COVID-19 Updates

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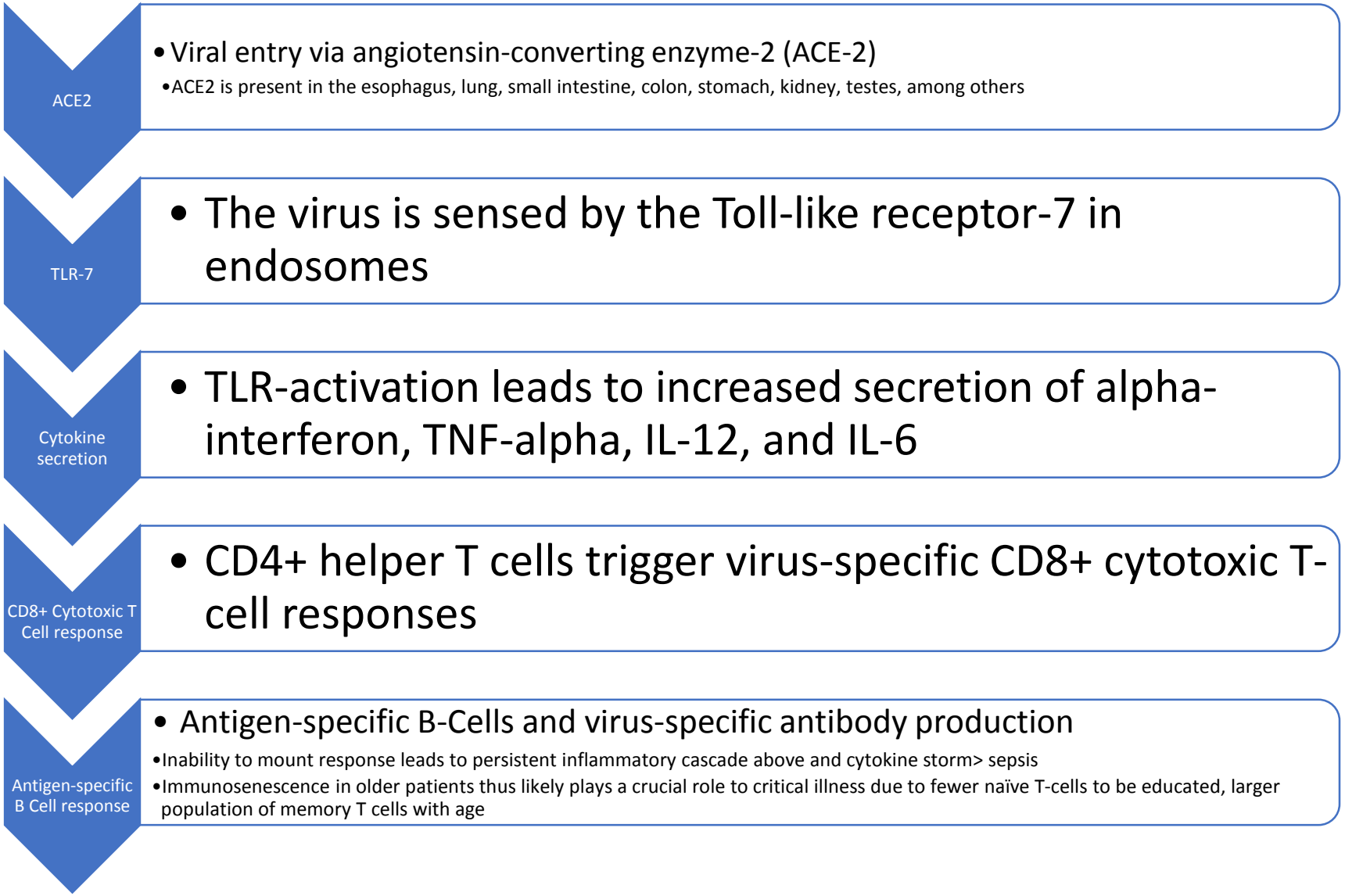
Adaptive Immune Response related to COVID19



Reference: Ahmadpoor P, Rostaing L. Why the immune system fails to mount an adaptive immune response to COVID-19 infection. Transpl Int. 2020 Apr 1. doi: 10.1111/tri.13611. [Epub ahead of print]

SARS-CoV2 virology

- Single-stranded, enveloped, positive sense RNA Beta-coronavirus
- Diverse group of viruses responsible for zoonotic outbreaks
- Other coronaviruses: NL63, 229E, OC43, HKU1, SARS-CoV, MERS-CoV

He F, Deng Y, Li W. J Med Virol. 2020. https://doi.org/10.1002/jmv.25766

SARS-CoV2 virology

- S protein: coronavirus envelope spike
  - ACE2 receptor binding and fusion
  - Determines host tropism and transmission capability
- Nucleocapsid protein: major structural protein
  - Involved in transcription and replication of viral RNA
  - Packaging and encapsulating genome into virions
  - Interfaces with host cell cycles
  - Highly immunogenic, abundant expression during active infection

He F, Deng Y, Li W. J Med Virol. 2020. https://doi.org/10.1002/jmv.25766

SARS-CoV2 Antibody Testing

Rapid point-of-care immunoassays (lateral flow assays)

Enzyme linked immunoassays (ELISA)

Neutralizing and anti-SARS-CoV2 Total antibody assays

Rapid POC Lateral Flow Assays

- Rapid turn around
- Low cost

- Generally low sensitivity
  - Hindered by missed cases/antigen detection in situations of low infectious burden or sampling variability
  - IgM reactions tend to be non-specific to many coronaviruses, thus cross-reactivity a problem
  - IgG antibodies take weeks to develop

ELISA (Enzyme Linked Immunosorbent Assay)

- Higher sensitivity

- Not yet rigorously validated for use
- Cross-reaction with other Coronaviruses lower but not zero
  - **SARS-CoV**, NL63, 229E, OC43, HKU1, MERS-CoV
- More technically difficult
- Longer turn-around time

ELISA formats

ELISAs can be performed with a number of modifications to the basic procedure. The key step, immobilization of the antigen of interest, can be accomplished by direct adsorption to the assay plate or indirectly via a capture antibody that has been attached to the plate. The antigen is then detected either directly (labeled primary antibody) or indirectly (labeled secondary antibody). The most powerful ELISA assay format is the sandwich assay. This type of capture assay is called a "sandwich" assay because the analyte to be measured is bound between two primary antibodies – the capture antibody and the detection antibody. The sandwich format is used because it is sensitive and robust.

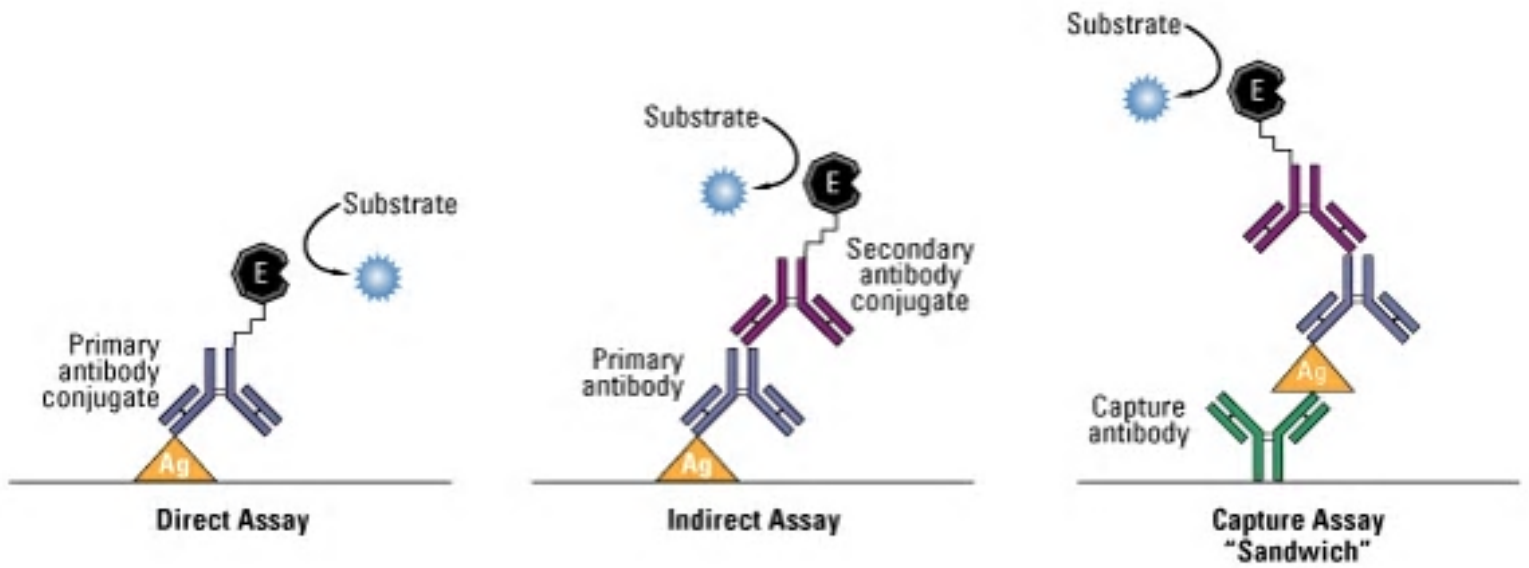


Diagram of common ELISA formats (direct vs. sandwich assays). In the assay, the antigen of interest is immobilized by direct adsorption to the assay plate or by first attaching a capture antibody to the plate surface. Detection of the antigen can then be performed using an enzyme-conjugated primary antibody (direct detection) or a matched set of unlabeled primary and conjugated secondary antibodies (indirect detection).

Schematic from: Thermo Fischer Scientific. 2020. https://www.thermofisher.com/us/en/home/life-science/protein-biology/protein-biology-learning-center/protein-biology-resource-library/pierce-protein-methods/overview-elisa.html#2

Research-based antibody assays

- Gold standard

- Highest sensitivity
- Neutralizing antibody titer > 1:640 correlates with immune protection
- Not widely available outside of clinical/lab research settings
- Highly technical
- Labor intensive

Bloch EM et al. J Clin Invest. 2020. https://doi.org/10.1172/JCI138745.