

Sema4 Launches Newborn Screening Targeted Sequencing Test

Feb 12, 2018 | [Monica Heger](#)

SAN FRANCISCO (GenomeWeb) – Sema4, the Mount Sinai Health System [spinout](#) that launched last year, has added a sequencing-based newborn screening test to its menu that looks for 193 disorders and analyzes pharmacogenomic genes related to 38 common pediatric medications.

The test, Natalis, can be ordered by parents online for \$649, although a physician ultimately has to approve it.

Sema4 CEO Eric Schadt said that the goal was to focus on early-onset, severe, highly penetrant conditions for which early detection is associated with a treatment or intervention to either reduce symptoms or, in some cases, to prevent them altogether. It's "focused on being medically actionable," he said, and guidelines exist for how to treat the disorders.

Targeted next-generation sequencing is used to assess the genes involved in the 193 conditions, while a genotyping array is used for the pharmacogenomics genes. Parents can order the test online and will receive a kit in the mail. Turnaround time from when Sema4 receives the sample until results are reported is around two weeks. Sampling is done at home via a cheek swab, and the Sema4 team asks for samples from the baby as well as both biological parents to help filter results.

Sema4 has partnered with PWN, an independent network of doctors and genetic counselors, to provide the test. A PWN physician approves test orders and one consultation with a PWN genetic counselor is also included.

The test includes the 34 disorders recommended by the federal government for testing as well as additional ones, like some childhood cancers, glucose-6-phosphate dehydrogenase (G6PD) deficiency, and atypical epilepsy. Some of the disorders, such as G6PD deficiency, can be treated with simple dietary changes. In addition, G6PD is highly prevalent in certain populations, for instance in African Americans, where 10 percent of males are affected.

Aside from more common disorders, the test also screens for rarer ones, which can help shorten time to diagnosis. "If you're affected with a rare genetic disorder, the odyssey averages around five to seven years for a diagnosis," Schadt said. The goal with an expanded newborn screening panel is that "you can know on day one, before clinical manifestation, and then you can start treatment, which can reduce the damage," he said. For some disorders, by the time there is clinical manifestation, testing, and a diagnosis, there can be irreversible mental development problems, he added.

Standard newborn screening varies state to state. While most states test for the 34 federally recommended conditions, some states test for additional disorders. New York, for instance, tests newborns for around 50 conditions.

Such testing is predominantly biochemical rather than genetic, Schadt said. Tests typically use mass spectrometry to look at analytes or other markers in blood. Natalis, by contrast, uses sequencing to look at DNA from babies' saliva. "It's a complementary panel that

covers all the disorders screened for across the 50 states, but also other conditions that are not on any of the panels," Schadt said.

The Natalis test is designed for asymptomatic babies whose parents want the extra information, Schadt said. Order requests for tests will first be reviewed and must be approved by a physician, he said. Sema4 wouldn't perform testing on newborns who were already showing symptoms of a disorder or on children above a certain age, Schadt said. Since the disorders tested for all manifest typically by the time a child is a few years old, if a parent wanted to order a test for a 10-year-old, that would not be approved, since chances are that child would be in the clear, Schadt said.

Currently, the test is self-pay, but Schadt said that Sema4 plans to launch research studies to demonstrate its clinical utility. Such studies would compare the Natalis test with standard newborn screening, including the rates of detection as well as healthcare utilization, to see what the impact of having an earlier diagnosis would be on the child's outcome and use of healthcare services. The firm estimates that rates of a positive test will vary depending on the child's population from one in four to one in 250.

"We're trying to build the evidence that if we start screening with this technology at birth or shortly after, it enhances diagnosis and enables early treatment," he said.

Schadt anticipated that its first customers would likely be those within the Mt. Sinai Health System, but he said the firm would also be targeting other large healthcare systems and would work with some select Ob/Gyns.

Large-scale newborn screening research projects funded by the National Institutes of Health have demonstrated [mixed results](#) in terms of whether parents want the additional information, as well as challenges with using the technology as a first-line screening test.

For instance, BabySeq, one of four NIH-funded Newborn Sequencing in Genomic Medicine and Public Health (NSIGHT) projects, has had difficulty recruiting parents into the study. BabySeq has two arms, one focused on screening healthy newborns and another that screens babies who have been admitted to the NICU. For healthy babies, just over 8 percent of the parents approached about enrolling actually did, Joel Krier, clinical chief of the Division of Genetics at the Brigham and Women's Hospital, reported last year. Similarly, the NSIGHT project at the University of North Carolina has also struggled with low enrollment rates.

However, one reason many cite for not enrolling is logistical hurdles. Participants must complete forms and questionnaires and go through a multi-step enrollment process, which they reported as being burdensome.

In addition, some conditions have proven difficult to screen for. For instance, under the NSIGHT project NBSeq at the University of California, San Francisco and UC Berkeley, researchers found that exome sequencing of newborns had a hard time identifying pathogenic variants that cause isovaleric acidemia, a condition that causes problems breaking down the amino acid leucine. Standard testing identified two positive cases that the exome pipeline missed, although manual inspection and whole-genome sequencing was able to find the pathogenic deletions.

Nonetheless, Sema4 is not the only one looking to move into sequencing-based newborn screening. Last year, [PerkinElmer](#) began offering whole-genome sequencing for healthy newborns of families who are also customers of its cord blood and tissue banking business.

In addition, Natera has indicated that it is interested in whole-genome [sequencing of newborns](#), eyeing its patient portal and cord blood and tissue banking business as a means through which it could eventually offer newborn sequencing services.

Aside from Natalis, Sema4 also offers sequencing-based carrier screening, including an expanded carrier screening test for 281 inherited conditions and a narrower version for 67 inherited conditions. That narrower version, CarrierCheck, is available through the online portal of consumer genomics company Helix.

Schadt said Sema4 does not currently have plans to make Natalis available through Helix. He said that although Sema4 is "interested in that channel, which may be able to broaden access to genomic information," it wants to first "assess in a more targeted way what the appetite is" for newborn screening.