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1. What is SARS-CoV-2 and how is it different from other coronaviruses?

2. What is COVID-19 and what is unexpected in it?

3. How is our immune response dealing with this virus in adult and older populations (including duration of immunity)?

4. What is the basis of potential immune vulnerability in older adults? How will it relate to protection by vaccination?
Selecting antigenic targets for SARS-CoV-2 serological assays

What is new in this virus?

- S RBD mutated, binds better to hACE2
- Persists and spreads better than SARS-1 or MERS
- Sheds from the infected person 2-3 days before symptoms
- Respiratory; always difficult to contain
- Asymptomatic spread (?)
**SARS-CoV-2**

- Severe acute respiratory syndrome coronavirus 2 (SARS-Cov2)
- Coronaviridae family
- Coronavirus disease 19 (COVID-19)
  - Fever
  - Cough
  - Fatigue
  - Shortness of breath; ARDS; cytokine storm

**Pronounced vulnerability in older adults:**

- Ages 45-54 have 3x higher mortality than those 21-45;
- Mortality goes up to 10-fold in those 55-64,
- Mortality culminates at 50-fold in those >65 years relative to adults 21-45 years old.

Arizona Department of Health COVID Dashboard
New T cell production diminishes early (puberty). Peripheral maintenance takes over, but fails by the last third of life, with naïve T (Tn) cells reduced to 20-40% of youthful numbers in mice and men......
NEW IMMUNE RESPONSES CRITICALLY DEPEND ON ACTIVATION OF NAÏVE T CELLS

- Upon infection, immature tissue DCs take up Ag from tissues, begin maturation and migrate into peripheral lymph nodes (LN).
- This is where they are scanned by thousands naïve T cells; the ones that can bind antigen on DC will get activated.
Mounting an immune response
CUMULATIVE PROBLEMS WITH AGING
Late February/Early March 2020:

- Can we detect immunity to this virus?
- What parts of the virus are targeted by the immune system (immunodominance, immune protection vs immune evasion)?
- What is the duration of immunity?
- Is there an immunological base to vulnerability to SARS-CoV2 (older adults primarily)?
March 28, 2020—The Beginning of it All

The Beginning of it All

HEALTH

UA researchers working on tests to detect COVID-19 antibodies in people without symptoms

Amanda Morris  Arizona Republic
Published 6:00 a.m. MT Mar. 28, 2020 | Updated 1:38 p.m. MT Apr. 1, 2020

Because of limited resources and time, Nikolich said the UA’s antibody testing will not be used to conduct widespread testing of the population to figure out who has and hasn't had the virus already. Instead, they will be coordinating with health care providers to select the best patients to test in order to have good data to analyze.
April 14, 2020—Wait, what?

Ducey says UofA will produce 250K tests for COVID-19 antibody

By Jeremy Duda  April 14, 2020
Last Updated: April 14, 2020 9:48 pm
Highly accurate ELISA test for SARS CoV-2 exposure developed at University of Arizona

- Total Ig assay (A+G+M)
- False positives: <1/6000
- False negatives: ~5%
- FDA EUA filed 4/27/20; approved August, 2020
- PPV 100%, NPV 99%

- 20,102 healthcare workers, first responders, general public, and students tested by July 29, 2020
- Overall seroprevalence: 1.5%
- Student seroprevalence: 2.7%
- Seroprevalence May-mid-June ~1%; after mid-June >3%.
Coronavirus herd immunity may be 'unachievable' after study suggests antibodies disappear after weeks in some people

Immunity to Covid-19 could be lost in months, UK study suggests

Exclusive: King’s College London team found steep drops in patients’ antibody levels three months after infection

Coronavirus - latest updates
See all our coronavirus coverage

Ian Sample Science editor
Sun 12 Jul 2020 12:31 EDT
Duration of antibody production varies widely depending on the infection or vaccine

<table>
<thead>
<tr>
<th>Antigen</th>
<th>Protective Titer</th>
<th>Subjects Protected</th>
<th>Total Population</th>
<th>Antibody Half-Life:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>IU/ml no. (%)</td>
<td></td>
<td>year (95 percent confidence interval)</td>
<td>§</td>
</tr>
<tr>
<td>Tetanus</td>
<td>0.01 42 (93)</td>
<td>11 (10–14)</td>
<td>12 (10–16)</td>
<td>0.23</td>
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<tr>
<td>Diphtheria</td>
<td>0.01 40 (89)</td>
<td>19 (14–33)</td>
<td>26 (17–51)</td>
<td>0.11</td>
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<tr>
<td>VZV</td>
<td>NA NA</td>
<td>50 (30–153)</td>
<td>63 (28–∞)</td>
<td>0.51</td>
</tr>
<tr>
<td>Vaccinia</td>
<td>3.8 28 (62)</td>
<td>92 (46–∞)</td>
<td>99 (48–∞)</td>
<td>0.91</td>
</tr>
<tr>
<td>Rubella</td>
<td>10.0 39 (87)</td>
<td>114 (48–∞)</td>
<td>85 (43–∞)</td>
<td>0.60</td>
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<tr>
<td>EBV</td>
<td>NA NA</td>
<td>11,552 (63–∞)</td>
<td>No decay (84–∞)</td>
<td>0.99</td>
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<tr>
<td>Mumps</td>
<td>NA NA</td>
<td>542 (90–∞)</td>
<td>124 (53–∞)</td>
<td>0.16</td>
</tr>
<tr>
<td>Measles</td>
<td>0.2 41 (91)</td>
<td>3014 (104–∞)</td>
<td>369 (67–∞)</td>
<td>0.56</td>
</tr>
</tbody>
</table>

*Ammana et al., NEJM, 2007*
Antibody production decays in a non-linear pattern after acute infections

Baumgarth et al., JI, 2020
Stable $\alpha$-Spike and neutralizing antibody titers over time following mild SARS-CoV-2 infections

Ripperger, Uhrlaub, Watanabe, Wong et al., Immunity, 2020
Confirmed lymphopenia in severe COVID-19 cases

SQL and Hemavet combined data. Neutrophil counts mostly zero on our hemavet *
Preliminary conclusions

• Correlations between immunity and disease severity in the literature appear stronger than those with age, but studies well-controlled for age still rare

• Interpretation confounded by unknown viral loads (how much virus did you get initially and how well you are controlling it)

• Severe remodeling of immune cells in blood is found with severe diseases

• Signatures of innate and adaptive cell transcriptomes starting to provide initial clues

• Tons of things to do .............