Update: COVID-19 Serology and Immunology Capacity Building

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

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

The New England Journal of Medicine

Remdesivir for the Treatment of Covid-19 — Preliminary Report


April 29, 2020

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)

<table>
<thead>
<tr>
<th>Treatment Group (Number Enrolled)</th>
<th>Deaths</th>
<th>%</th>
<th>Hazard Ratio Estimate</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Remdesivir (538)</td>
<td>32</td>
<td>7.1%</td>
<td>0.70</td>
<td>(0.47, 1.04)</td>
</tr>
<tr>
<td>Placebo (521)</td>
<td>54</td>
<td>11.9%</td>
<td></td>
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</tbody>
</table>

% 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
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 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
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• 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

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

RFP (due July 22)

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

Up to $3M total costs per year, per site
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
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Budget set-aside for collaborative projects proposed post-award
Network Coordinating Center at Frederick National Lab

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

With Special Thanks to:

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