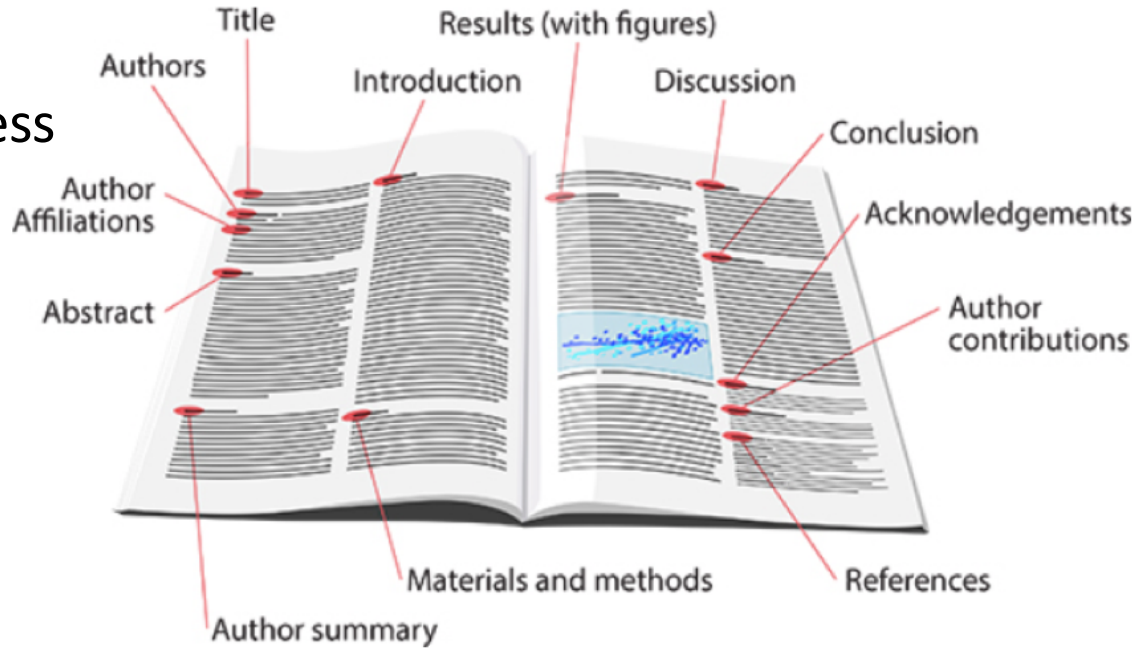
Journal 1: COVID-19 Vaccines In Development

BMES Cell Team

Fall 2020

Outline

- Introduction to Reading Scientific Articles
    - Purpose of a Scientific Paper
    - Dr. Meyer's Recommended Reading & Writing Order
- Background on SARS-CoV-2
- Vaccine Development Process
- Article Background
- Discussion Questions
    - Breakout Rooms



https://mindthegraph.com/blog/read-scientific-papers/#.X6IHRy9h1QI

Introduction to Reading Scientific Articles

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Material is largely based on Dr. Meyer's Recommendations

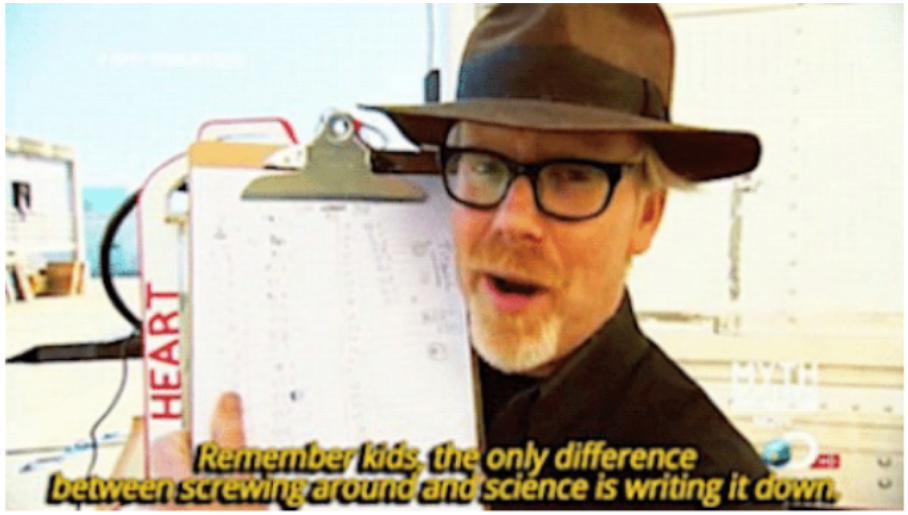
Purpose of a Scientific Paper

A scientific paper communicates what you have done to other scientists.

Allows other researchers to:

→ accurately replicate your experiments

→ use conclusions from your research as a basis for future experimentation



https://twitter.com/sciencechannel/status/867373382714761217

Written Order of a Paper vs. Reading Order of a Paper

Title
↓
Authors
↓
Abstract
↓
Introduction
↓
Results
↓
Discussion
↓
Experimental Procedures
↓
Acknowledgements
↓
References

Title
↓
Abstract
↓
Introduction
↓
Discussion
↓
Figures (Part of Results)
↓
Rest of Results
↓
Experimental Procedures
↓
Everything Else

Title

The title concisely explains the information provided by the article.

ELSEVIER

Current Opinion in Microbiology

Volume 52, December 2019, Pages 55-63

Fantastic yeasts and where to find them: the hidden diversity of dimorphic fungal pathogens

Marley C Caballero Van Dyke [1], Marcus M Teixeira [1, 2], Bridget M Barker [1] ✉

Review > Neuro Oncol. 2018 Feb 19;20(3):313-323. doi: 10.1093/neuonc/nox106.

miR miR on the wall, who's the most malignant medulloblastoma miR of them all?

Xin Wang [1 2], Borja L Holgado [1], Vijay Ramaswamy [1 3], Stephen Mack [1], Kory Zayne [1], Marc Remke [4], Xiaochong Wu [1], Livia Garzia [1], Craig Daniels [1], Anna M Kenney [1 5 6], Michael D Taylor [1 2 7]

Actin' like actin?

R D Mullins [1], J F Kelleher, T D Pollard

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Human Microbiome Journal

Volume 13, August 2019, 100058

Letter to the Editor

The effect of having Christmas dinner with in-laws on gut microbiota composition

Nicolien C. de Clercq [a] ✉, Myrthe N. Frissen [a] ✉, Evgeni Levin [a, b] ✉, Mark Davids [a] ✉, Jorn Hartman [a] ✉, Andrei Prodan [a, b] ✉, Hilde Herrema [a] ✉, Albert K. Groen [a, c] ✉, Johannes A. Romijn [a] ✉, Max Nieuwdorp [d, e] ✉

Understanding the Dynamics of Emerging and Re-Emerging Infectious Diseases Using Mathematical Models, 2012: 157-177 ISBN: 978-81-7895-549-0 Editors: Steady Mushayabasa and Claver P. Bhunu

7. A mathematical model of Bieber Fever: The most infectious disease of our time?

Valerie Tweedle[1] and Robert J. Smith?[2]

[1]Department of Biology, The University of Ottawa, 585 King Edward Ave, Ottawa ON K1N 6N5 Canada; [2]Department of Mathematics and Faculty of Medicine, The University of Ottawa 585 King Edward Ave, Ottawa ON K1N 6N5, Canada

Snakes on a Spaceship—An Overview of Python in Heliophysics

A. G. Burrell ✉, A. Halford, J. Klenzing, R. A. Stoneback, S. K. Morley, A. M. Annex, K. M. Laundal, A. C. Kellerman, D. Stansby, J. Ma

https://www.sciencealert.com/scientists-sharing-their-best-pun-filled-paper-titles-has-us-in-stitches https://pubmed.ncbi.nlm.nih.gov/15157457/ https://www.sciencedirect.com/science/article/abs/pii/S136952741930013X

Abstract

The abstract provides a brief overview of every section of the paper.

- Roughly 5-6 sentences long
    - Contains about a sentence for each section of the paper
    - Emphasizes novel / important research findings
    - Convinces audience to read the paper

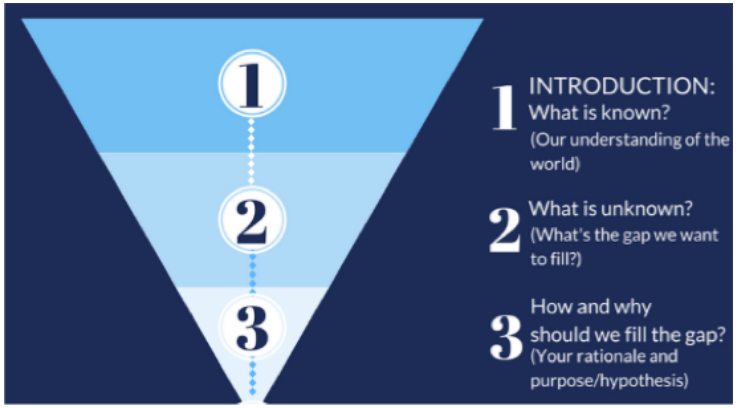
- Read the abstract **first**
- Write the abstract **last**

https://absolutelymaybe.plos.org/2018/06/06/building-a-great-scientific-abstract-a-quick-checklist/

Introduction

The introduction provides background information on the research topic and explains the researcher's motivation for their experiments.

- Background information
  - First, explains general, textbook-level information on the topic
  - Then, delves into more specific research conducted by peers
  - Ends with precise focus of this paper
  - Setup for results section
- Read the introduction **second**
- Write the introduction **with the discussion**



https://wordvice.com/video-how-to-write-a-compelling-research-paper-introduction/

Discussion

The discussion synthesizes the results of the paper.

- Places results in a broader context and interprets experimental findings
    - First, explains the findings of independent research
    - Then, links these findings to general understanding of the topic
    - Specifies areas of focus and next steps for future research
- Read the discussion **third**
- Write the discussion **as you write the introduction**
    - If there is a conclusion, read it **after reading the discussion** and write it **with the introduction**

Figures (Part of Results)

The figures visually depict what was done in the experiment.

- Three main types of figures in bioengineering papers:
  - Cartoon depictions of the procedure
  - Pictures of the experimental setup, colorimetric assays, and microscope images
  - Graphs synthesizing quantitative data
- Examine the figures **before you read the results section**
- Make the figures **second to last (with the rest of the results section)**

Example of Figure Types: Engler Paper

Matrix Elasticity Directs Stem Cell Lineage Specification

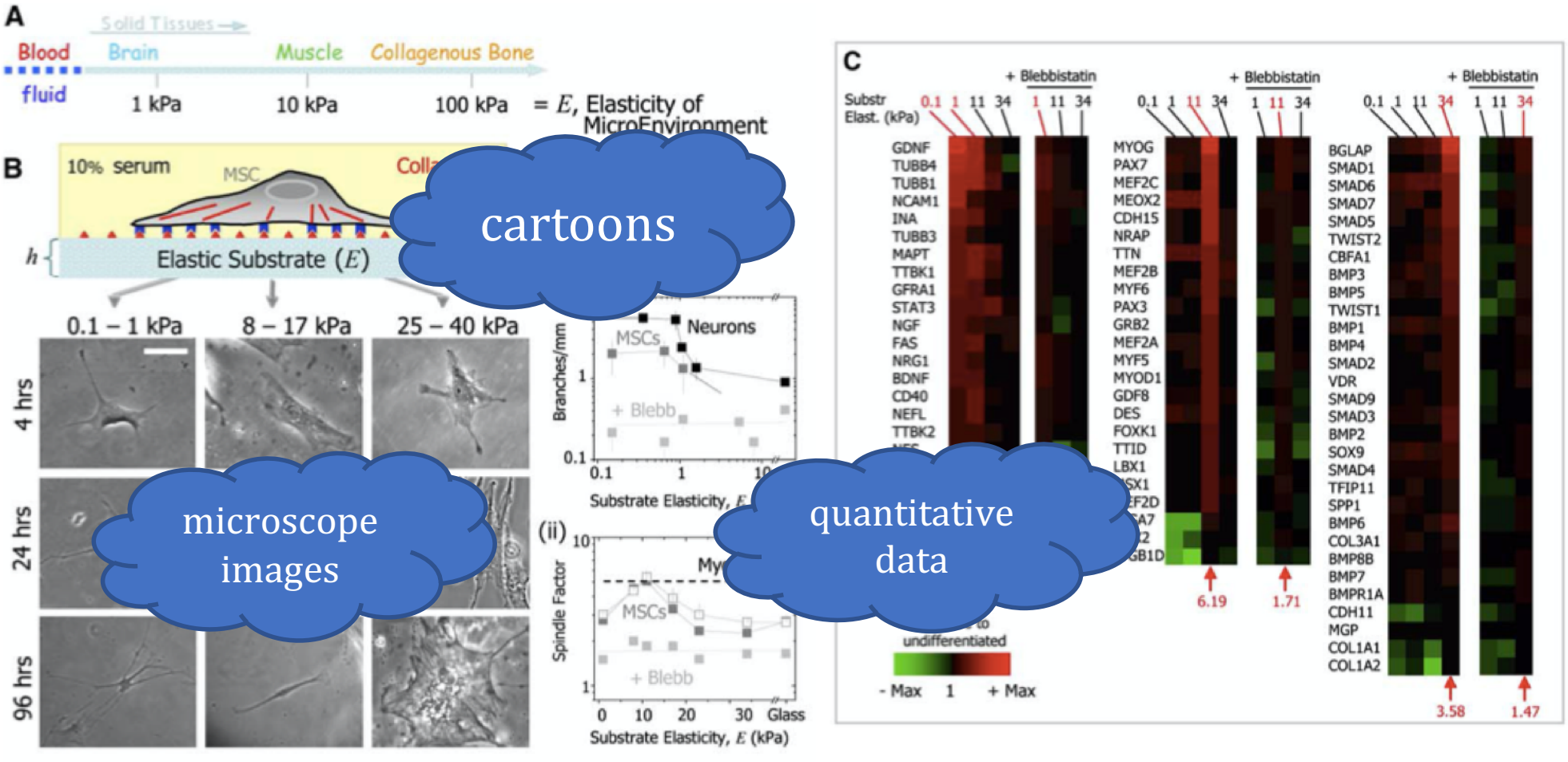


Figure 1. Tissue Elasticity and Differentiation of Native MSCs

https://www.cell.com/action/showPdf?pii=S0092-8674%2806%2900961-5

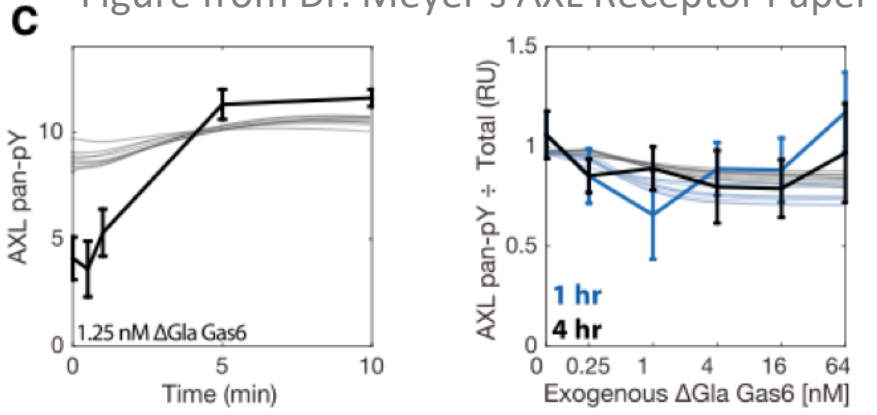
Rest of Results

The results communicate important experimental findings.

- Guide the reader through the experiments
- List important quantitative and qualitative findings
- Broken into sections that are interwoven with the appropriate figures
- Experimental findings are not interpreted in the results section

- Read the results **second to last**
- Write the results **second**

Figure from Dr. Meyer's AXL Receptor Paper



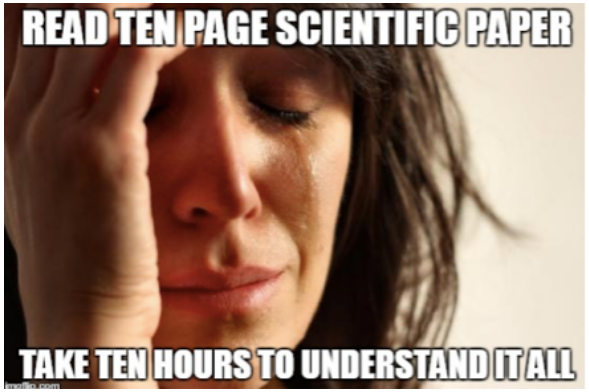
https://www.cell.com/action/showPdf?pii=S2405-4712%2815%2900007-1

Experimental Materials and Methods

Materials and methods provide instructions for experimental replication.

- Most technical section of the paper
- Typically broken down into distinct experiments
    - Ex: Dr. Meyer's AXL Receptor Article in *Cell Systems*
        - Preparation, Quantification, Transfection, Immunofluorescence, Modeling, Calculations

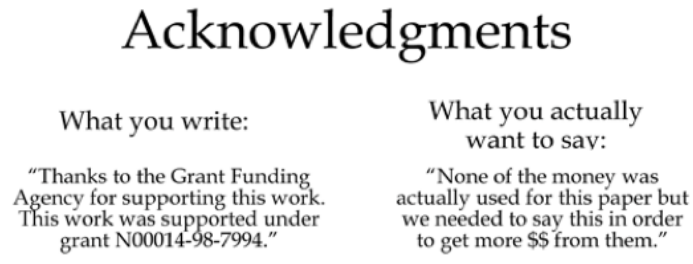
- Read the materials and methods **last**
- Write the materials and methods **first**



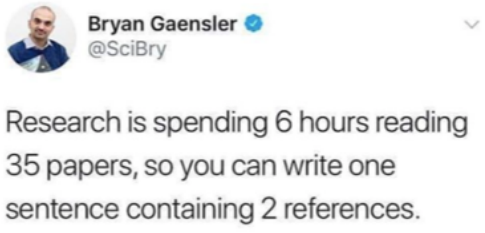
https://mindthegraph.com/blog/read-scientific-papers/#.X6IGrS9h1QJ

Everything Else

- **Authors**
  - Lists major contributors to experimental design and execution
  - The primary researchers are listed first
  - The principle investigator (PI) is listed last
  - An asterisk * marks contact person for inquires about the article



- **Acknowledgements**
  - Specifies sources of funding
    - government grants, private companies, non-profits
  - Lists consultants, advisors, and material contributors
  - Everyone that helped make the project happen should be acknowledged for their contribution



- **References**
  - Useful when researching a specific topic discussed in the paper

https://www.pinterest.com/pin/548313323382597911/

Background: SARS-CoV-2

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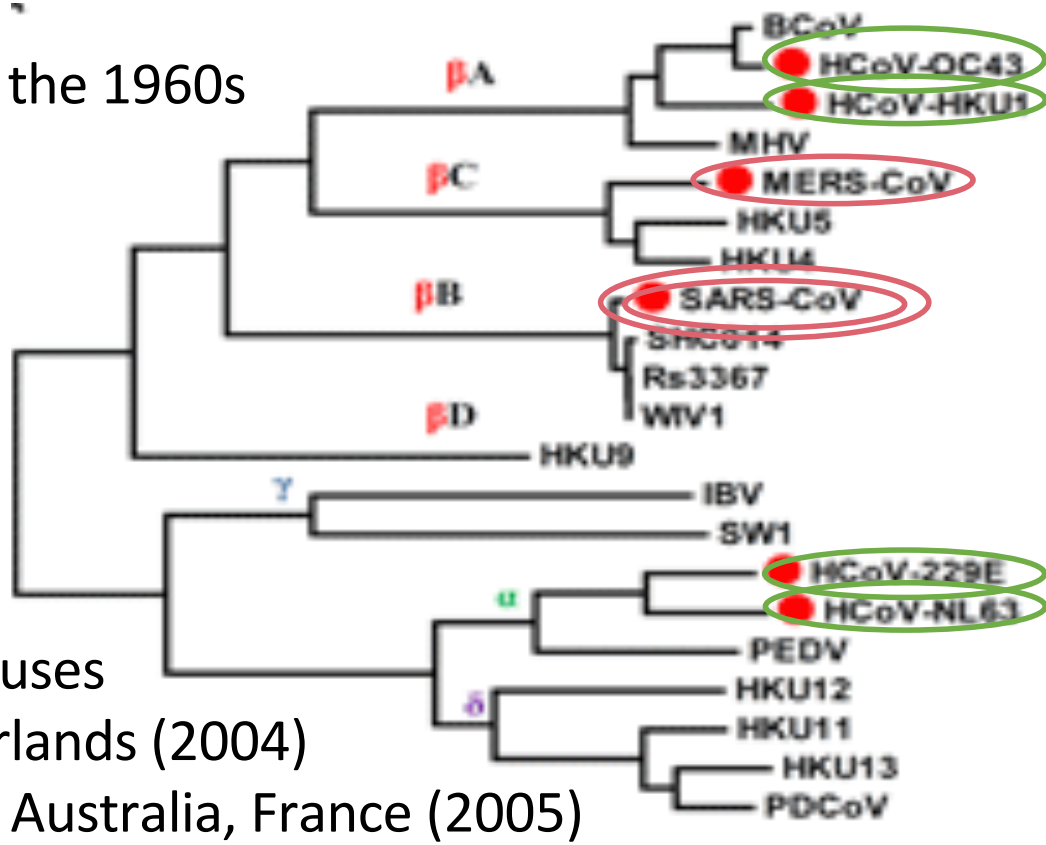
Material is largely based on Dr. Niemz's KGI Presentation

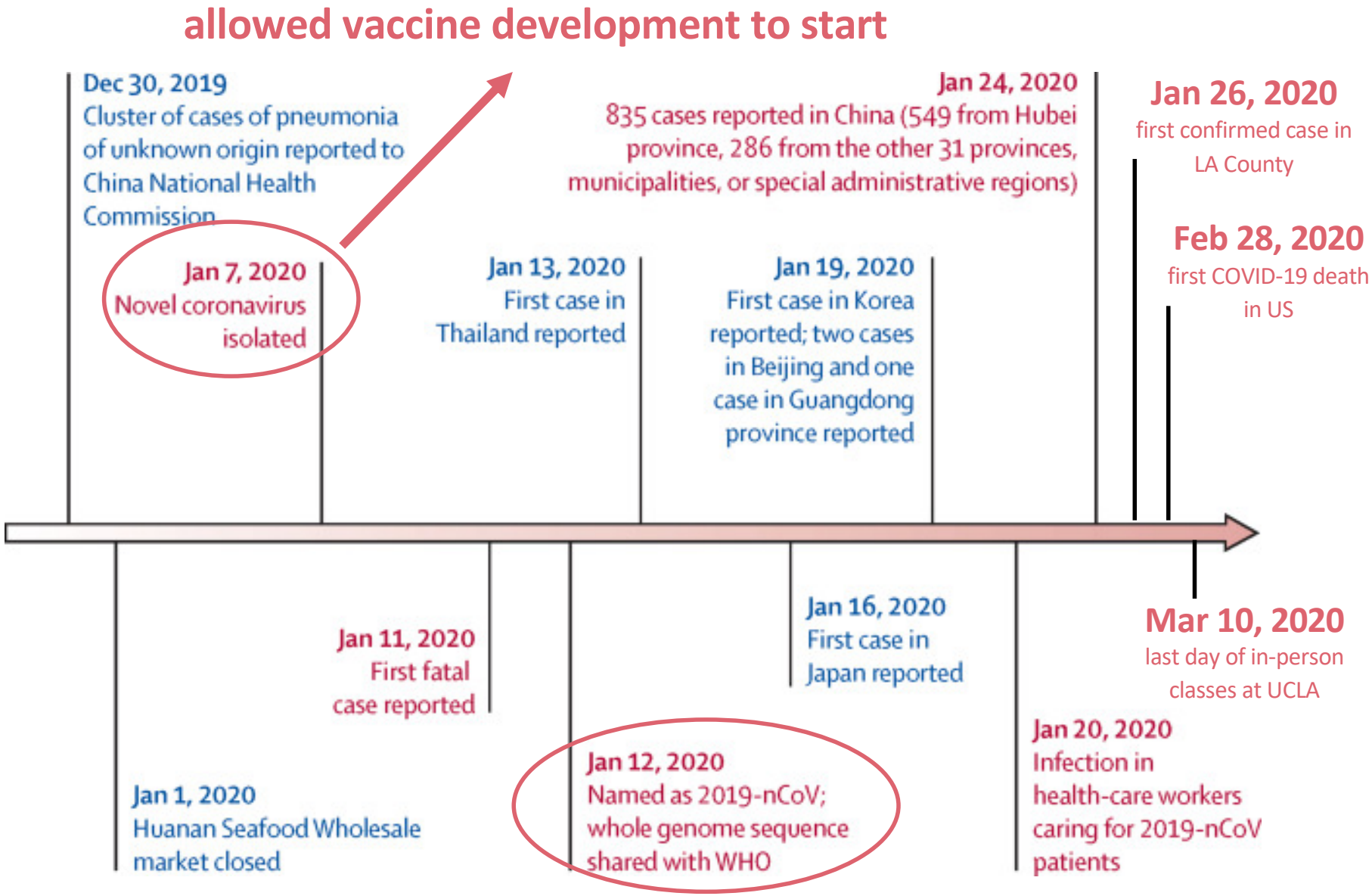
Human History with Coronavirus

- Coronaviruses were first studied in the 1960s
  - OC43 and 229E
  - Common cold
- SARS-CoV Outbreak (2002-2004)
  - Killed ~10% infected
  - 774 deaths worldwide
  - Research wake up call
  - Similar virus found in bats
- Looking for other human coronaviruses
  - NL63 found in US & Netherlands (2004)
  - HKU1 found in Hong Kong, Australia, France (2005)
- MERS-CoV (2012)
  - Killed ~34.4% infected
  - 881 deaths worldwide (September 2012 – November 2019)
- SARS-CoV-2 (2019)
  - According to the CDC, 216,459 in the US alone (Feb – Nov 2020)



https://www.the-scientist.com/news-opinion/a-brief-history-of-human-coronaviruses-67600 https://www.cdc.gov/coronavirus/types.html https://advances.sciencemag.org/content/5/4/eaav4580

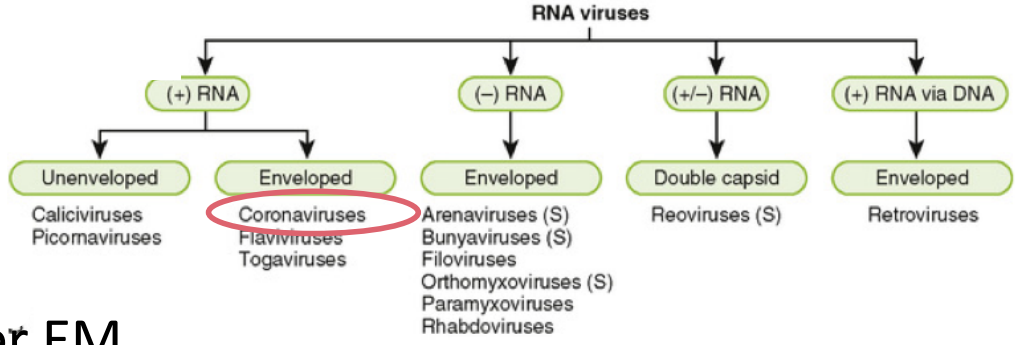
Early Timeline of SARS-CoV-2

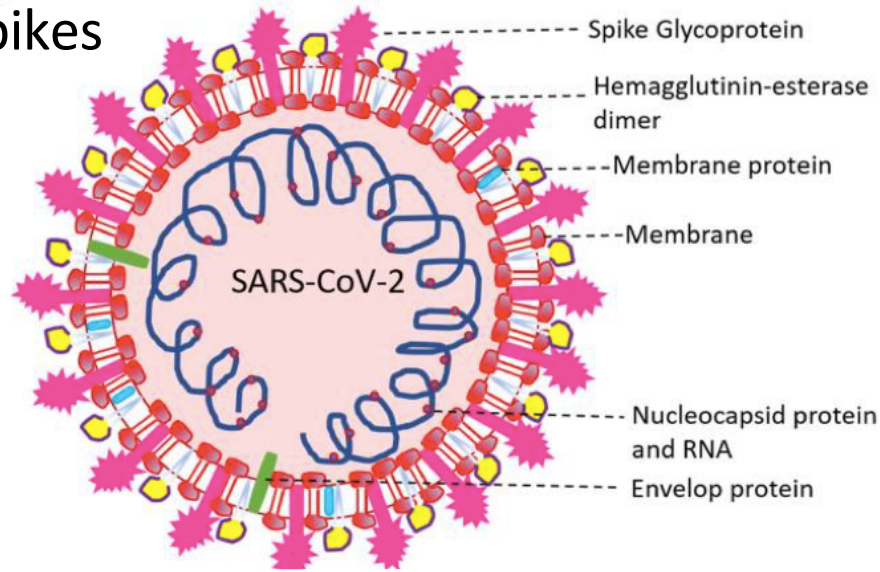


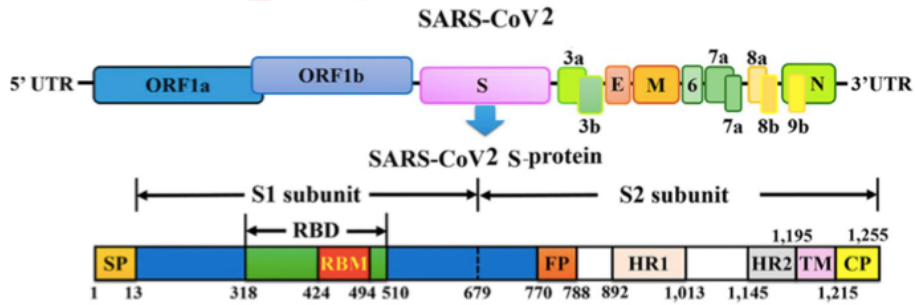
https://www.nbclosangeles.com/news/local/a-coronavirus-timeline/2334100/https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)30185-9/fulltext

Structure of SARS-CoV-2

- Large, single-stranded RNA virus
  - Positive-sense (~mRNA)
  - Enveloped (protection)
- Origin of the name
  - “Corona” (halo) shape under EM
  - Shape comes from envelope spikes
- Coronavirus Genome
  - ~30,000 nucleotides (large!)
  - 4 structural proteins:
    - Nucleocapsid (N)
    - Membrane (M)
    - Envelope (E)
    - Spike (S)
  - Spike Protein
    - Receptor Binding
    - Membrane Fusion
    - Antibody Target



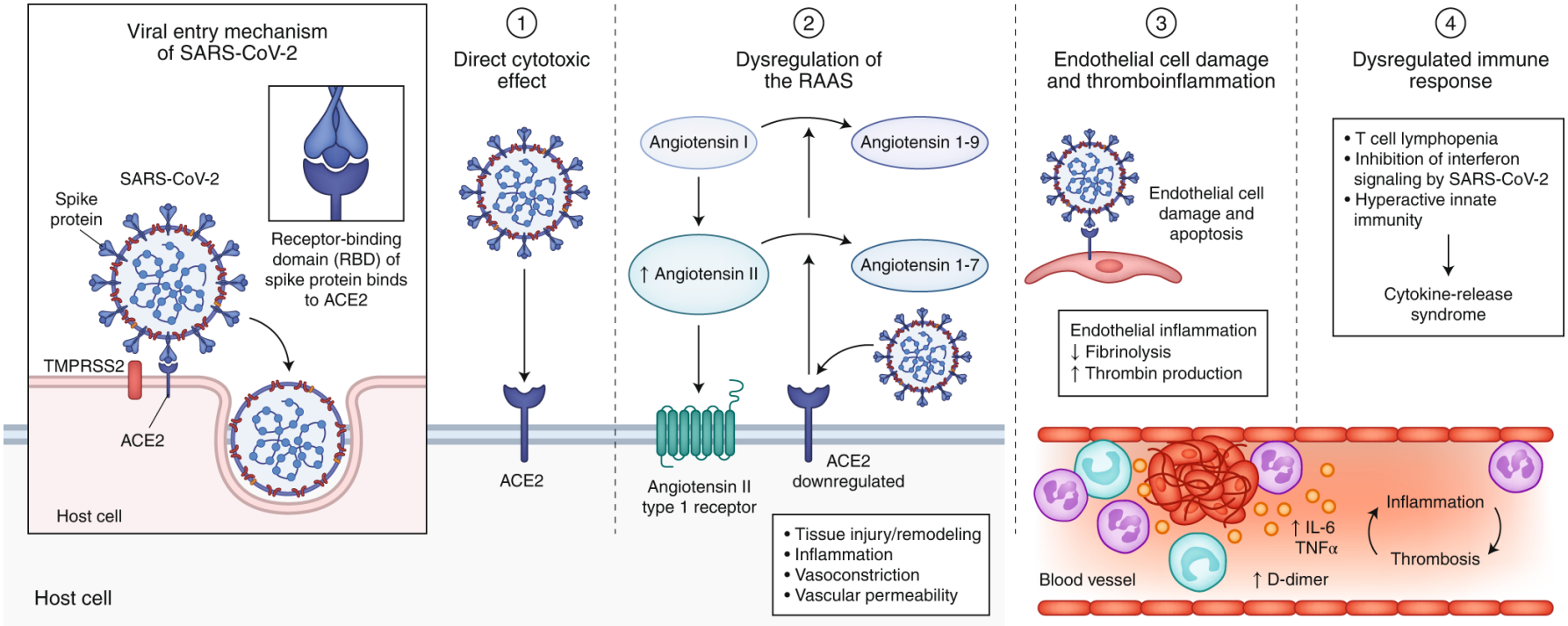




https://www.cdc.gov/coronavirus/mers/photos.html#:~:text=Coronaviruses%20derive%20their%20name%20from,%2C”%20or%20halo.https://oncohemakey.com/viral-structure-classification-and-replication/https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7196923/#!po=1.25000

SARS-CoV-2 vs. COVID-19 & Disease Progression

- Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is the virus that causes coronavirus disease 2019 (COVID-19)



- Vaccines target SARS-CoV-2 to prevent COVID-19
  - SARS-CoV-2 binds to angiotensin-converting enzyme 2 (ACE2)
  - After binding, SARS-CoV-2 is endocytosed and can replicate
- COVID-19's mechanism of action is currently being investigated
  - Associated with a "cytokine storm"
  - One current idea: Dysregulation of RAAS

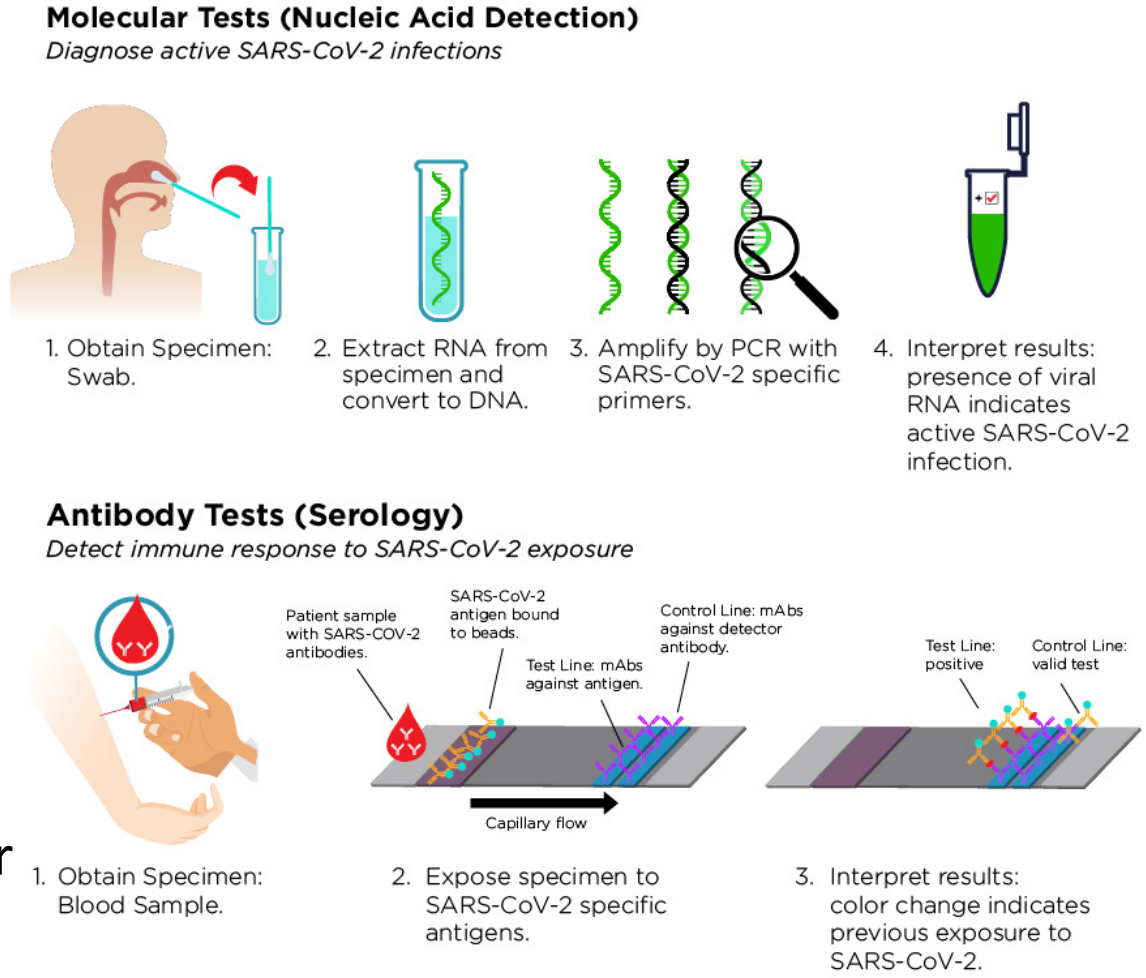
https://www.nature.com/articles/s41591-020-0968-3

Testing for SARS-CoV-2

- Two main testing methods: Nucleic-Acid Based and Antibody Based

- **Nucleic-Acid Based**
  - Respiratory specimen
  - Detects viral RNA
  - Active infection
  - Used for diagnosis

- **Antibody Based**
  - Blood sample
  - Detects IgM & IgG
  - Produced 1-2 weeks after infection
  - Not currently used for diagnosis, but can indicate exposure to viral RNA



https://asm.org/Articles/2020/April/COVID-19-Testing-FAQs

Background: The Vaccine Development Process

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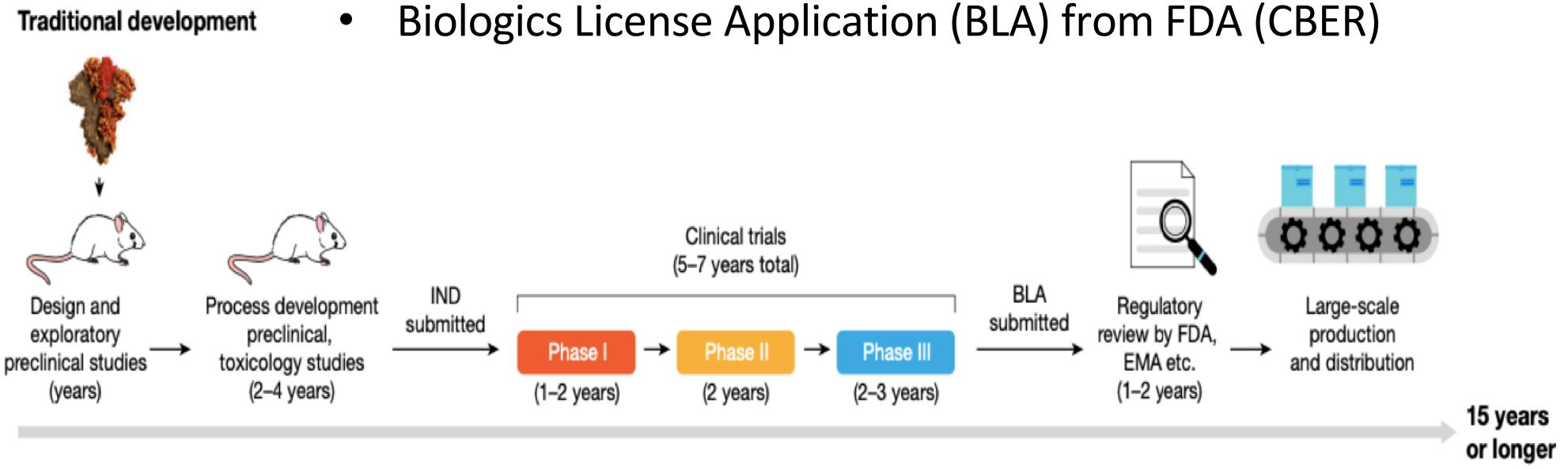
Normal Vaccine Development

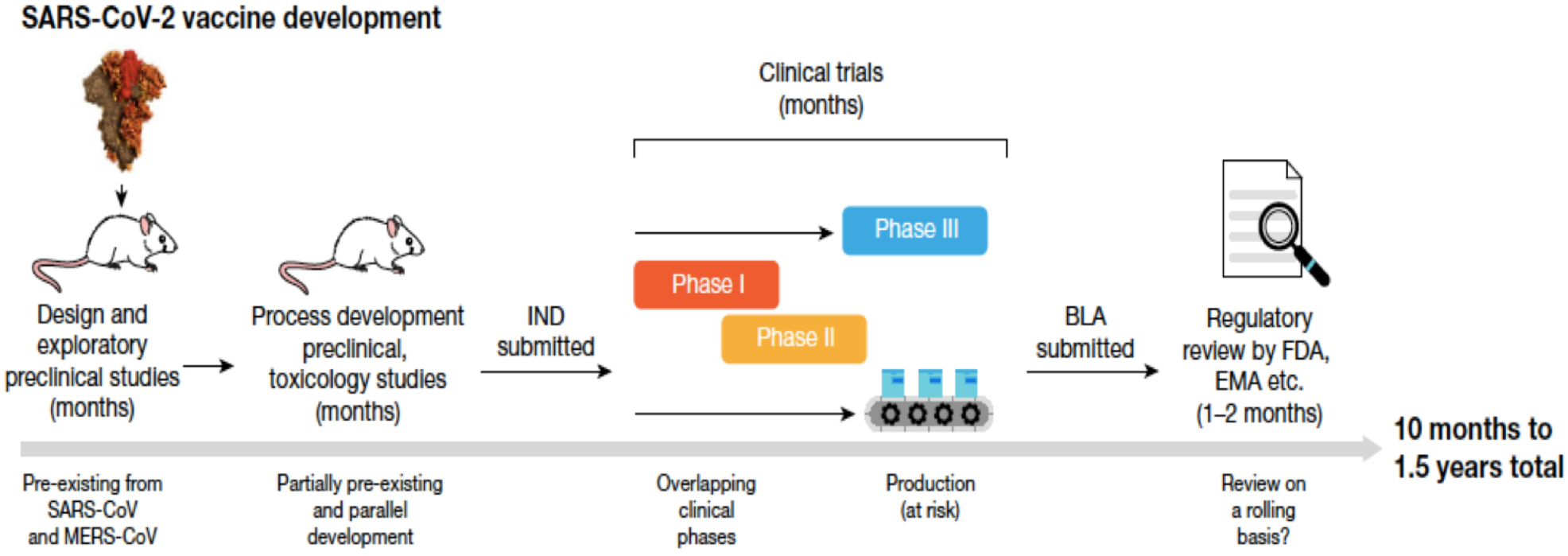
- Vaccine development is a VERY long process
  - 10-15 years from discovery to market availability
  - Fastest known vaccine development timeline was still ~4 years
- Why does vaccine development take so long?
  - The sponsors of a vaccine need to demonstrate the long-term safety and efficacy of their product
    - Years of preclinical animal studies and clinical trials
  - Regulatory agencies require the submission of documentation
    - Investigational New Drug (IND) Application before trials
    - Biologics License Application (BLA) from FDA (CBER)



https://www.fda.gov/about-fda/fda-organization https://khn.org/morning-breakout/its-rare-a-vaccine-is-developed-in-five-years-can-the-world-really-pull-it-off-in-one/

SARS-CoV-2 Accelerated Vaccine Development Timeline

- Leveraging existing preclinical research on SARS-CoV-2 and MERS-CoV
  - ~20 years of research since the first SARS-CoV outbreak
  - Improved ability to isolate viruses and decode genomes
- FDA expedited processes for biotechnology tackling the SARS-CoV-2 virus
  - Emergency Use Authorization (EUA)
  - Approval granted for simultaneous vaccine development from many different companies with overlapping clinical trail phases



https://www.fda.gov/about-fda/fda-organization https://khn.org/morning-breakout/its-rare-a-vaccine-is-developed-in-five-years-can-the-world-really-pull-it-off-in-one/

Journal 1: SARS-CoV-2 Vaccines in Development

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Fall 2020

UCLA BIOMEDICAL ENGINEERING SOCIETY @

Article Overview

- Review article published September 23, 2020 in Nature
    - Synthesizes research conducted by vaccine sponsors
- Author Information: Florian Krammer
    - Professor of Vaccinology in the Microbiology Department of Icahn School of Medicine at Mount Sinai (NYC)
    - PI of SEM-CIVIC (focuses on improving flu vaccines)
    - Krammer laboratory is an NIH-funded CEIRS
- Review Structure
    - Overview on SARS-CoV-2 history and its known mechanisms
    - Types of SARS-CoV-2 vaccines in development
    - Results from preclinical (NHP) and clinical trials

https://labs.icahn.mssm.edu/krammerlab/dr-krammer/

Discussion Questions

- What was your main takeaway from this review article?
- What are the advantages and disadvantages of the different types of vaccines in development (inactivated vs. live-attenuated, etc.)?
- Examine Figure 4. What do you notice about the distribution of vaccine candidates? Discuss both the vaccine type and trial stage.
- What conclusion does Krammer reach on the outlook of a SARS-CoV-2 vaccine? What evidence does Krammer use to support this conclusion? What case would a skeptical scientist make against Krammer's conclusion? Based on this article, provided background information, and your personal experience, what is your assessment of this conclusion?

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