

The Role of Laboratory Testing in the Covid-19 Pandemic

Department of Diagnostic & Health Sciences

College of Health Professions





Introduction

Hassan Aziz, PhD, FACSs, MLS(ASCP)^{cm} Professor

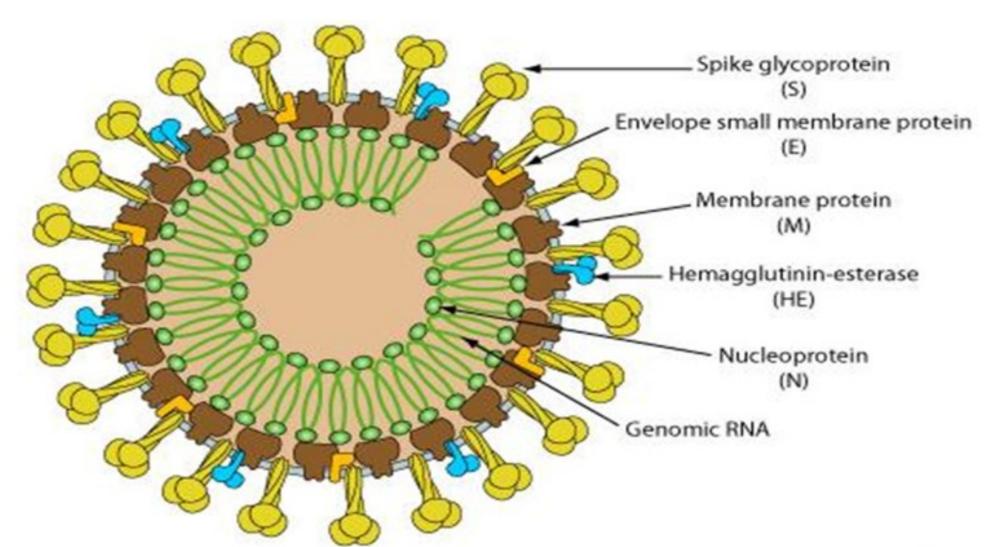




Update/Overview of COVID-19

Linda Williford Pifer, PhD, SM (ASCP), GS (ABB)
Professor

LITHSC





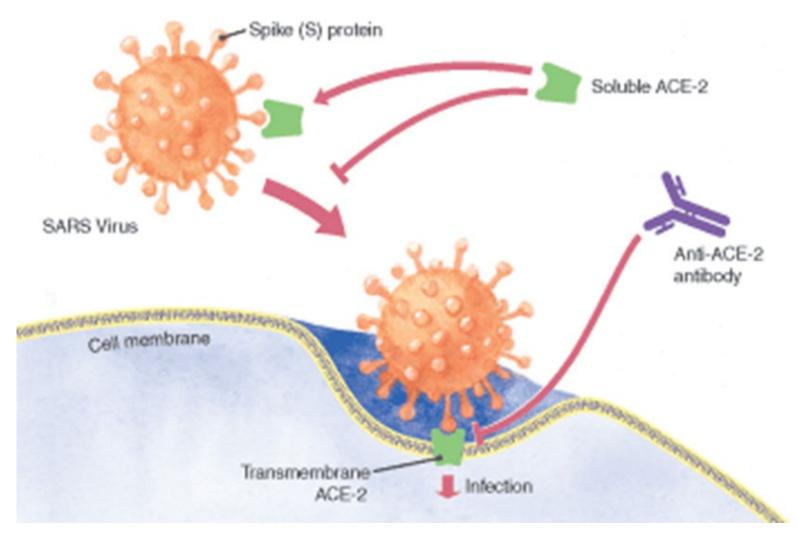
Angiotensin-I converting enzyme 2 (ACE-2) is the receptor for coronaviruses

This enzyme acts to reduce blood pressure and inflammation

UTHSC.

COVID-19 VIRIONS BIND TO ACE-2 RECEPTORS ON CELL

MEMBRANE





6 KNOWN CORONAVIRUSES & 3 OUTBREAKS

- 1. 229E, NL63, OC43, or HKU1 relatively insignificant
- 2. SARS-1 Coronavirus...

Severe Acute Respiratory Syndrome (outbreak in 2003. Guangdong Province, China); CFR= 10% (Case/fatality ratio)

3. MERS Coronavirus

Middle Eastern Respiratory Syndrome; CFR = 34%

4. SARS-2 (COVID-19)

Wuhan, China ... 2019-2020? CFR = 2-3% (CFR = 2-3%) Ro = 1.4 - 2.5 (Transmission rate/patient)

UTHSC

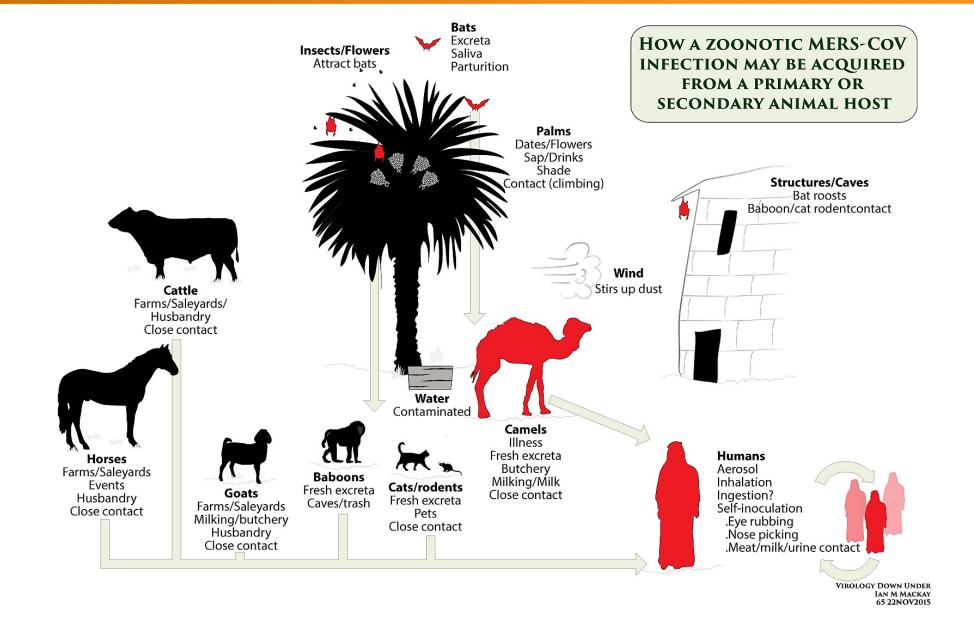




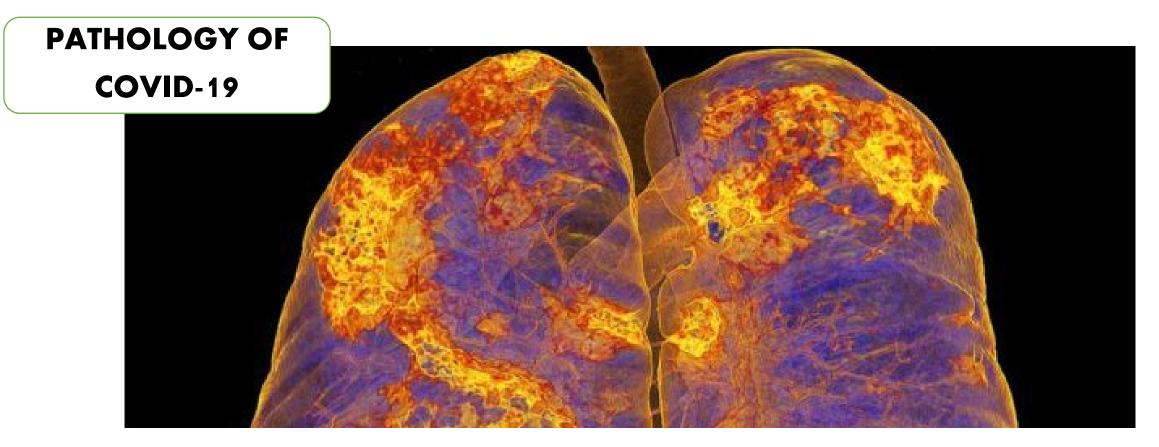


PANGOLIN, HORSESHOE BAT & CIVET CAT... ALL CORONAVIRUS VECTORS

UTHSC.







DYSPNEA, FEVER, COUGH, WEAKNESS, SORE THROAT, ACHES, HEADACHE EXTREME WEAKNESS SOMETIMES REQUIRING PHYSICAL THERAPY

UTHSC.





OTHER: FOOT LESIONS, LOSS OF SENSE OF SMELL & TASTE, CONFUSION, INFLAMMATORY ENCEPHALITIS, NEUROLOGIC, DEFICITS, STROKE, HEADACHE, DIARRHEA, PRESENCE OF VIRAL SHELLS SEEN IN EM'S OF BOWEL SECTIONS.

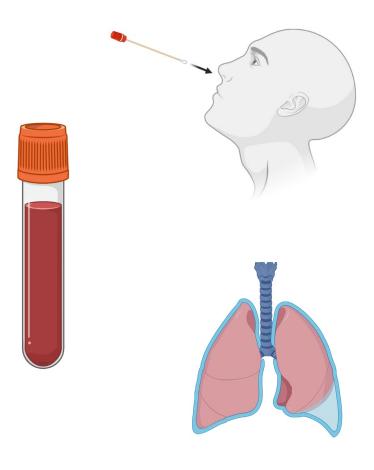


Specimen Collection Antigen versus Antibody Testing for SARS-CoV-2

Jacen Moore, PhD, MA, MT (ASCP)
Assistant Professor



COVID-19 Specimen Collection

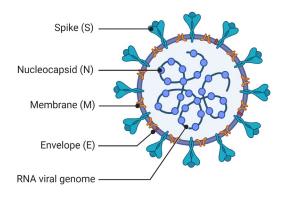


- Nasopharyngeal or Oropharyngeal swabs
 - Swabs must be plastic with artificial cotton
- Blood or tissue (autopsy)
- Respiratory
 - Respiratory aspirate
 - Bronchial alveolar lavage
 - Sputum
 - Productive, not induced
- Stool or Urine
 - Less reliable



What is a SARS-CoV-2 antigen or antibody?

- SARS-CoV-2 'Antigen'
 - Portions of the virus that the body recognizes as foreign or non-self



- Testing for portions of virus directly
- Determines if person is acutely or chronically infected

- Antibodies
 - Y-shaped proteins made by the body in response to virus

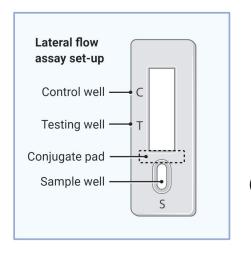




 Can provide protection against the virus and indicate viral exposure

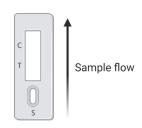


Serologic-Based Testing for COVID-19 Antibodies

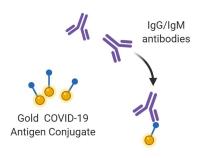




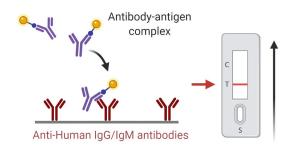




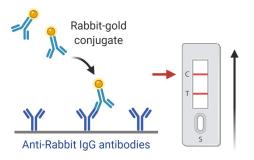
2 Sample incubation



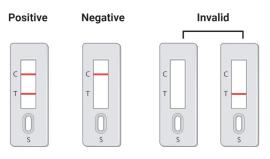
(3) Antibody-antigen recognition



(4) COVID-19 antibody detection



(5) Control antibody detection



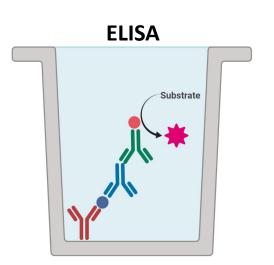
6 Interpreting results

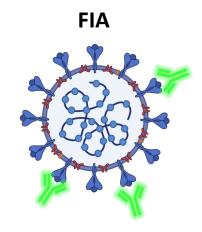


Antigen-Based Testing for SARS-CoV-2

- Enzyme-linked immunosorbent assay (ELISA)
 - Antibodies 'capture' COVID antigen
 - Secondary antibodies bind to captured antigen
 - Enzyme-labelled tertiary antibodies detect bound secondaries
 - Substrate allowed to react with enzyme
 - Direct relationship between antigen quantity and substrate intensity

- Fluorescence Immunoassay (FIA)
 - Fluorescently labelled antibodies bind COVID antigen
 - Instrument measures fluorescence intensity
 - Direct relationship between antigen quantity and fluorescence intensity







Antigen versus Antibody Testing

	Antigen	Antibody
What test identifies	Viral proteins or RNA	Host antibodies to virus
What test can tell you about infection status	Actively infected	Has been infected or exposed
When the test can be used accurately	During the acute phase of infection	Days-years in late or post-infection
Testing complexity	Highly complex and requires trained personnel and instrumentation	Easy to perform-can be done as point of care using rapid test devices
Sensitivity and specificity	Varies depending on test system	Varies depending on test system
Sample requirements	Swabs, BAL, Aspirates, Sputum, tissue biopsy, blood	Blood, saliva



Current Status of Diagnostic and Screening Tests for COVID-19

Anami Patel, PhD Vice President, Poplar Healthcare

FDA- Emergency Use Authorization (EUA)

- Guidance issued Feb. 29, 2020 describes a policy regarding certain laboratories immediately using tests they developed and validated in order to achieve more rapid testing capacity in the U.S.
- To address the COVID-19 public health emergency, the FDA has determined that prior public participation for this guidance is not feasible or appropriate and issued this guidance without prior public comment.
- This guidance document is immediately in effect, but it remains subject to comment in accordance with the FDA's good guidance practices













EUA: Scope

- The new policy is limited to:
- Laboratories certified to perform high complexity testing, consistent with the requirements under the CLIA – Molecular diagnostics for SARS-CoV-2

- The new policy does NOT impact:
- Requirements under the CLIA
- CDC recommendations for who should be tested













EUA: Policy

The guidance includes recommendations regarding:

- Validating newly developed SARS-CoV-2 tests prior to clinical use
- Notifying FDA when clinical use of a validated test begins
- Confirming the first 5 positive and negative samples with an EUA authorized test
- Indicating in test reports that the test has been validated but independent review by FDA is not yet complete
- Submitting an EUA within 15 days of initiating testing
- Steps to take if any specimens fail confirmatory testing or if FDA is unable to authorize the EUA













EUA: Test Validation

- The guidance includes recommendations regarding the minimal testing to be performed for validation:
 - Limit of Detection (LoD)
 - Clinical Evaluation
 - Inclusivity
 - Cross-Reactivity
- Limited viral materials are available
 - FDA, BARDA, and CDC prioritize and coordinate shipments to labs when ready to validate













Poplar Healthcare Testing Workflow

- Roche cobas 6800 EUA: SARS-CoV-2 RNA detection
- ThermoFisher: SARS-CoV-2 RNA detection
- CDC-IDT: CDC 2019-nCoV RNA









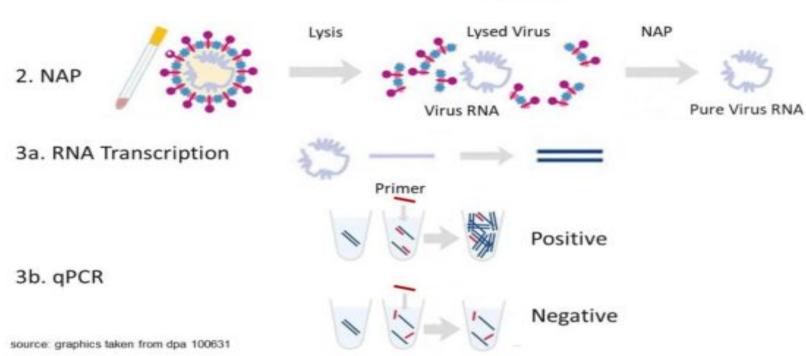




Test Workflow

1. Sample Collection (Swabs, Lavage, Sputum)

















Test Workflow

Sample collection

Sample prep

Real-time PCR

Data analysis



Samples collected using BD Universal Viral Transport Collection Kits:

- · Bronchoalveolar lavage
- · Nasal aspirate
- Nasopharyngeal swabs



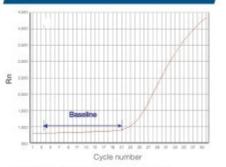
KingFisher Flex Purification System with MagMAX Viral/Pathogen Nucleic Acid Isolation Kit



QuantStudio 5 Real-Time PCR System or 7500 Real-Time PCR System

TaqMan 2019-nCoV Assay and Control Kits

TaqPath 1-Step RT-qPCR Master Mix, CG



Amplification curves using the 7500 or QuantStudio 5 Real-Time PCR System software













^{*} For Research Use Only. Not for use in diagnostic procedures.

Roche cobas 6800

- EUA: cobas SARS-CoV-2 RNA detection
- Detection of SAR-COV-2 and pan-Sarbecovirus
- Specimen Types: Nasopharyngeal & Oropharyngeal swab in UTM, UVT, or Saline
- Specimen Transport: 15°C to 30°C
- Specimen Transport & Storage: 2°C to 25°C and processed within 48 hrs. OR dry ice if >48 hrs.
- Capacity: 94 samples can be resulted in 6 hrs.













Roche cobas 6800 Result Interpretation

- Target 1: SARS-CoV-2, Target 2: pan-Sarbecovirus
- If both targets positive SARS-CoV-2 detected
- If only Target 1 positive SARS-CoV-2 detected
- If only Target 2 positive SARS-CoV-2 Presumptive positive
- All positive/negative results are called back to providers
 & state













ThermoFisher: TaqPath COVID-19 Combo Test

- EUA*: SARS-CoV-2 RNA detection
- Detection of SAR-COV-2
- Specimen Types: Nasopharyngeal & Oropharyngeal swab in UTM, UVT, or Saline
- Specimen Transport: 15°C to 30°C
- Specimen Transport & Storage: 2°C to 25°C and processed within 48 hrs. OR dry ice if >48 hrs.
- Capacity: 94 samples can be resulted in 6 hrs.

* Poplar Healthcare has submitted for EUA













ThermoFisher: COVID-19 Result Interpretation

- Target 1: ORF1ab, Target 2: N gene, Target 3: S gene
- If any two targets positive SARS-CoV-2 detected
- If Two or more Targets positive SARS-CoV-2 detected
- If only one Target positive SARS-CoV-2 Inconclusive
- All positive/negative results are called back to providers
 & state













CDC (IDT): 2019-nCoV

- EUA*: CDC 2019-nCoV RNA
- Detection of 2019-nCoV RNA
- Specimen Types: Nasopharyngeal & Oropharyngeal swab in UTM, UVT, or Saline
- Specimen Transport: 15°C to 30°C
- Specimen Transport & Storage: 2°C to 25°C and processed within 48 hrs. OR dry ice if >48 hrs.
- Capacity: 60 samples can be resulted in 6 hrs.

* Poplar Healthcare has submitted for EUA













CDC (IDT): 2019-nCoV Result Interpretation

- Target 1: 2019 nCoV_N1, Target 2: 2019 nCoV_N2 gene
- If both targets positive 2019 nCoV detected
- If only one Target positive 2019 nCoV Inconclusive
- All positive/negative results are called back to providers
 & state













Assay limitations

- Reliable results depend on proper sample collection, storage and handling procedures
- Mutated virus strain
- Not for monitoring treatment
- Not for screening of blood or blood products















Pathology and Lab Medicine and its role in a deadly pandemic: How the UTHSC Pathology Department responded to the Coronavirus crisis in the first 45 days

Mahul B. Amin, MD Professor and Chairman





PATHOLOGY AND LAB MEDICINE AND ITS ROLE IN A DEADLY PANDEMIC:

HOW THE UTHSC's PATHOLOGY DEPARTMENT RESPONDED TO THE CORONAVIRUS CRISIS
IN THE FIRST 45 DAYS

Mahul Amin, MD

Professor and Chairman

UTHSC Gerwin Chair of Cancer Research

Department of Pathology and Laboratory Medicine





SHOUT OUT!!



- National Medical Laboratory Professionals Week is an annual celebration of the medical laboratory
- Originated in 1975: 44th year
- Recognition & awareness of the important work by these professionals
- Lab professionals are engaged as vital partners in clinical care: 24/7/365
- Lab results are an integral part of the medical records of any patient
- More than 60% of medical diagnoses are dependent significantly on pathology and laboratory results.







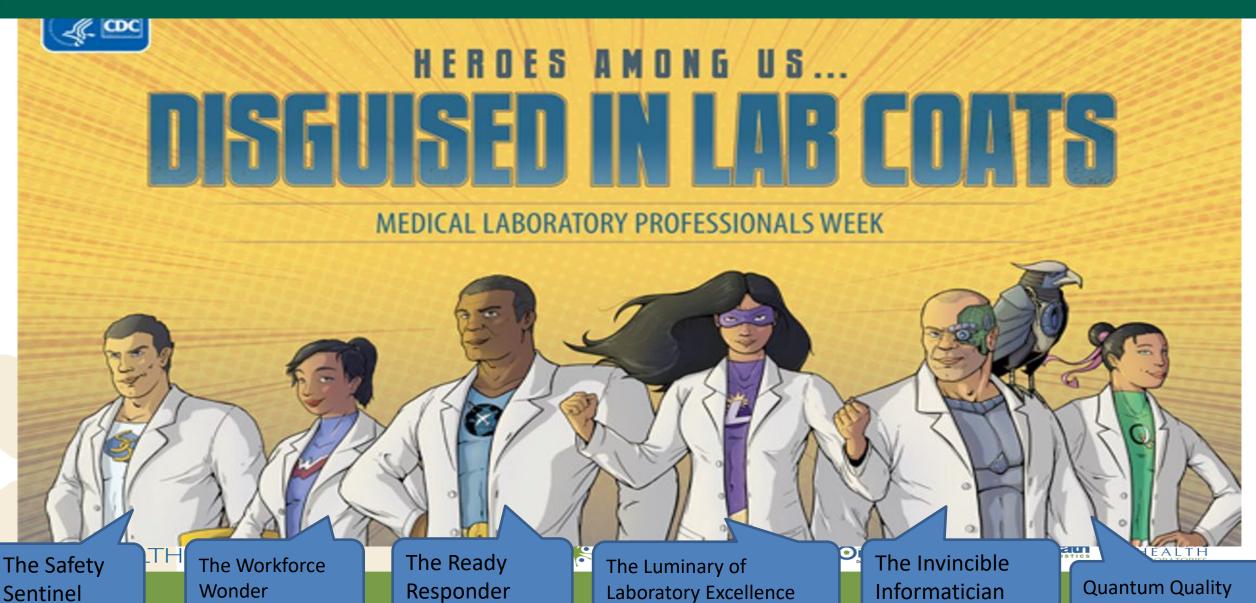




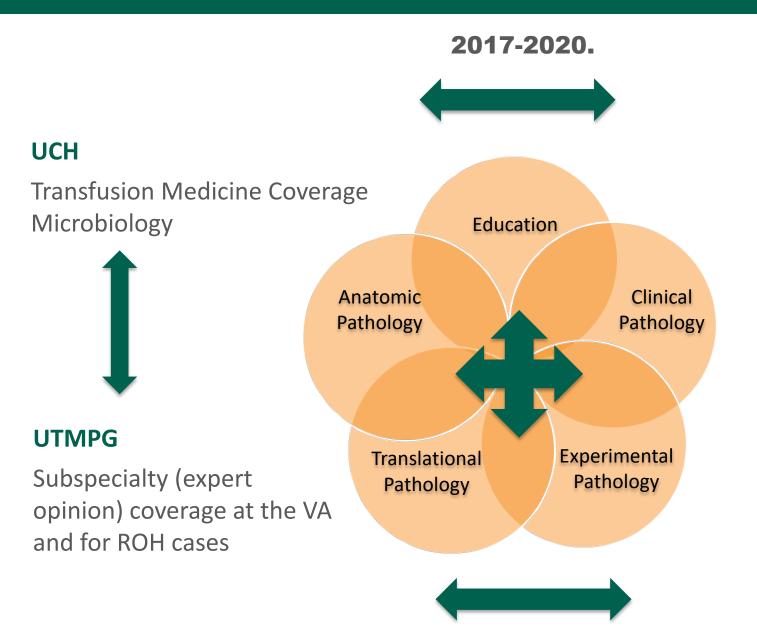












West Clinic

CLINICAL



RESEARCH

St. Jude
National &
International
Collaborations



DEPT. OF PATHOLOGY & LAB MEDICINE RESPONSE



CONSULTATIVE SERVICES

2

DEVELOP

& OFFER

PCR TEST

3

DEVELOP SEROLOGIC TESTING

PARTICIPATE IN
CORONAVIRUS
CONVALESCENT
PLASMA PROGRAM

FACILITATE FUTURE RESEARCH

5

PUBLIC HEALTH REPORTING

&

FACILITATING PREDITICTION MODELS

















CONSULTATIVE SERVICES

- Test selection
- Test Implementation
- Test Interpretation
- Send out testing
- Logistics arrangement











1

6

2

DEVELOP

& OFFER

PCR TEST

3

4

5



TRANSLATIONAL RESEARCH INIATITIVE:

TISSUE REPOSITORY

2016



2019



- Tissue repository from Methodist University 1992-2005
- Tissue repository 2003-2008 data "digital and searchable" with over 100,000 specimens
- Histology core in partnership with Office of VC of Research
- Cancer translational research initiatives...

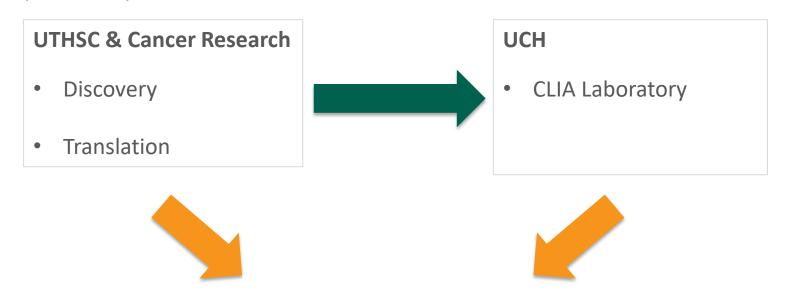


TRANSLATIONAL RESEARCH INITIATIVE:

GENOMICS

Overview

- Acquired: 2018
- In partnership with the UTHSC Center for Cancer Research



UTHSC PIONEERED "PRECISION/PERSONALIZED"

INNOVATIVE DIAGNOSTIC APPROACHES



TRANSLATIONAL RESEARCH INITIATIVE:

GENOMICS

Overview

- Started: 2018
- In partnership with UTHSC Center for Cancer Research

Capabilities

- Nucleic acid extraction
- Library preparations
- Sequencing (exome & custom cancer panels)
- Robust Informatics platforms [LIMS, LORA (UT designed)]

Specimen registration

Specimen tracking

Computational analysis



Accomplishments

475 Custom cancer panels



THE UTHSC COVID-19 TEST:

RAPIDLY REPURPOSING A CANCER TRANSLATIONAL AND HISTOLOGY LABORATORY TO A HIGH THROUGHPUT MOLECULAR SARS-CoV-2 TESTING FACILTY TO MEET THE NEEDS OF THE COMMUNITY IN A DEADLY PANDEMIC

- **TIMELINE**: Project day: 40 (April 22):
- March 13: Executive decision to bring the test to UTHSC
- March 15: Initiated planning for data collection for an FDA EUA submission using a CDC based test format, and testing expansion in an existing CLIA high complexity laboratory and compatible with State of TN laboratory regulations
- March 13-27: Design test and perform test validation: Preanalytical, analytic and postanalytical systems developed.
- March 27: First sample collection for testing at UT collection site
- March 30: First clinical sample testing performed; FDA notified of test initiation

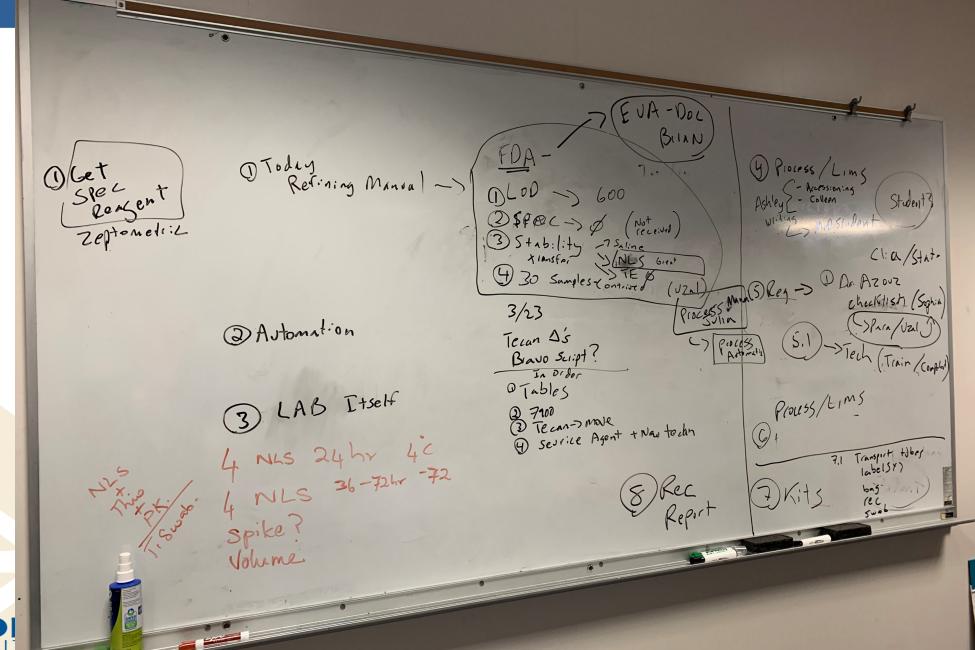










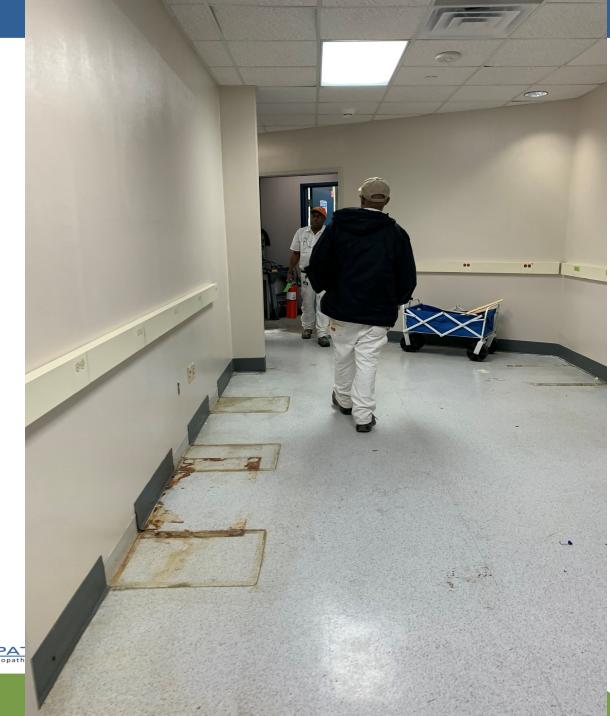


















WOMEN'S HEALTH





HEALTH















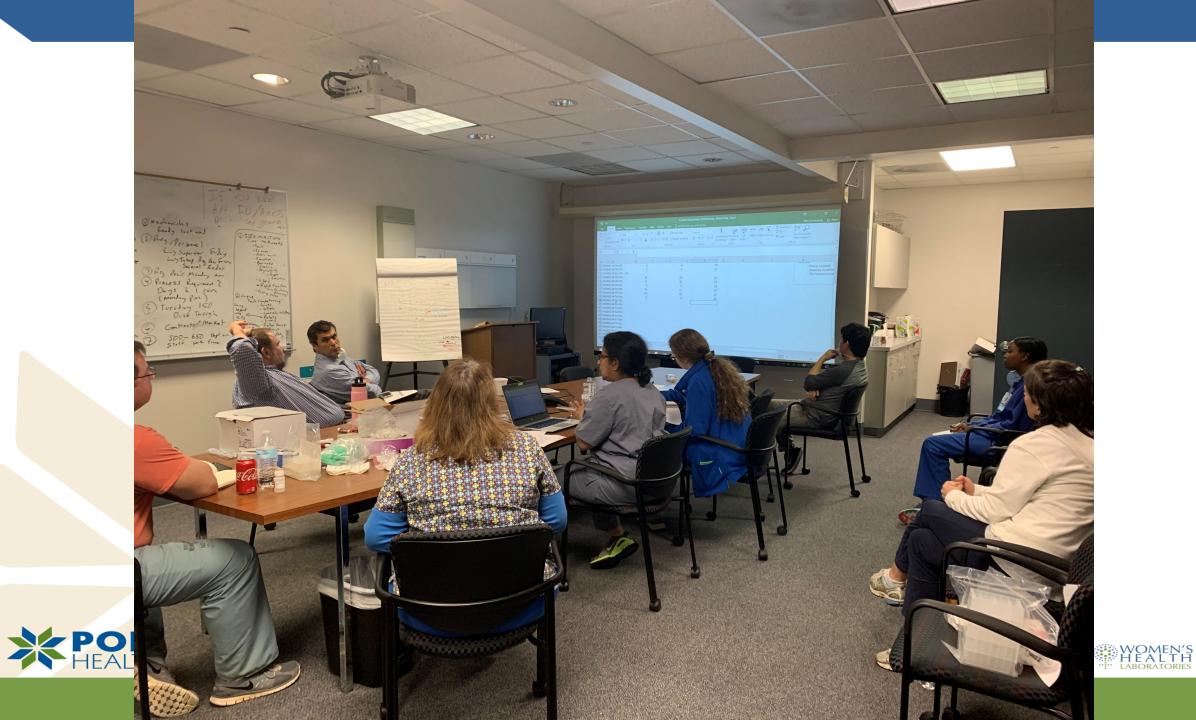














THE UTHSC COVID-19 TEST:

- Week of March 30th: Resulted our first CLINICAL tests (within 15 days of project initiation) and since April 1, UT Lab has performed all testing on samples collected at Liberty Bowl/Tiger
 Stadium UTHSC collection site.
- Week of April 9: Worked out experimental conditions, automation programming for the high throughput automation and more efficient processes
- Week of April 13: Began evaluation of automated testing in human specimens, logistics, compliance, regulatory, supply chain, training personnel and required mandated validation for a separate and unique EUA submission.
- Week of April 20: Develop and offer automation of up of 1000-1500 test

















































930 Madison Avenue, Suite 500 Memphis, TN 38103 901.866.8067 • Fax: 901.302.2067

Pathology Report

Patient Information Specimen Information Physician Information

Name: John Doe Address:

123 Main St Memphis, TN 38103

Phone: 901-555-1234 DOB: 7/4/1976 Gender: M Specimen ID: S000002-99999-000

Order#: 9876ZXY Collected: 4/6/2020 Received: 4/7/2020

Reported: 4/7/2020

Dr. David Schwartz

1407 Union Ave. STE 700 Memphis, TN 38104 (901) 209-9678

Ordered Items:

U697 - COVID 19 SARS-COV-2 LR *

Results:

U697 - COVID 19 SARS-COV-2 LR *

Not Detected

Comment:

*This test was developed and its performance characteristics determined by University of Tennessee Clinical Health and University of Tennessee Health Science Center. This test has not been FDA cleared or approved. This test has been authorized by FDA under an Emergency Use Authorization (EUA). This test has been validated in accordance with the FDA's Guidance Document (Policy for Diagnostics Testing in Laboratories Certified to Perform High Complexity Testing under CLIA prior to Emergency Use Authorization for Coronavirus Disease-2019 during the Public Health Emergency) issued on February 29th, 2020. FDA independent review of this validation is pending. This test is only authorized for the duration of time the declaration that circumstances exist justifying the authorization of the emergency use of in vitro diagnostic tests for detection of SARS-CoV-2 virus and/or diagnosis of COVID-19 infection under section 564 (b) (1) of the Act, 21 U.S.C. 360bbb-3 (b) (1), unless the authorization is terminated or revoked sooner.



930 Madison Avenue, Suite 500 Memphis, TN 38103 901.866.8067 • Fax: 901.302.2067

Pathology Report

Patient Information

Specimen Information

Physician Information

Name: John Doe Address:

123 Main St

Memphis, TN 38103 Phone: 901-555-1234

DOB: 7/4/1976 Gender: M

Specimen ID: S000002-99999-000

Order#: 9876ZXY Collected: 4/6/2020 Received: 4/7/2020

Reported: 4/7/2020

Dr. David Schwartz

1407 Union Ave. STE 700 Memphis, TN 38104 (901) 209-9678

Ordered Items:

U696 - COVID 19 SARS-COV-2 HR *

Results:

U696 - COVID 19 SARS-COV-2 HR *

DETECTED

Comment:

*This test was developed and its performance characteristics determined by University of Tennessee Clinical Health and University of Tennessee Health Science Center. This test has not been FDA cleared or approved. This test has been authorized by FDA under an Emergency Use Authorization (EUA). This test has been validated in accordance with the FDA's Guidance Document (Policy for Diagnostics Testing in Laboratories Certified to Perform High Complexity Testing under CLIA prior to Emergency Use Authorization for Coronavirus Disease-2019 during the Public Health Emergency) issued on February 29th, 2020. FDA independent review of this validation is pending. This test is only authorized for the duration of time the declaration that circumstances exist justifying the authorization of the emergency use of in vitro diagnostic tests for detection of SARS-CoV-2 virus and/or diagnosis of COVID-19 infection under section 564 (b) (1) of the Act, 21 U.S.C. 360bbb-3 (b) (1), unless the authorization is terminated or revoked sooner.



Complex testing and operational capability from ground zero in such a short timeframe: Perfect coming together and smart use of some key existing strengths

- <u>High throughput robotics</u> used for high throughput DNA sequencing of hundreds and thousands of genes is repurposed rapidly and validated for high throughput automated viral assay output of around 1000 tests per day.
- State of the art lab information management system (LIMS) for the cancer translational lab funded by
 Cancer Research Institute is used throughout the testing cycle from requisition to the many steps of testing
 and reporting.
- Research and Development (Scientific) team: The molecular translational lab team has several years' experience (prior to arrival here at UTSHC) developing and performing over 10,000 unique molecular high throughput assays (and 20M individual tests) have patents in the area.
- <u>UTHSC Regional Biocontainment Laboratory:</u> one of few in the state, we have had access to live CoV2 virus (handled in their BSL-3 research facility) and viral RNA for validation of tests and running appropriate













Complex testing and operational capability from ground zero in such a short timeframe: Perfect coming together and smart use of some key existing strengths

- <u>Clinical Deployment team:</u> Experienced lab leadership with decades of cumulative experience in test deployment, medical and scientific directorship of clinical labs, including microbiology and molecular labs.
- <u>Clinical, University and hospital partners:</u> UCH and UTHSC personnel, medical students, residents, research PhDs, Medical Laboratory Scientists from partner clinical laboratories.
- <u>Team commitment</u> with high clinical and academic standards with a can-do attitude and to do whatever it takes to make a difference in a global pandemic.















Overarching Value Summary

Unique UTHSC Lab Developed FDA, CLIA, and Tennessee compliant test performed using standardized CDC molecular targets, with high throughput capacity, likely greater sensitivity, 24 hours resulting, serving community and partner hospitals, with a comprehensive process that could impact public health and medical care decision-making for our city and paving the way for new research avenues, discovery and innovation.















2

3

DEVELOP SEROLOGIC TESTING 6

5

SEROLOGIC TESTING Invaluable complement to PCR testing for COVID19

- STRATEGICALLY: to offer full range of COVID19 lab testing at UTHSC
- Offer a UTHSC (scientists at UTHSC) developed novel serologic test
- Leverage the capabilities of our evolving and transformed clinical lab at 930 Madison building
- Clinically onboard commercially available test on existing platforms at partner hospitals of Regional One Health and MLH hospitals





PARTICIPATE IN
CORONAVIRUS
CONVALESCENT
PLASMA PROGRAM



ROLE IN CORONAVIRUS CONVALESCENT PLASMA PROGRAM CCP

- Use of convalescent plasma has been studied in other respiratory infections, such as the 2003 SARS-CoV-1, 2009 H1N1, and 2012 MERS-CoV epidemics & other serious epidemics such as Ebola
- UTSHC transfusion pathologists play at active role at Regional One Health and all MLH hospitals as a team identifying donors and matched convalescent plasma
- First two patients are ready for CCP this week

















ROLE IN CORONAVIRUS CONVALESCENT PLASMA PROGRAM

DONOR AWARNESS EFFORTS

- individuals who have previously tested positive
- You may help save a life of someone with symptomatic advanced coronavirus illness









2

3

4

5

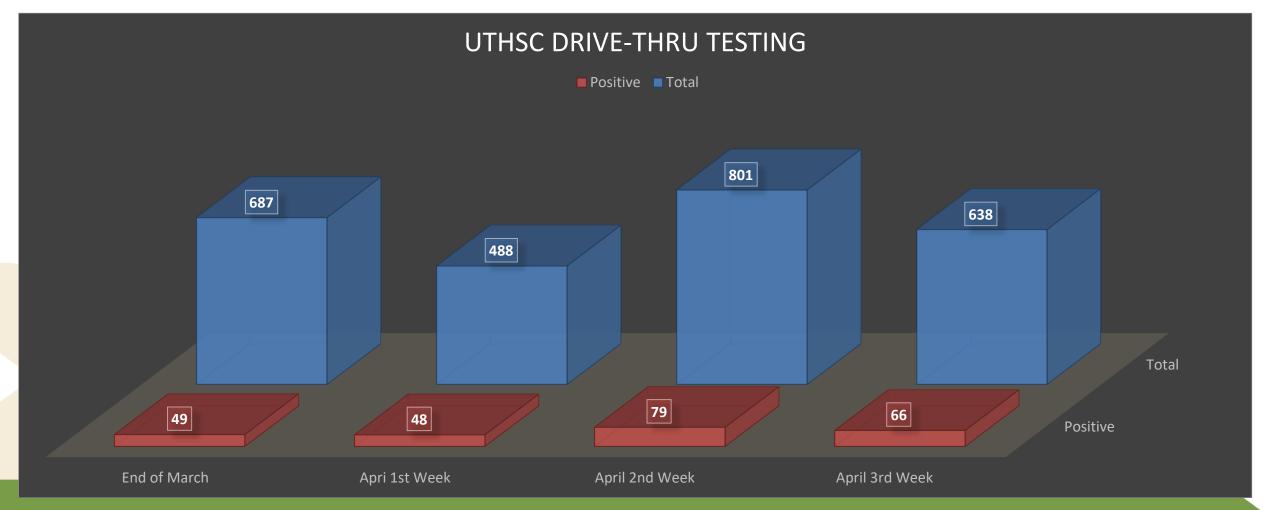
PUBLIC HEALTH REPORTING

&

FACILITATING PREDITICTION MODELS



State and County Health Department Reporting





CURRENT NUMBERS

- UTHSC Community Drive
 - Negative 1934
 - Positive 214
 - Presumptive Positive 186
 - Total 2334
 - Percent Positive 17.14%
- Cumulative:
 - Negative 8124
 - Positive 923
 - Presumptive Positive 216
 - Total 9263
 - Percent Positive 12.29%











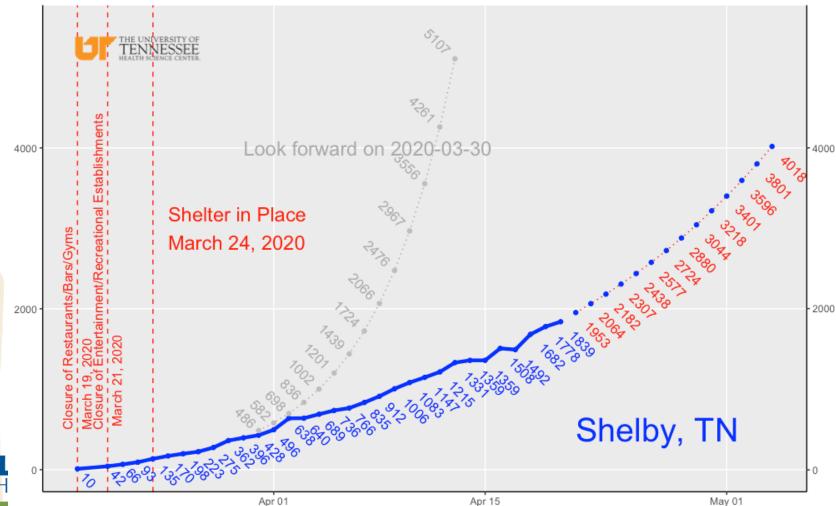


The number of days until no. of cases double is an essential measure of how fast the virus spreads

We were doubling numbers every 4 days, currently about every 12 days

Shelby County: COVID-19 confirmed cases

Short-term forecasts for Shelby County extrapolated from past 7 days

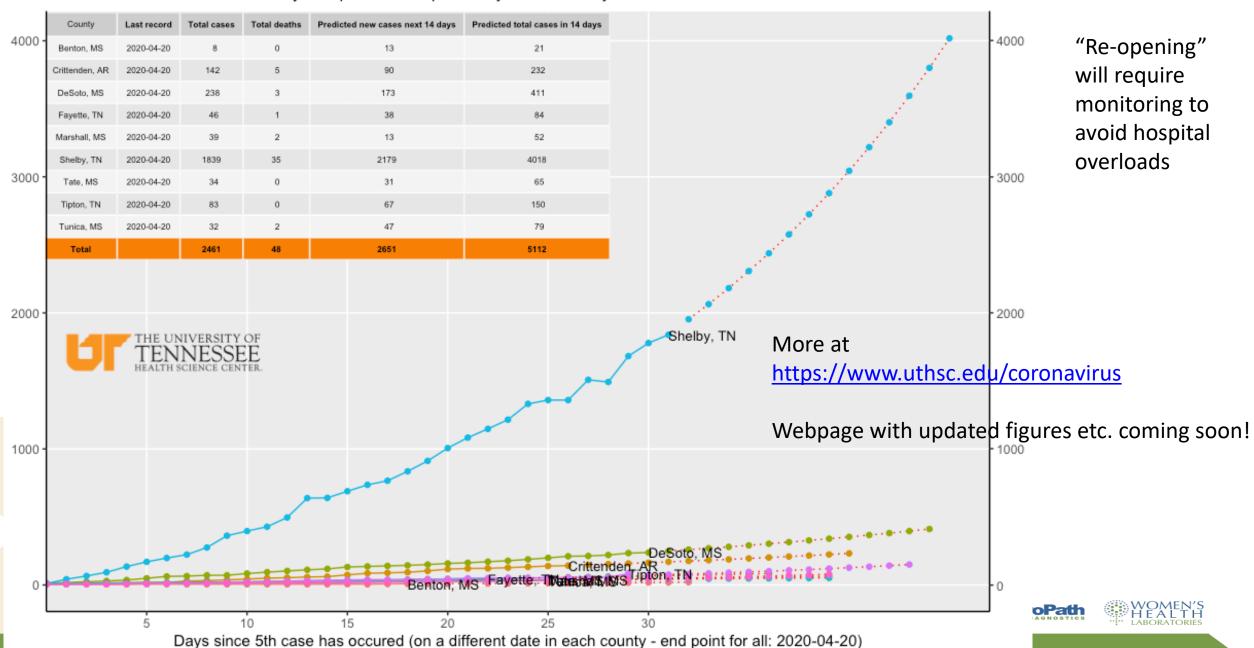






Memphis Metropolitan Area: COVID-19 confirmed cases trajectories by county

Short-term forecasts for each county extrapolated from past 7 days in that county



Source: Data from Johns Hopkins University (github; accessed Tue Apr 21 16:46:06 2020); UTHSC College of Medicine | Preventive Medicine | Biostatistics.



2

3

4

FACILITATE FUTURE RESEARCH

5



Enabling Research – IRB

• Leveraging Cancer Research Institute biobanking protocols and personnel, IRB compliant research protocols for genomic and other relevant research questions.









Summary:

- Unfortunate international pandemics, such as the current coronavirus infection, provide an accelerated opportunity for Pathology and Lab Medicine professionals and personnel to play a pivotal role in the care of those affected by the virus
- The role extends beyond diagnostic and clinical service needs: it should be ideally comprehensive and meets the needs of the medical community and the society we serve: such as we have humbly attempted to do.















THANK YOU

- Vice Chancellor Brown, Dean Strome, Dr. Jon McCullers
- Partners at UT, UTHSC, UCH, medical school and GME program
- Pathologists, PhDs and Lab personnel working round the clock on the effort
- Physicians, patients and community who inspire us to bring out the best in us.













Questions?

cls@uthsc.edu



Thank You!



