

ACCELERATING A CURE FOR COVID-19

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Gatehouse Bio

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The number of COVID-19 cases continues to grow exponentially. In an effort to slow and contain the spread of the disease federal and local governments around the world are closing public spaces and requesting that citizens practice social distancing. Despite these restrictions it is estimated that over 1 billion people (15% of the world's population) could become infected over the next 18 months. Based on current modeling, roughly 70 million of those individuals (6% cases) will develop severe infections requiring hospitalization. Individuals with severe COVID-19 infections ultimately succumb to organ failure and death within 18 days of symptomatic presentation, creating an extremely narrow window of opportunity for doctors to treat these patients.

We are confident there is an effective treatment strategy for COVID-19 infected patients, and if we are to change the projected scenarios, we need to act quickly and execute on an accelerated path to identify successful therapies. Gatehouse Bio is bringing together an ecosystem of partners aligned around a common mission to accelerate a cure.

We know the combination of heterogeneity within the population and likely across SARS-CoV-2 strains is playing a huge role in virulence, as some infected people are completely asymptomatic, while others die within days. Right now, COVID-19 diagnosis relies solely on detecting the presence of the virus but provides no information as to the infectivity of the virus or to the varied molecular responses the body makes as it tries to fight off the virus, both of which will ultimately determine a given patient's disease course. By taking an integrated approach to correlate the molecular mechanisms of SARS-CoV-2 infection and the body's response to infection with the known mechanism-of-action of FDA approved drugs we can create a short-list of therapeutic candidates with the potential to slow or forestall the consequences of COVID-19 infection and increase the likelihood of identifying potential treatments more quickly.

Gatehouse Bio has developed a technology platform that identifies disease signatures using a class of genes called small RNAs. We currently have a portfolio of small RNA signatures that define biological processes (e.g. inflammation, interferon response, cytokine release, receptor signaling, T-cell activation, and other relevant pathways) known to be affected by past SARS and MERS coronaviruses. Here, we propose a study to correlate our small RNA signatures with the new SARS-CoV-2 strains currently infecting populations around the world. The results of our study will uncover host pathways that are impacted by COVID-19 infection. Matching this information to our database of FDA approved drugs will result in a short-list of therapeutic candidates that can accelerate clinical trials and the identification of effective drugs. Because we'll be analyzing patient response signatures to COVID-19 infection, an additional benefit and outcome of our work could be a rapid prognostic test for aggressive disease to facilitate clinical triage.

We welcome all help and assistance, including resources, people and capital. The list of current needs is provided below.

Please contact us to get involved:

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Our Plan

To create a short-list of FDA approved drugs to treat COVID-19, we propose the following plan and timeline:

1. Collect matched, saliva and blood samples from 576 COVID-19 infected patients in New England, Tri-State Area, and Texas Metro Cities.
2. Samples will be processed and sequenced in Gatehouse Bio's BSL2 lab.
3. Data will be analyzed for sRNA-Signatures correlated to inflammation, cytokine release, T-cell activation, fibrosis and others using our platform.
4. Results will be a short-list of FDA approved drugs to test in clinical trials within 30 days.
5. Clinical trials will be executed with pharma using sRNA-Signatures to direct targeted therapy.

Under an IRB Approved Protocol, samples will be collected from 576 COVID-19 positive patients. Samples will be batch processed in groups of 96 every 4 days. Data analysis is estimated to take 6 days. Start-to-finish we will have a short-list of high-confidence FDA approved drugs in 30 days.

Sample Collection

To collect patient samples, we're taking a multi-pronged approach including:

- Contacting hospitals, using social media, and setting up sampling stations alongside existing drive-through test locations. Patient registration will be handled through a dedicated web portal that will include information about the study.
- Patients will Opt-In to our clinical study by signing informed consent. Sampling will include collecting matched saliva and blood samples, as well as clinical metadata including: lung function, temperature, symptom profile, blood pressure, sex, race, age and BMI.

Saliva will be collected using the RNeasy Protect Saliva Mini Kit from QIAGEN. Saliva is a proven efficacious biological material for SARS-CoV-2 viral RNA detection. Samples collected using the RNeasy Protect Saliva Mini Kit are stable for up to 14 days at room temperature (15-25°C), which provides enough time for samples to be collected, stored and shipped in batches.

Blood will be collected using a PAXgene RNA Blood Tube from QIAGEN. Whole blood contains the entire composition of B-cells, T-cells, platelets and circulating small RNAs required for detecting small RNA signatures correlated to the mechanism of SARS-CoV-2 infection. Samples collected using the PAXgene RNA Blood Tubes are stable for up to 14 days at room temperature (15-25°C), which provides enough time for samples to be collected, stored and shipped in batches.

Samples will be collected by trained specialists wearing the appropriate personal protective equipment required to come into close contact with potentially infected individuals.

Gatehouse Bio was issued clearance from the AstraZeneca Biosafety Committee to work with saliva and blood samples from COVID-19 patients. Our staff has undergone Bloodborne Pathogen Training from the American Red Cross and has all the necessary training to perform the work. Our

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laboratory at the Boston BioHub Incubator is outfitted with state-of-the-art liquid handling robots and certified to handle biohazardous material that have high-throughput capability allowing us to process approximately 2,000 samples per week, while minimizing human exposure to bloodborne pathogens.

Data Analysis

We will analyze the data for the following endpoints

1. We will test COVID-19 patients with unique SARS-CoV-2 strains for sRNA-signatures of inflammation, cytokine release, T-cell activation, fibrosis, glucocorticoid response and others.

Timeline: 30 days.

Deliverables: short-list of FDA approved drugs with panels of sRNA-signatures that will serve as the prospective companion diagnostics for Phase II clinical trials.

2. Correlate sRNA-signatures to SARS-CoV-2 viral load and metadata variables such as lung function, temperature and symptomatic profile.

Timeline: 35 days

Deliverables: a predictive diagnostic tests for 14-day progression, disease severity and outcome.

Resources Needed:

People:

- Registered Nurses
- Lab Technicians
- Data Scientists
- Web designer

Consumables for sample collection:

- 20 RNeasy Protect Saliva Mini Kits (QIAGEN)
- 11 PAXgene RNA Blood Tubes from (QIAGEN)
- 1000 phlebotomy kits and consumables (BD)

Consumables for laboratory work:

- 11 NextFlex Rapid Directional RNA-seq Kits v2.0 (PerkinElmer)
- 11 NextFlex Small RNA Library Prep Kits v3.0 (PerkinElmer)
- 11 NovaSeq 6000 S2 Flow Cells 200 cycle kits (Illumina)
- Sterile pipette tips, 96-well plates, ethyl alcohol and isopropyl alcohol

IT infrastructure:

- AWS compute
- Webhosting and site

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Private Protection Equipment:

- Gloves
- Masks
- Faceshield
- Disposable gown
- Hair bonnet
- Hand sanitizer
- Informed consent form
- iPad with LIMS for Metadata
- Infrared Thermometer
- Marker
- RNeasy Protect Saliva Tube
- Eppendorf 1.0mL Pipette
- eTIPS 1.0mL Pipette Tips
- Eppendorf 1.7mL Tubes
- PAXgene Blood RNA Tube
- Biohazard Plastic Bags
- Absorbent Pads
- Styrofoam box
- Turnicate
- Alcohol Prep Pads
- Sterile Gauze
- Sterile Band-aids (large)
- Butterfly Needles
- Biohazard Sharps Container
- Biohazard Bag
- Biohazard Box