Update: COVID-19 Serology and Immunology Capacity Building

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Principal Deputy Director

2nd Virtual Meeting of the National Cancer Advisory Board and the Board of Scientific Advisors

June 15, 2020

Topics for today

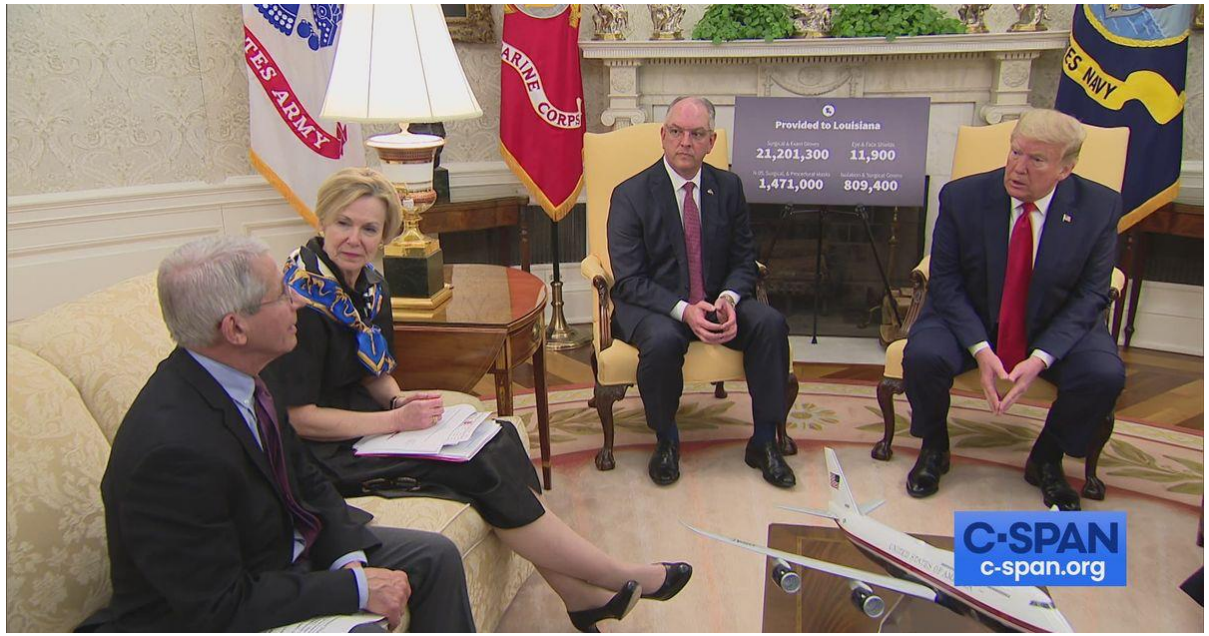
- Use of FNLCR by NIAID to respond rapidly to epidemics
- Use of FNLCR expertise in serology as an NCI response to COVID-19 epidemic
- Proposed Serological Sciences Network for SARS-CoV-2

NCI and NIAID are the major users of FNLCR

- **NIAID has made extensive use of FNLCR in responding rapidly to other epidemics:** Examples include SARS (2003), Ebola (2013), Zika (2015)
- **One example from current SARS-CoV-2 epidemic:** Developing a global therapeutic trial of **Remdesivir** in COVID-19 patients
  - A nucleoside analog, functions as an RNA chain terminator
  - Originally developed for treatment of Ebola and Marburg virus infections
  - Subsequently found to inhibit replication of other RNA viruses, including coronaviruses

Adaptive Coronavirus Treatment Trial (ACCT): Hospitalized COVID-19 patients on Remdesivir treatment improved faster than those on placebo

The White House



April 29, 2020

The NEW ENGLAND JOURNAL of MEDICINE

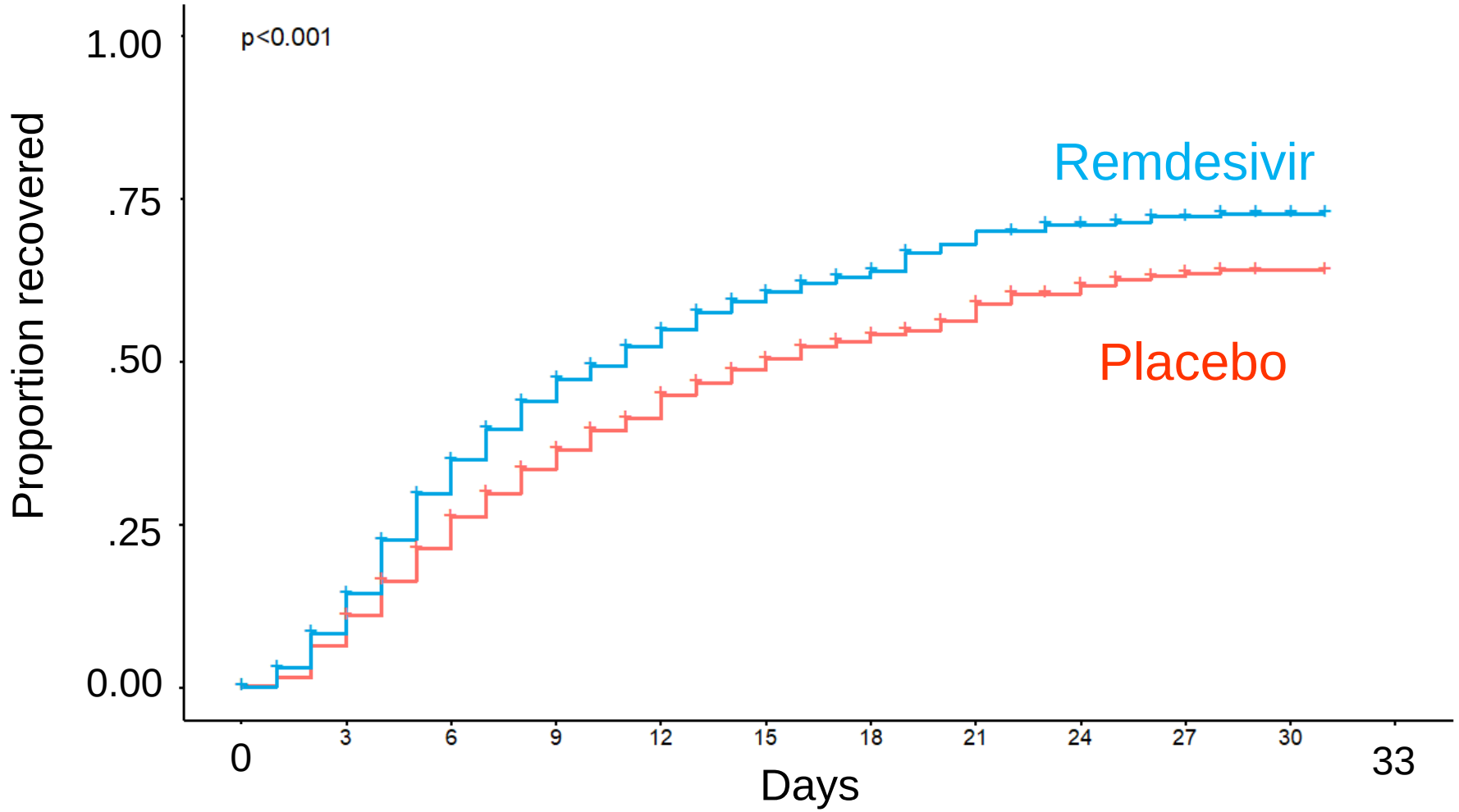
ORIGINAL ARTICLE

Remdesivir for the Treatment of Covid-19 — Preliminary Report

J.H. Beigel, K.M. Tomashek, L.E. Dodd, A.K. Mehta, B.S. Zingman, A.C. Kalil, E. Hohmann, H.Y. Chu, A. Luetkemeyer, S. Kline, D. Lopez de Castilla, R.W. Finberg, K. Dierberg, V. Tapson, L. Hsieh, T.F. Patterson, R. Paredes, D.A. Sweeney, W.R. Short, G. Touloumi, D.C. Lye, N. Ohmagari, M. Oh, G.M. Ruiz-Palacios, T. Benfield, G. Fätkenheuer, M.G. Kortepeter, R.L. Atmar, C.B. Creech, J. Lundgren, A.G. Babiker, S. Pett, J.D. Neaton, T.H. Burgess, T. Bonnett, M. Green, M. Makowski, A. Osinusi, S. Nayak, and H.C. Lane, for the ACTT-1 Study Group Members*

May 22, 2020

Hospitalized COVID-19 patients on Remdesivir treatment were discharged 31% faster than patients on placebo



Beigel et al, NEJM 2020

Lower 14-Day mortality rate for Remdesivir group than placebo group, but difference did not achieve statistical significance (p=0.059)

Treatment Group (Number Enrolled)	Deaths	%	Hazard Ratio	
			Estimate	95% CI
Remdesivir (538)	**32**	**7.1%**	**0.70**	**(0.47, 1.04)**
Placebo (521)	**54**	**11.9%**		

% is from the Kaplan-Meier estimate

28-day mortality data still being collected

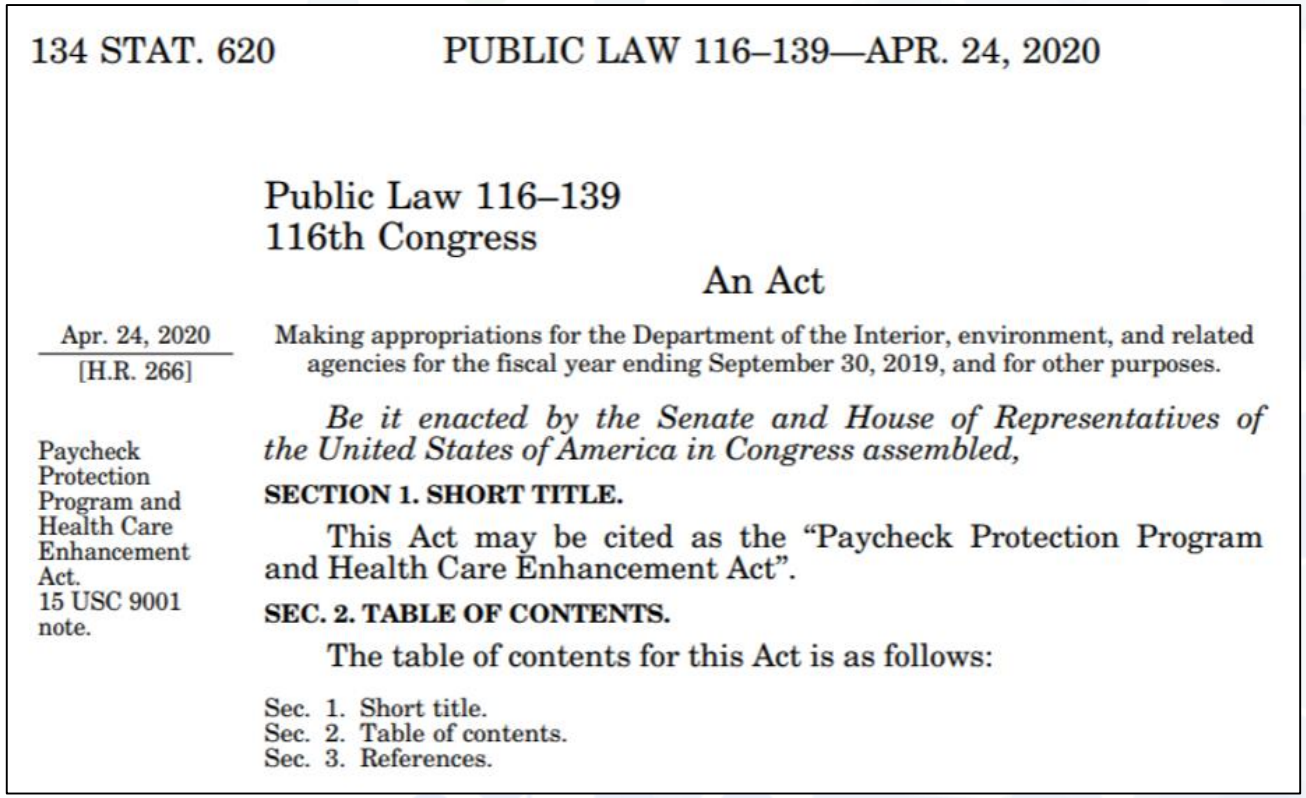
Beigel et al, NEJM 2020

"No one wants to have COVID-19, but everyone wants to have had it."

Maura Judkis
Washington Post
May 7

NCI supplemental funding from Congress

- Enacted April 24th
- $306M for NCI to **develop**, **validate**, **improve**, and **implement** serological testing and associated technologies
- COVID-19 focused and *distinct* from annual appropriation



134 STAT. 620 PUBLIC LAW 116–139—APR. 24, 2020

Public Law 116–139
116th Congress

An Act

Apr. 24, 2020
[H.R. 266]

Making appropriations for the Department of the Interior, environment, and related agencies for the fiscal year ending September 30, 2019, and for other purposes.

Be it enacted by the Senate and House of Representatives of the United States of America in Congress assembled,

Paycheck Protection Program and Health Care Enhancement Act.
15 USC 9001 note.

SECTION 1. SHORT TITLE.

This Act may be cited as the "Paycheck Protection Program and Health Care Enhancement Act".

SEC. 2. TABLE OF CONTENTS.

The table of contents for this Act is as follows:

Sec. 1. Short title.
Sec. 2. Table of contents.
Sec. 3. References.

Convert part of HPV serology lab to SARS-CoV-2 serology

A collaborative research effort with several groups: NIAID, FDA, CDC, BARDA, Mt. Sinai, others

Shorter term goals

1. Characterize performance of different serologic assays, correlate with neutralization assays, understand possible cross-reacting sera from prior to epidemic;
2. correlations with serologic tests submitted to FDA

Longer term goals

Understand implications of being seropositive (e.g., resistance to reinfection), duration of seropositivity

Cohort oriented research projects: COVID-19 longitudinal trial of cancer patients, others

FDA and commercial SARS-CoV-2 serology devices

- **March 16:** FDA permits sale of commercial laboratory-based and rapid lateral flow SARS-CoV-2 serology devices without its own assessment of their performance
  - Serology devices are not used to diagnose current infection; devices that measure viral RNA or viral protein are used to to diagnose current infection
- **May 4:** Emergency use authorization (EUA) by FDA given to several commercial devices; FDA requires all other manufacturers to submit EUA requests within 10 business days
- **June 4:** FDA gives EUA for several additional devices

Summary of initial 40 commercial serology devices evaluated by FNLCR serology laboratory

- **Focus on IgG antibody tests;** IgM becomes positive at about the same time as IgG and decreases faster than IgG
- **Sensitivity** (detect true positives): Varied from 30% to 100%
- **Specificity** (does not detect false-positives): Varied from 87% to 100%
- **Results sent to FDA;** to help FDA determine suitability for EUA; FDA has made some of the NCI evaluation results publicly available, others to be released in near future
- In near future, only devices with high sensitivity and high specificity should be available

Importance of specificity at low rates of seroprevalence

- If a test has 99% specificity and the seroprevalence rate is found to be 5%,
  - **20% of the positives will be false-positives**

- If a test has 95% specificity and the seroprevalence rate is found to be 5%,
  - **50% of the positives will be false-positives**

Seropositivity: characteristics and questions

- Being antibody-positive means either the person is currently infected with SARS-CoV-2 or has been previously infected
- Can be used now for seroprevalence studies; should identify most people who had asymptomatic or symptomatic infection (a small minority may remain antibody-negative)
- **It is not currently known: 1) whether being antibody-positive is associated with protection against reinfection; 2) what antibody levels may be associated with protection; 3) how long protection and antibody levels will last**
  - **Antibody titers are likely to become important**
- For candidate polyclonal antibodies from convalescent sera and neutralizing monoclonal antibodies: will they reduce the risk of serious disease?
- For candidate SARS-CoV-2 vaccines, will induction of neutralizing antibodies confer protection?

Thanks to

- **Ligia Pinto, Troy Kemp, Jim Cherry: NCI Frederick Serology lab**
- Cristina Cassetti, Hilary Marston, Maureen Beanan, Barney Graham, Kizzmekia Corbett: NIAID
- Michele Owen, Natalie Thornburg: CDC
- Rosemary Humes: BARDA
- Steve Gitterman, Brendan O’Leary, Jeet Guram: FDA
- Florian Krammer, Carlos Cordon-Carlo: Mt. Sinai Medical Center
- Mike Busch: Vitalant

COVID-19 SeroTracker: Data Resource for Strategic Assessment

Serology Data Warehouse

to collect and manage COVID-19 serology test results; to serve as a research resource to the NCI/NIAID/CDC and the broader research community

Serology Tracking Dashboard

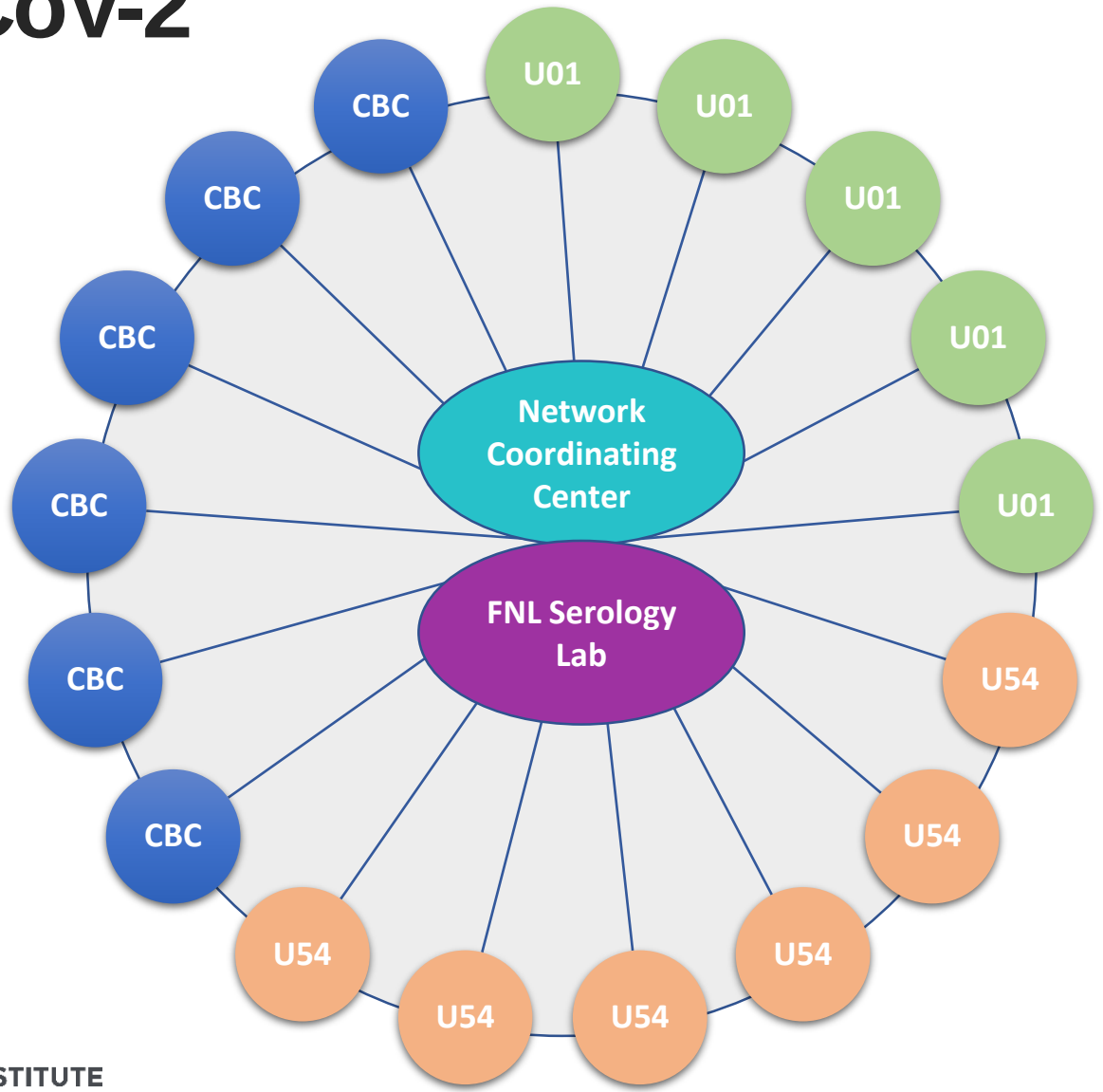
To display: 1) Summary of global serology studies, assay types, and results generated; and 2) SARS-CoV-2 antibody prevalence in the US with ability to filter results by geography and demographics

- **Requirements are currently being developed by experts from NCI/NIAID/CDC**

- Aim to have prototype in two stages:

1. Summary Dashboard this Summer
2. Larger Prototype this Fall

Proposed Serological Sciences Network for SARS-CoV-2

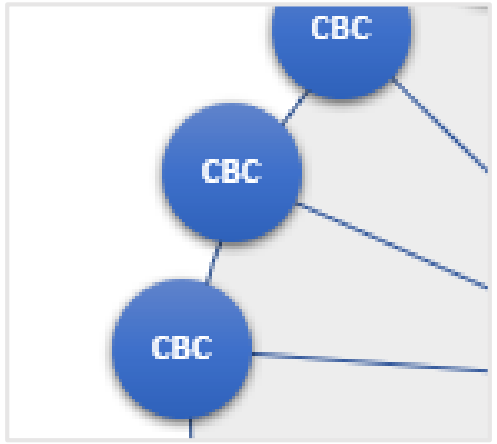


4-8 CBCs: Serological Sciences **Capacity Building Centers** (RFP)

4-8 U54s: Serological Sciences **Centers of Excellence** (RFA)

5-10 U01s: Serological sciences projects (RFA)

Serological Sciences Capacity Building Centers



RFP (due July 22)

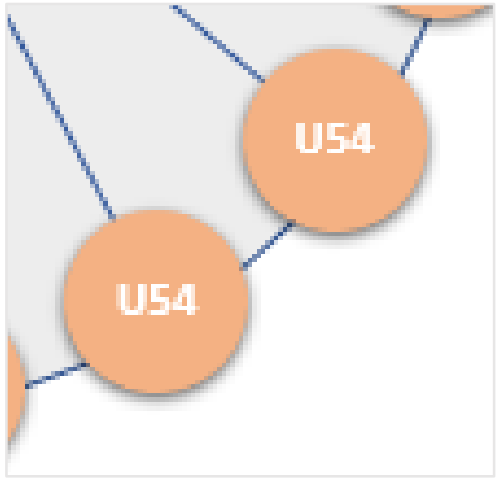
4-8 contracts with academic and/or private sector through FNLCR

Up to $3M total costs per year, per site

Goals

- Develop and expand serological testing capacity and practice in the community
  - Implementation of serological standardization, assay development and availability of FDA-EUA authorized SARS-CoV-2 testing to identify those who may have been exposed to the virus.
  - Scale up acquired serological testing to provide increased national capacity by screening at least 10,000 patients per week with FDA-EUA authorized assays
- Acquire convalescent sera from recovered COVID-19 patients who are seropositive and conduct surveillance clinical trials in patients who have recovered from COVID-19 and are seropositive
- Pursue focused serological science

Serological Sciences Centers of Excellence (RFA)



4-8 U54 awards (due July 22)

Up to $1.5M total costs per year for up to 5 years

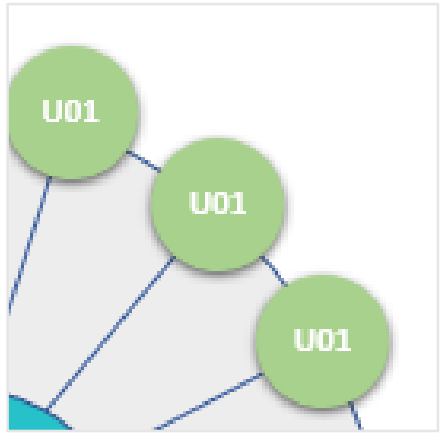
Goals

- Understand the mechanisms driving the serological, humoral and cellular immune responses to SARS-CoV-2 viral infection to inform the development of novel serological tests
- Determine the serological correlates with disease pathogenesis and protection against future infection
- Improve population-based models of outbreak and susceptibility through serology-focused studies
- Preference for cancer relevant component

Each Center will have 2-3 projects, administrative core and the possibility of technical core

Budget set-aside for collaborative projects proposed post-award

Serological sciences projects (RFA)



5-10 U01 awards (due July 22)

Up to $500K direct costs per year, up to 5 years

Goals

- Understand the mechanisms driving the serological, humoral and cellular immune responses to SARS-CoV-2 viral infection to inform the development of novel serological tests
- Determine the serological correlates with disease pathogenesis and protection against future infection
- Improve population-based models of outbreak and susceptibility through serology-focused studies
- Preference for cancer relevant component

Budget set-aside for collaborative projects proposed post-award

Network Coordinating Center at Frederick National Lab

FNLCR Task Order

$750K total costs per year

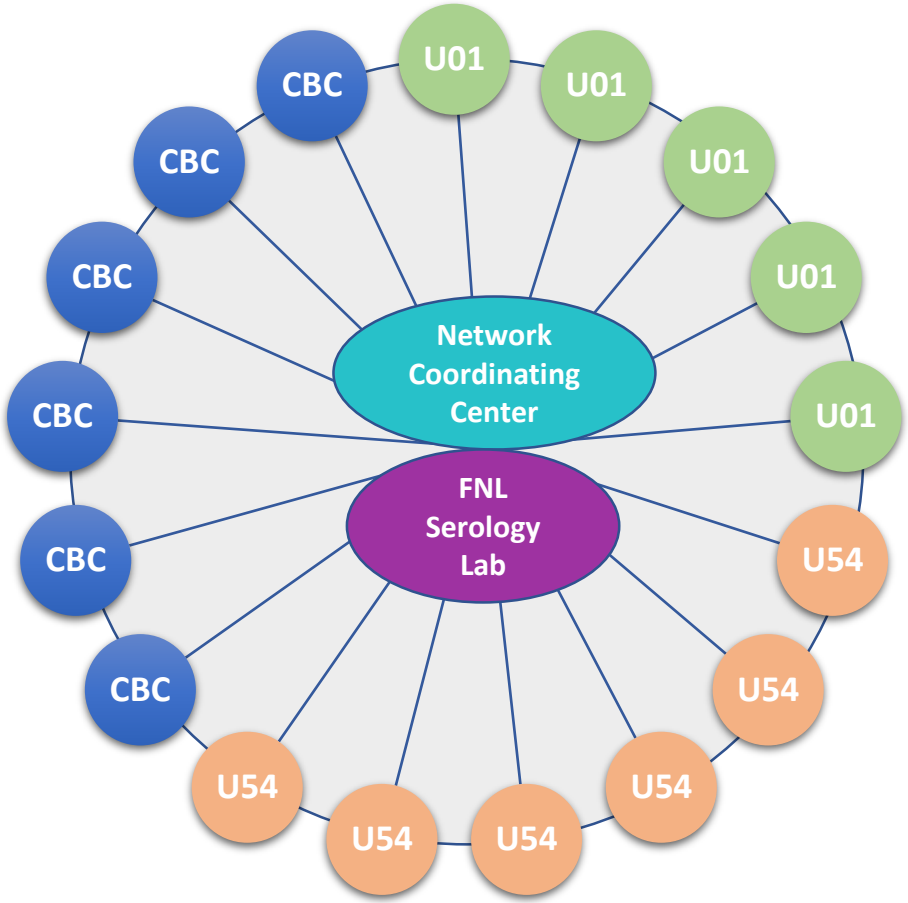
Goals

- Provide program management, coordination and communication across the Serological Sciences Network for SARS-CoV-2
- Coordinate sharing of the data, reagent, sample, and assays
- Coordinate comparison of results among different centers and assays through inter-Center collaborative studies, leading to international serology standardization
- Coordinate partnerships with national and international associates such as the FDA, CDC, WHO, National Institute for Biological Standards and Control (NIBSC), and others
- Work in close collaboration with NCI program staff

Request for Information:
Strategy for Research in Coronavirus Serology Testing and Serological Sciences

- To seek input from research community on scope of Serological Sciences Network
- RFI closed May 26
- Some responses are being incorporated into the scope of the Network

The Serological Sciences Network



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