Pathology researchers took the lead of a multidisciplinary NYU Langone SARS-CoV2 sequencing team to track the genetic evolution of the coronavirus in New York City. The team, composed by the NYU Genome Technology Center, the Institute for System Genetics (ISG), the Vaccine Center and the Center for Biospecimen Research & Development (CBRD), determined the genetic code of SARS-CoV2 isolated from 91 NYU Langone Health patients, the most complete study in New York City during the current pandemic.

“The value of determining viral local sequences is that – the more that become available – the better we can monitor the spread and severity of the disease – and the more it can clarify which drugs, vaccines, or social interventions are effective here,” says Adriana Heguy, PhD, director of the Genome Technology Center (GTC) and Professor of Pathology at NYU Langone Health, and leader of the sequencing team.

SARS-CoV-2, the new virus which causes coronavirus disease 2019 or COVID-19 has infected more than 1.2 million patients worldwide as of April 6. According to the World Health Organization (WHO), the illness has resulted in more than 70,000 deaths to date, more often among elderly patients with underlying health conditions. The New York State Department of Health has reported more than 67,500 cases to date in New York City.

Samples for this project were collected from the nasal swabs of patients at Tisch Hospital, NYU Winthrop Hospital and NYU Langone Hospital Brooklyn, classified by CBRD and genetic sequence of the viruses were generated by the GTC in collaboration with the ISG and the Vaccine Center, then immediately submitted to GISAID EpiFlu – the Global Initiative on Sharing All Influenza Data. Founded in 2008 to promote the international sharing of data on influenza infections, the GISAID database is now tracking the evolution of the new coronavirus.

The early data suggests that the coronavirus has been spreading in the New York City community for a couple of months since before testing started. Further, the particular genetic codes in most local viral samples indicates that they originated in Europe.

“This global effort does not just determine the code of a single version of the virus, but tracks how its genetic code changes as it moves through a population, and with what consequences,” says Matija Snuderl, MD, director of Molecular Pathology and Diagnostics and Associate Professor of Pathology. “As viruses evolve during transmission from person to person, their sequences can help researchers to zero in on the provenance, or place of origin, of that specific infection,” adds Dr. Snuderl, who leads the clinical testing team.

SARS-CoV-2 is a single-stranded RNA virus with 29,900 nucleotides in total. Mutations occur in the code as viruses copy themselves after invading human cells, such that viral genomes continually, randomly evolve

“Slight changes in the genetic code of a virus that happen during transmission from person to person can help to guide the public health response,” says Matthew Maurano, PhD, one of the lead
investigators at the ISG and Assistant Professor of Pathology. Samples from NY patients sequenced so far show that, compared with other GISAID sequences, the NY region has numerous infection chains, some likely derived from Europe, others possibly directly from Asia. Further, the NY region shows extensive mixing with other US states across the continent.

For the current project, the NYU Langone team used a technique called “capture sequencing” to determine the order of the virus’ RNA sequence from each patient sample. The team first used "baits" – pieces of genetic material designed specifically to attach to the SARS-CoV-2 RNA – to detect its sequence out of the mix of genetic material retrieved from each patient’s nose and throat. The team used high-throughput instrumentation to determine the sequences by breaking RNA chains into pieces, and amplifying each fragment attached to an identifying bar code tag making enough copies to be picked up by fluorescently labelled oligonucleotide probes to identify the virus’ RNA sequence.

“Capture sequencing has enabled us to instantly sample all genes in all organisms present in a complex patient sample, and to more accurately identify ongoing changes in genes,” says Dr. Heguy. “We’re just starting this project, but will soon be sequencing 192 viral samples per week with the goal of offering thousands of sequences for analysis in the near future.”

Please see next page for Figure.
Figure: Dendrogram showing relationship of SARS-CoV2 sequences from around the world. Most sequences from NY (in purple) group with those from Europe at top. Samples from across the entire US are mixed in to the same groups, suggesting there has been broad domestic transmission.