RUTGERS
School of Arts and Sciences

30 Days from Genetics to Coronavirus: A Strange Journey

Jay A. Tischfield, PhD, FFACMG, Duncan and Nancy MacMillan Distinguished Professor of Genetics, Pediatrics and Psychiatry; Director, Human Genetics Institute of NJ; CEO, RUCDR Infinite Biologics®

HGINJ

RUCDR INFINITE BIOLOGICS

SARS-CoV-2? Never heard if it (5 months ago)

- The Human Genetics Institute of New Jersey is a RU Research Institute on Busch campus in Piscataway

- Its members, all of whom are SAS faculty in the Division of Life Sciences, research diverse subjects ranging from cancer, kidney disease, fear, the evolution of limbs, genomics and neuropsychiatric disorders such as schizophrenia and Tourette disorder.
- RUCDR Infinite Biologics® is a Center within HGINJ

HGINJ

RUCDR INFINITE BIOLOGICS

But RUCDR is a highly automated and programmable genomics laboratory

RUCDR is a BIOBANKING world leader!!

RUCDR grant and contract research funding on the genetic bases of common diseases

NIMH National Institute of Mental Health

NIDA NATIONAL INSTITUTE ON DRUG ABUSE The Science of Drug Abuse & Addiction

NIAAA National Institute on Alcohol Abuse and Alcoholism of the National Institutes of Health

National Institute of Allergy and Infectious Diseases National Institutes of Health

NJCTS New Jersey Center for Tourette Syndrome and Associated Disorders, Inc.

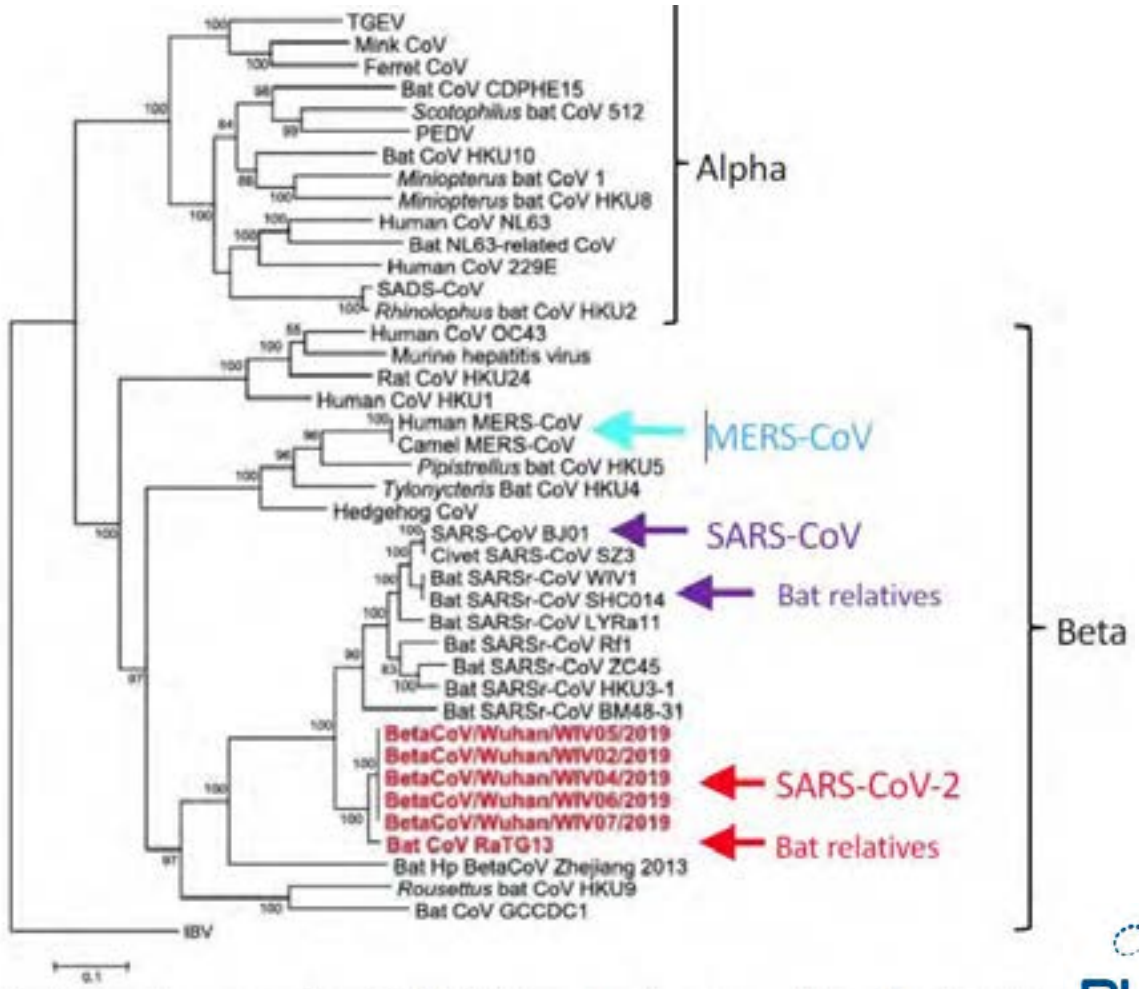
Pfizer

SFARI Simons Foundation Autism Research Initiative

MERCK

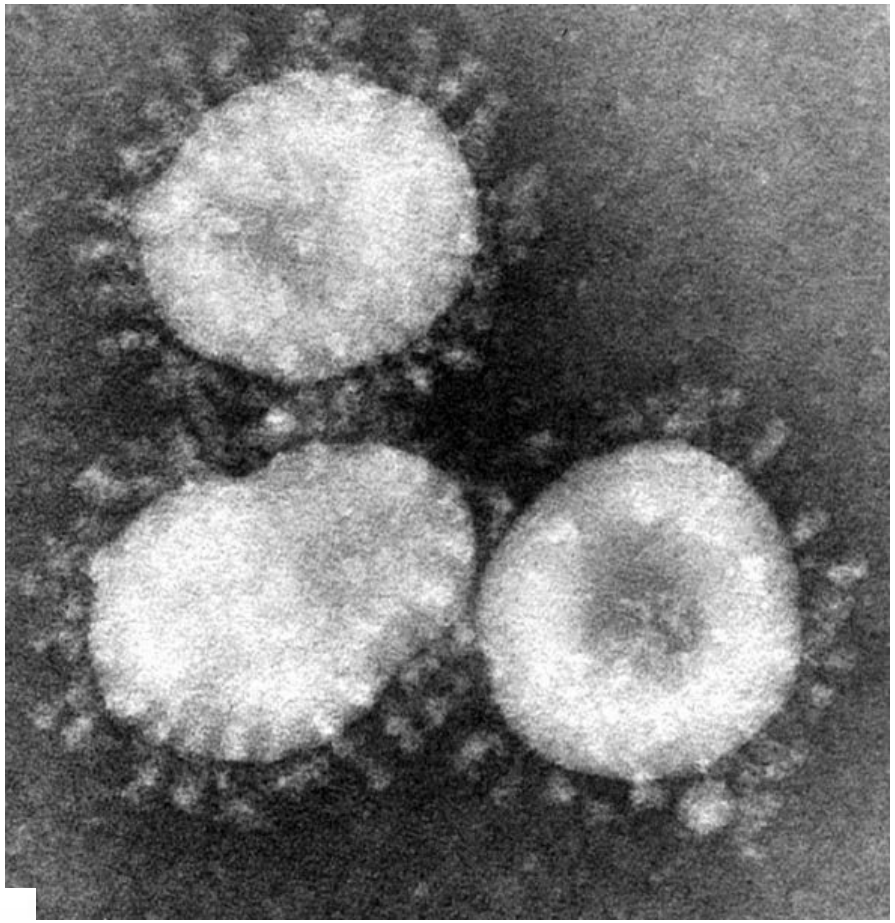
And then we learned about Coronaviruses

- Coronaviruses are positive-strand RNA viruses with large genomes (≥27,000 bases). SARS-CoV-2 is 29,811 bases
- Both alpha and beta types cause disease in humans, account for 10-30% of cases of the common cold (Pubmed 31971553).
- Very stable for RNA viruses – CoV OC43 isolates from 1960s and 2001 had only 2 amino acid changes (Pubmed 15280490)!
- Easily hops between species
  - MERS-CoV hopped from camels to humans
  - SARS-CoV hopped from bats to civets and humans
  - SARS-CoV-2 hopped from bats to humans
  - It seems humans with colds gave mice hepatitis, or vice versa

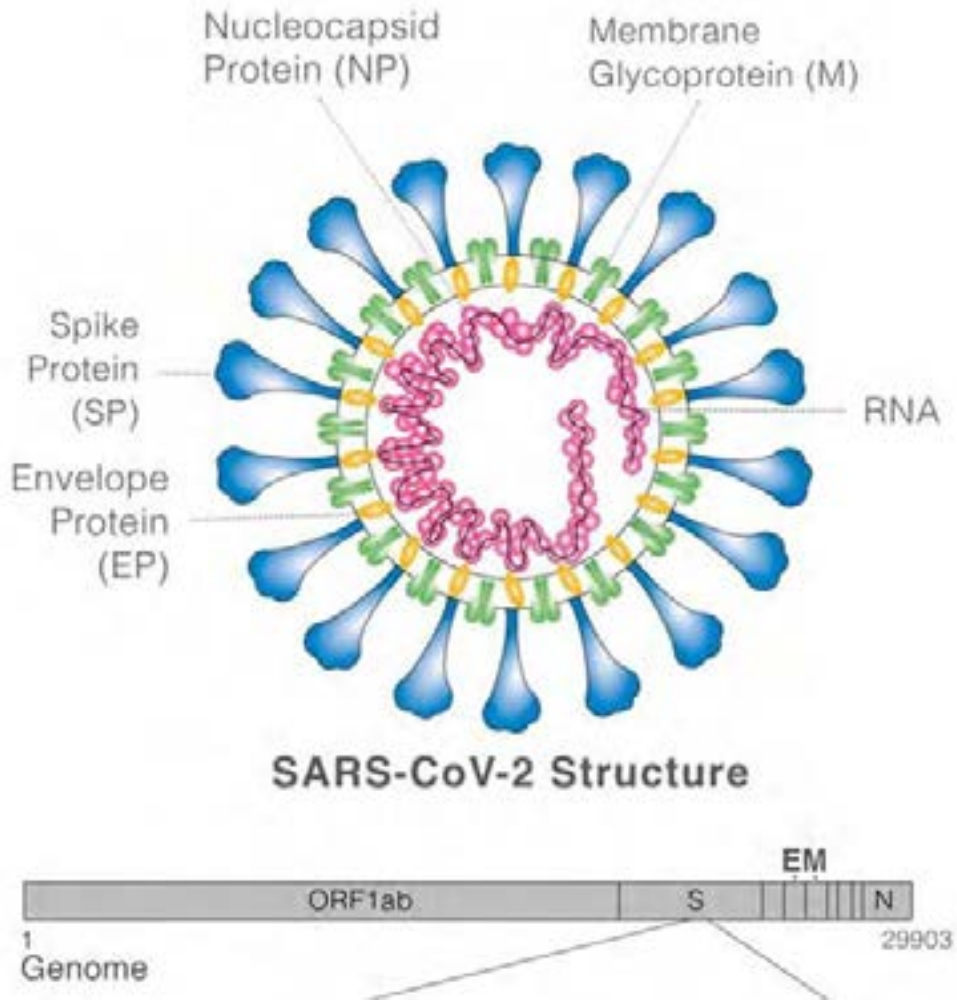


https://www.sciencemag.org/news/2020/01/mining-coronavirus-genomes-clues-outbreak-s-origins

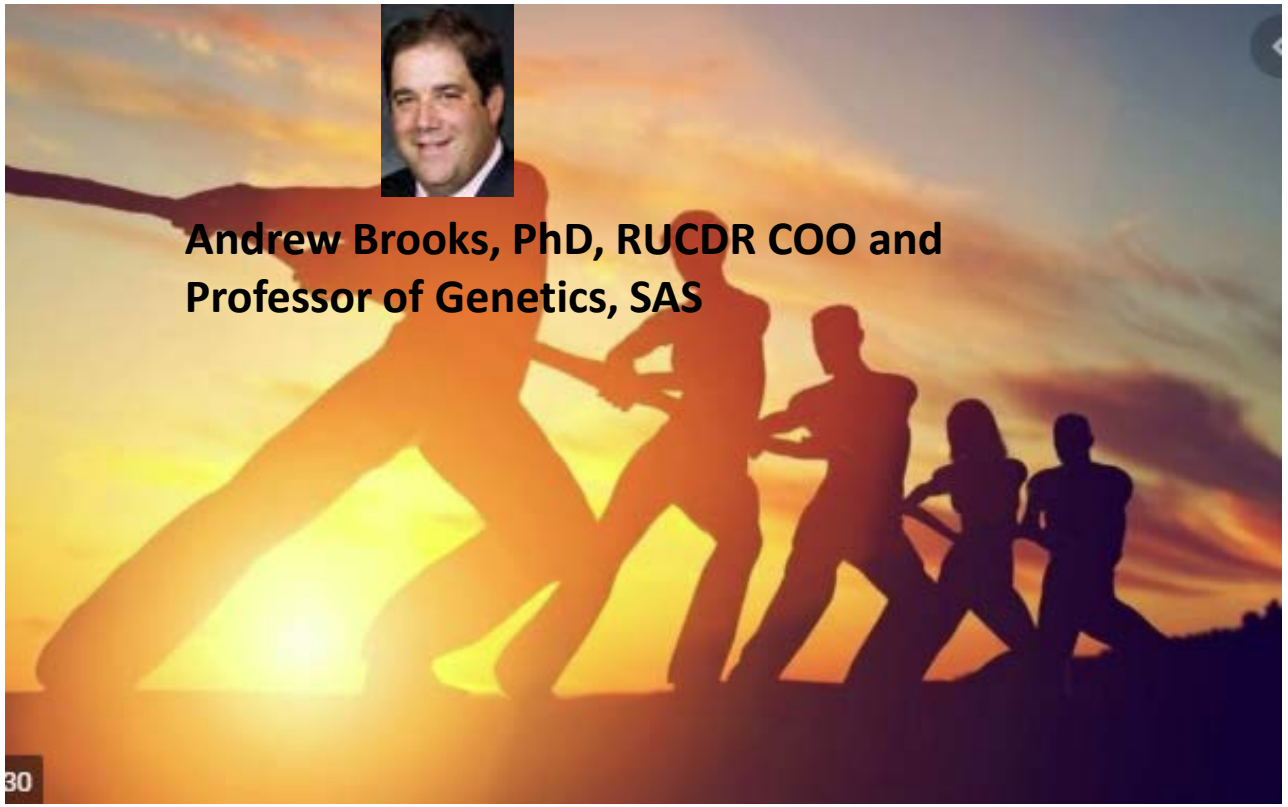
SARS-CoV-2 Coronavirus



Electron microscope image



Hard work & teamwork develop novel saliva test for SARS-CoV-2



Assay development started in March: EUA approved April 10, Home collection approved May 7, 2020

U.S. FOOD & DRUG ADMINISTRATION

April 10, 2020

Christian Bixby,
Assistant Director, Research and Clinical Lab Services, RUCDR
Rutgers Clinical Genomics Laboratory-Rutgers University
604 Allison Road,
Piscataway, NJ 08854 US

Re: EUA200090
Trade/Device Name: ThermoFisher - Applied Biosystems TaqPath COVID-19 Combo Kit
Laboratory: Rutgers Clinical Genomics Laboratory-Rutgers University
Dated: March 28, 2020
Received: March 30, 2020

Dear Christian Bixby:

This letter is in response to your request that the Food and Drug Administration (FDA) add your test as an authorized test to the March 31, 2020 Emergency Use Authorization (EUA), pursuant to Section 564 of the Federal Food, Drug, and Cosmetic Act (the Act) (21 U.S.C. §360bbb-3). We have reviewed the EUA submission package and determined that your test meets the criteria for issuance under section 564(c) of the Act because your test is eligible for authorization under the March 31, 2020 EUA for Molecular-based Laboratory Developed Tests for Detection of Nucleic Acid from SARS-CoV-2 (Molecular LDT COVID-19 Authorized Test). As such, your test is hereby added to Appendix A[1] as an authorized test.

Having concluded that the criteria for issuance of this authorization under Section 564(c) of the Act are met, I am adding this test to Appendix A as an authorized test, as described in the Scope of Authorization (Section II) and pursuant to the Conditions of Authorization (Section IV) of the attached letter of authorization[2] for use by the authorized laboratory to detect SARS-CoV-2 in specimens collected from individuals suspected of COVID-19 by their healthcare provider. Accordingly, in addition to this letter, you will receive copies of the FDA Letter of Authorization and the authorized Healthcare Provider and Patient Fact Sheets that must be used in conjunction with your authorized test pursuant to the Conditions of Authorization (Section IV) of the Letter of Authorization.

Sincerely yours,

Uwe Scharf, M.Sc., Ph.D.
Director, Division of Microbiology Devices
OHT7: Office of In Vitro Diagnostics and Radiological Health
Office of Product Evaluation and Quality
Center for Devices and Radiological Health

[1] Appendix A is available at: https://www.fda.gov/medical-devices/emergency-situations-medical-devices/emergency-use-authorizations
[2] The Letter of Authorization is available at: https://www.fda.gov/medical-devices/emergency-situations-medical-devices/emergency-use-authorizations

U.S. Food & Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993
www.fda.gov

ACCELERATED EMERGENCY USE AUTHORIZATION (EUA) SUMMARY
SARS-CoV-2 ASSAY
(Rutgers Clinical Genomics Laboratory)

For in vitro diagnostic use
Rx only
For use under Emergency Use Authorization (EUA) Only

(The Rutgers Clinical Genomics Laboratory TaqPath SARS-CoV-2 Assay will be performed in the Rutgers Clinical Genomics Laboratory, a Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a certified high-complexity laboratory, per the Instructions for Use that were reviewed by the FDA under this EUA).

INTENDED USE

The Rutgers Clinical Genomics Laboratory TaqPath SARS-CoV-2 Assay is intended for the qualitative detection of nucleic acid from SARS-CoV-2 in oropharyngeal (throat) swab, nasopharyngeal swab, anterior nasal swab, mid-turbinate nasal swab and saliva specimens from individuals suspected of COVID-19 by their healthcare provider. Testing is limited to Rutgers Clinical Genomics Laboratory (RCGL) at RUCDR Infinite Biologics – Rutgers University, Piscataway, NJ, that is a Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a certified high-complexity laboratory.

Results are for the detection and identification of SARS-CoV-2 RNA. The SARS-CoV-2 RNA is generally detectable in respiratory specimens during the acute phase of infection. Positive results are indicative of the presence of SARS-CoV-2 RNA; clinical correlation with patient history and other diagnostic information is necessary to determine patient infection status. Positive results do not rule out bacterial infection or co-infection with other viruses. The agent detected may not be the definite cause of disease. Laboratories within the United States and its territories are required to report all positive results to the appropriate public health authorities.

Negative results do not preclude SARS-CoV-2 infection and should not be used as the sole basis for patient management decisions. Negative results must be combined with clinical observations, patient history, and epidemiological information.

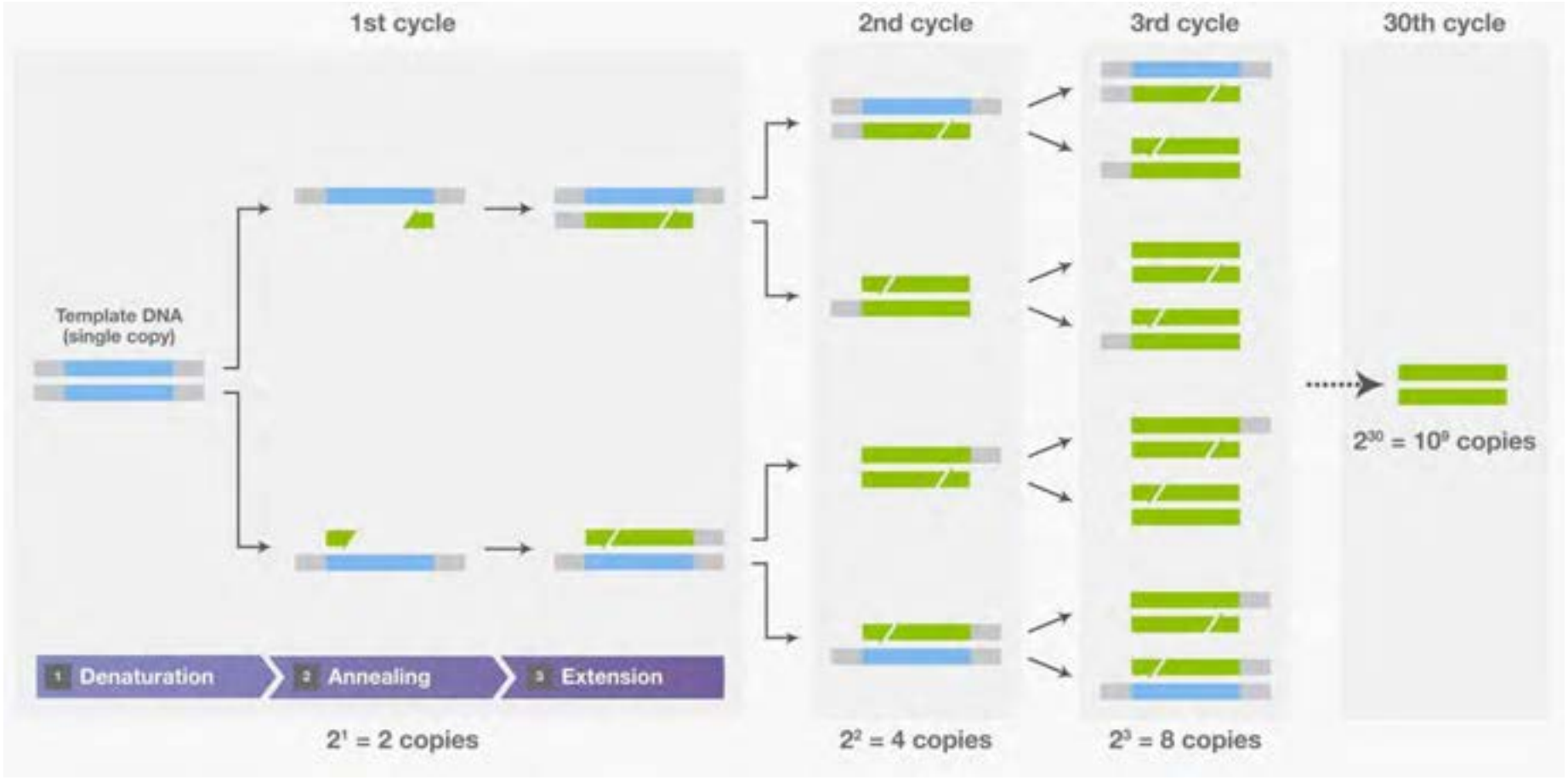

Foundation News
FDA Approves First At-Home Saliva Collection Test for Coronavirus

How to use the saliva collection kit

SARS-CoV-2 (COVID-19) diagnostic assay

- **1.** Extract viral RNA from saliva (Chemagic bead method) - 96 samples
  - Afterwards, robots move extracted samples to 384 well format
- **2.** Reverse transcribe RNA into (stable) DNA
- **3.** Add short DNA probes (oligonucleotide) and perform real time quantitative PCR (polymerase chain reaction)
  - The assay targets three specific genomic regions of the SARS-CoV-2 nucleocapsid (N) gene, spike (S) gene, and ORF1ab region.
- **4.** Determine number of cycles (Ct value) for detection (or not)
  - A sample is considered positive for SARS-CoV-2 RNA if amplification is detected with at least two of the three SARS-CoV-2-specific target sequences.

PCR Basics

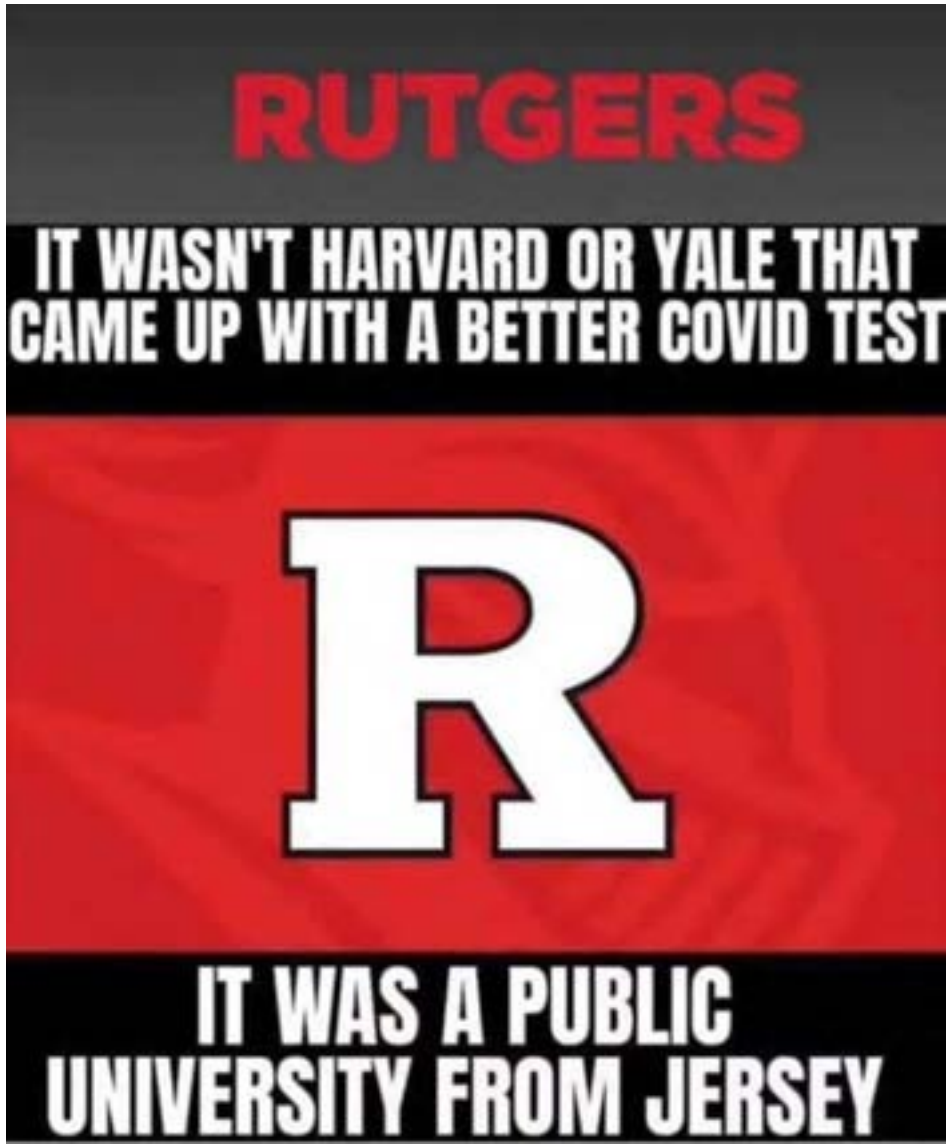

1st cycle
2nd cycle
3rd cycle
30th cycle
Template DNA
(single copy)
1 Denaturation
2 Annealing
3 Extension
2^1 = 2 copies
2^2 = 4 copies
2^3 = 8 copies
$2^{30} = 10^9$ copies

Advantages of the saliva test

- Sensitivity
- Home Collection
  - With or without telemedicine assistance
  - Does not require patient travel & potential exposure of others
- Huge reduction in risk to medical personnel
  - No virus exposure of healthcare workers if done at home
  - Obviates the need for PPE, a limiting resource
  - Requires far fewer healthcare workers
- Large numbers of tests can be done on any day
  - Testing lab capacity becomes the main issue

Caveats

- **1.** Test must be prescribed by a healthcare provider
- **2.** Healthcare provider must suspect COVID-19: Generally means patient must present with symptoms
- Interpretation: No test, including RUCDR test, is currently authorized for population screening of well individuals.


RUTGERS
IT WASN'T HARVARD OR YALE THAT CAME UP WITH A BETTER COVID TEST
R
IT WAS A PUBLIC UNIVERSITY FROM JERSEY