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Mt. Sinai to Open Clinical NGS Lab; Aims to Sequence 1 Million Individuals in Resilience Project

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By Monica Heger

NEW YORK (GenomeWeb) – Mt. Sinai said this week that it plans to open a new next-generation sequencing laboratory in Branford, Conn., at the site of Roche's former 454 Life Sciences facility.

Daniela Starcevic, who heads Mt. Sinai's molecular diagnostics efforts, led the development of the Connecticut lab, along with Eric Schadt, founding director of Mt. Sinai's Icahn Institute for Genomics and Multiscale Biology.

The team will seek CLIA certification and CAP accreditation for the lab and plans to run NGS panels for clinical diagnostics as well as translational research projects, including its flagship Resilience Project, which aims to understand why some people can carry severe disease-causing mutations, yet be disease free.

Schadt told *Clinical Sequencing News* that the lab would likely be operational in November and would run in a research mode until it receives CLIA certification and CAP accreditation, which he anticipated would occur in the summer of 2015.

Over the last several years, Mt. Sinai has been increasingly developing clinical NGS tests that it runs out of its Genetic Testing Laboratory in New York. For instance, it currently runs a targeted cancer hotspot panel on the Ion Torrent PGM, as well as an autism test, carrier screening, and exome sequencing for undiagnosed disorders on the Illumina HiSeq.

"As we started ramping that up, it became clear we needed to expand out," Schadt said. "We were maxed out, space-wise."

The old 454 lab in Branford was ideal for a number of reasons, Schadt said. Because it was formerly an NGS facility, it required less work to make it amenable for Mt. Sinai's purposes. In addition, it is large, giving Mt. Sinai plenty of space to grow and expand.

Mt. Sinai has also tapped into the expertise in Branford, hiring a number of former 454 employees, including the new managing director of the Connecticut lab, Todd Arnold, who was formerly vice president of research and development at 454. Mt. Sinai has also hired Daniel Sisco as director of laboratory operations. Sisco was previously director of the sequencing center at 454.

The Connecticut lab will initially be equipped with eight of Thermo Fisher's Ion Proton systems, eight Ion Chefs, the Torrent Suite Variant Caller and customized AmpliSeq panels. Mt. Sinai has also purchased a Pacific Biosciences RS that it will install in the new lab, and according to Schadt, the team will consider additional platforms as it scales up.

One of the first projects that will be run out of the lab is the Resilience Project, where researchers aim to identify disease-causing mutations in healthy individuals.

"We'll be screening for people that harbor highly penetrant mutations that should have caused catastrophic illness, like Huntington's disease," Schadt said, with the goal of trying to figure if they have any protective variants and if those variants can shed light on ways to combat disease.

The Resilience Project launched in August, and Schadt said that within the first year the team aims to use a targeted sequencing panel on the Proton to screen around 50,000 people, with the goal of screening 1 million people.

In collaboration with Thermo Fisher, Mt. Sinai researchers developed an AmpliSeq panel consisting of 26,000 amplicons covering 700 genes. Schadt said that a subset of this panel would be looked at for participants in the Resilience Project. However, he said, the goal is that by driving volume, the panel will be run at a low cost and can cover multiple projects at once. For instance, he said, while the panel covers the known Mendelian disease loci, there are also pharmacogenomic variants and variants that confer disease risk for a variety of common diseases.

For the research projects, Schadt said the team has institutional review board approval to return clinically relevant results to participants. In addition, he said, aside from becoming CLIA and CAP certified, the team is seeking approval from the New York State Department of Health and plans to develop tests that can be ordered by and reported back to patients' physicians.

Already, at Mt. Sinai's clinical lab in New York, the group offers a clinical cancer hotspot panel, run on the Ion Torrent PGM, and has NY State approval for a handful of the mutations on that panel that are clinically actionable, Schadt said.

The way that NY State approves NGS testing is usually for a few variants at a time, Schadt said. For instance, he said that in the case of the cancer hotspot panel, there are only a handful of mutations for a few cancer indications that are approved. Those are the ones that are actionable in the sense that there is a drug linked to the variant, and testing for it is reimbursable, he said.

He said the team will also develop NGS assays for carrier screening, pharmacogenomics, inherited cancer, and will be expanding the cancer hotspot panel.

While all of the assays will initially be developed as LDTs, Schadt said the team is developing the tests with an eye toward the US Food and Drug Administration and how it might regulate LDTs. In addition, he said, they will be working to get NY State approval for the tests, "a heavy regulatory hurdle to surpass."

Schadt said that the goal will be for all the panels to cost in the $100 range, which he thinks will be possible as the lab scales up. Initially, the tests will be offered for patients affiliated with Mt. Sinai hospital and its network of affiliated clinics, "but once we get this facility up and going … we fully anticipate offering those services to others outside the Mt. Sinai complex," Schadt added.

Aside from the fleet of Protons on which Schadt said the team would develop all of its targeted clinical assays, in the near term it also plans to bring in a PacBio RS system. Mt Sinai has two PacBio RS's in its New York location that it uses primarily for research, but Schadt said the third system, which will be installed in the new lab, will be for clinical diagnostics for things like HLA haplotyping, targeting structural variants in cancer, assays that involve long tandem repeats for diseases such as Fragile X syndrome, and other clinical applications for which long reads are necessary, Schadt said.

As the lab moves into more comprehensive sequencing like exome and whole-genome, it will bring in Illumina systems, Schadt said. "We'll ultimately have a variety of technologies there," he said.

Monica Heger tracks trends in next-generation sequencing for research and clinical applications for GenomeWeb's *In Sequence*and *Clinical Sequencing News*. E-mail Monica Heger or follow her GenomeWeb Twitter accounts at @InSequence and@ClinSeqNews.