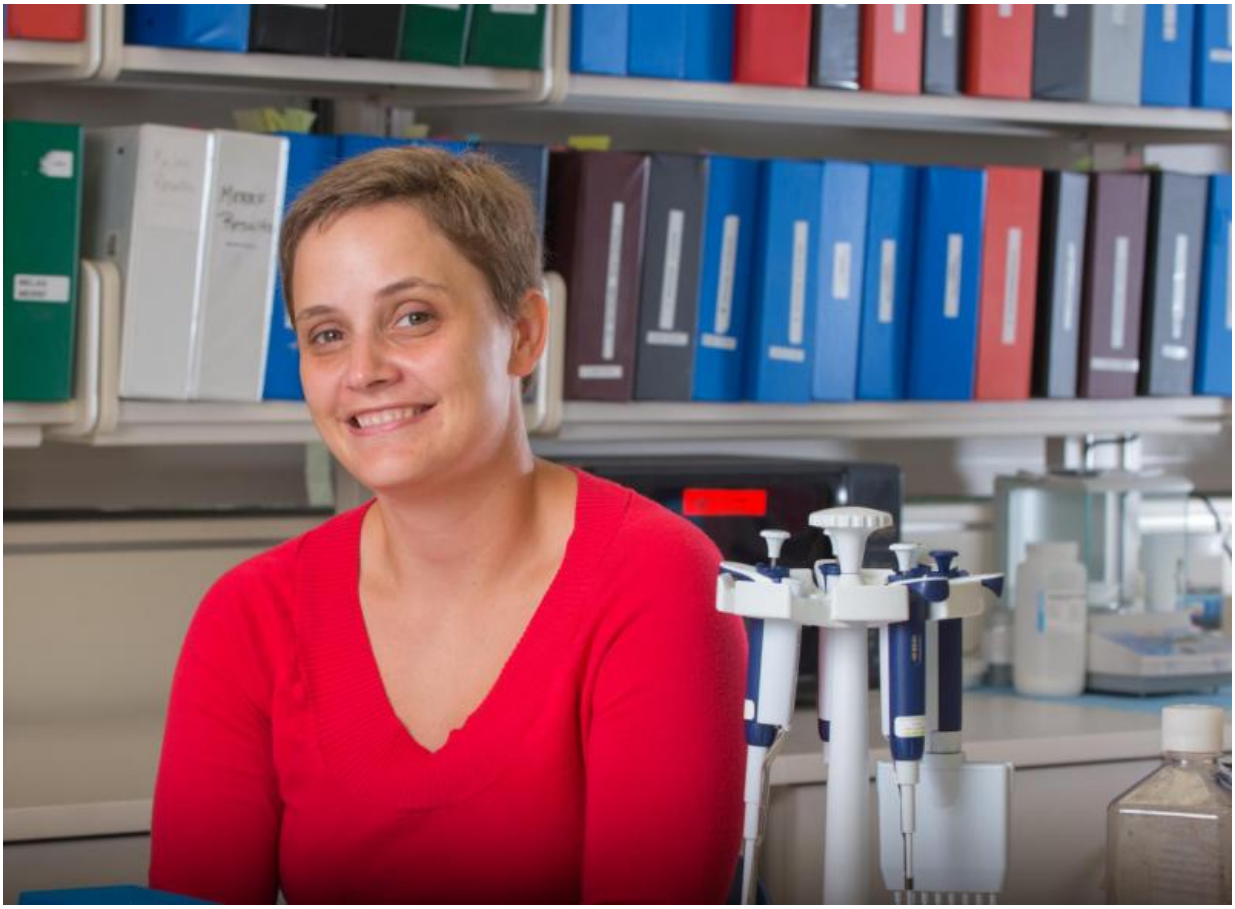

A study published today in *The Lancet Respiratory Medicine* and presented at the annual Pediatric Academic Societies Meeting revealed the early results of the clinical usefulness of rapid whole-genome sequencing in neonatal and pediatric intensive care units (NICUs and PICUs). Children's Mercy Kansas City's STAT-Seq test helped diagnose a genetic disease in more than one half of 35 critically ill infants tested, compared to just nine percent with standard genetic tests.

Credit: Children's Mercy Kansas City

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As a result of receiving a specific disease diagnosis, clinical care was refined in 62 percent of infants, including 19 percent who had a markedly favorable change in treatment, and palliative care was initiated in 33 percent. Lead authors of the study were Laurel Willig, MD, Josh Petrikin, MD, and Stephen Kingsmore, MB, ChB, BAO, DSc, FRCPath, of Children's Mercy Kansas City.

"Genomic diseases are the leading cause of death in NICUs and PICUs, but a timely and accurate diagnosis can significantly improve the precision of the care we provide. We've shown that rapid diagnosis using whole-genome sequencing is feasible and changed management for a majority of infants that were diagnosed," said Dr. Willig, a pediatric nephrologist. "We hope STAT-Seq will be instrumental in introducing precision medicine into the NICU and PICU."

Still a research protocol, STAT-Seq is the fastest whole-genome test in the world, taking less than 50 hours from test order to delivery of an initial report. STAT-Seq can identify mutations across the genome associated with approximately 5,300 known genetic diseases, and in some cases even identify previously unknown genetic diseases. In contrast, standard clinical practice calls for an array of genetic tests to be

performed (94 standard genetic tests were ordered on patients in this study), which are time-consuming and can only test for a limited set of disorders.

The symptoms and signs of genetic diseases in neonates are often overlapping, making identification of a specific diagnosis difficult. Further, infants frequently show only a fraction of the full set of symptoms and signs of genetic diseases, further complicating timely diagnosis and specific treatment. STAT-Seq bypasses these difficulties by casting the widest net in defining the underlying etiology.

"STAT-Seq dramatically improves our ability to rapidly detect thousands of genetic diseases, including those we wouldn't have anticipated or that have never been seen before," said Dr. Petrikin, a neonatologist. "Armed with a precise diagnosis, we may be able to try potentially effective treatments, stop ineffective treatments, or ease discomfort by instituting palliative care."

These retrospective results underscore the importance of a larger, prospective, randomized study now under way: In September 2013, Children's Mercy became one of four pilot projects to explore newborn genomics through funding by the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) and the National Human Genome Research Institute (NHGRI), both parts of the National Institutes of Health. Other projects include teams at Brigham & Women's Hospital at Boston Children's Hospital; University of California San Francisco and University of North Carolina Chapel Hill. Comprised of these four programs, the Newborn Sequencing In Genomic medicine and public HealTh (NSIGHT) program aims to explore, in a limited but deliberate manner, the implications, challenges and opportunities associated with the possible use of genomic sequence information in the newborn period. The four programs convened in April at the 6th Annual Pediatric Genomics Conference at Children's

Mercy Kansas City.

More information: *The Lancet Respiratory Medicine*, www.thelancet.com/journals/lan … (15)00139-3/abstract

Provided by Children's Mercy Hospital