

# Coronavirus Overview as it Relates to Vaccine Development

## Lawrence Stanberry, MD, PhD

### June 1, 2020

Course Number PB-VI01P: Development of a Vaccine During a Pandemic  
Course Directors: Philip LaRussa, MD and Lawrence Stanberry MD, PhD

Conflicts of Interest: None

# Outline

- Coronavirus Virology & Biology
- Transmission
- Pathophysiology
- Clinical features
- Diagnostics
- Immunology

# Coronavirus Virology

- >30 known animal CoVs in four genera – A,  $\beta$ ,  $\Delta$ ,  $\Gamma$
- Virus spillover occurs with bats and rodents likely sources of human CoVs
- Seven CoVs known infect humans
  - HCoV-229E, and HCoV-NL63 (alphaCoVs)
  - HCoV-OC43, and HCoV-HKU1 (betaCoVs)
  - SARS-CoV, SARS-CoV-2, and MERS-CoV (betaCoVs)

# Coronavirus Virology

- Positive-stranded RNA viruses –prone to mutation
- Genetic drift occurs with SARS-CoV-2 S, N and M proteins potentially complicating vaccine development

# Endemic Coronavirus Biology

- Worldwide distribution
- Major cause of common cold-like illness in all ages
- Infection marked seasonal and cyclical patterns
- ~50% of endemic CoV infections are asymptomatic
- Endemic CoVs have a high rate of reinfection; in volunteers it can occur within a year of prior infection

# Endemic Coronavirus Biology

- One study, 81.5 % of newly infected individuals had pre-existing virus specific neutralizing antibody
- Uncertain whether pre-existing neutralizing antibody modifies the severity of subsequent re-infections
- Endemic CoV infections involve mainly the surface of the respiratory tract, it is possible that secretory IgA antibody plays a more direct role in protection, as is the case with swine CoV infections

# SARS-CoV-2 Transmission

- Primarily human to human
- Respiratory –droplets/contact - portal of entry: eyes/nose
  - Medical students touch their eyes, nose and or mouth an average of 10 times an hour
- Oral-fecal?
- No recognized mother to fetus transmission



# COVID-19 Transmission Dynamics

- Research suggests that seasonality is likely to play only a minor role in the epidemiology of COVID-19
- Public health interventions strongly associated with reduced epidemic growth:
  - *restrictions of mass gatherings*
  - *school closures*
  - *measures of social distancing*

# COVID-19 Pathophysiology(?)

- Virus binds to ACE2 receptors on oral, nasal and ocular mucosal epithelial cells initiating infection
- Infection extends to lungs leading to pneumonia
- Viremia may develop in some patients with dissemination and injury of visceral organs, i.e., heart, renal, gastrointestinal tract (with fecal shedding)
- In some, infection triggers immune dysregulation and immunopathological (autoimmune) responses

# COVID-19 Clinical Features Important in Vaccine Development?

- Hypoxia
- Pneumonia
- Organ failure (heart, kidney, multi-organ)
- Hepatitis
- Shock
- Stroke
- Venous thromboembolism
- Pediatric Multi-System Inflammatory Syndrome

# SARS-CoV-2 Diagnostics

- Acute infection
  - Virus culture
  - Viral nucleic acid (RNA) detection
  - Antigen detection
- Serologic assays
  - ELISA
  - Lateral-flow
  - Virus neutralization
  - Pseudovirus neutralization

# SARS-CoV-2 Immunology

- Antibody seroconversion– IgM appears day 8-12 and is gone by week 13. IgG appears around day 14
  - Serum contains neutralizing antibody; convalescent plasma appears to have some therapeutic benefit
- Both CD4+ and CD8+ T cells are detected about 7 days after onset of symptoms
  - SARS- CoV-1 mouse studies showed that induction or passive transfer of virus- specific CD4+ and CD8+ T cells increased survival. Other studies found that some vaccines could induce detrimental T cell responses

# SARS-CoV-2 Unknowns

- What proportion of the population need to become infected and/or immunized to afford to community immunity (herd immunity)?
- Will COVID-19 infection protect against SARS-CoV-2 reinfection?

# References

1. Koyama T, et al. Emergence of Drift Variants That May Affect COVID-19 Vaccine Development and Antibody Treatment, *Pathogens* 2020, 9, 324; doi:10.3390/pathogens9050324
2. Ling Lin, et. al. (2020) Hypothesis for potential pathogenesis of SARS-CoV-2 infection—a review of immune changes in patients with viral pneumonia, *Emerging Microbes & Infections*, 9:1, 727-732, DOI: 10.1080/22221751.2020.1746199.
3. Juni P, et al, Impact of climate and public health interventions on the COVID-19 pandemic: a prospective cohort, *CMAJ* 2020. doi: 10.1503/cmaj.200920; early-released May 8, 2020.
4. Tay MZ, et. al, The trinity of COVID-19- immunity, Inflammation and Infection. *Nature Reviews - Immunology* April 2020