

Journal 1: COVID-19 Vaccines In Development

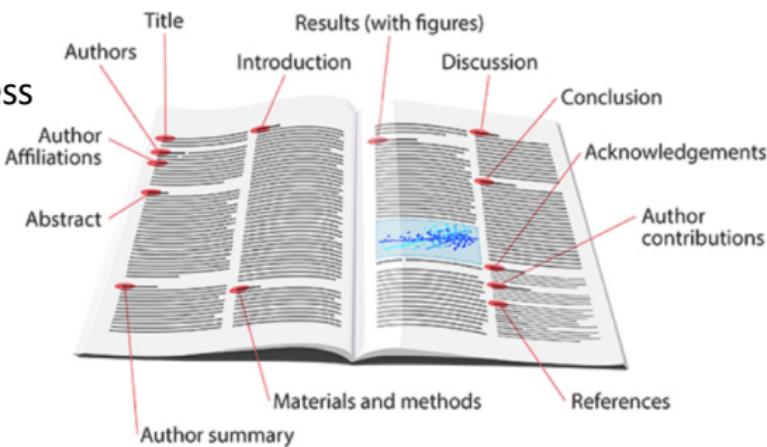
BMES Cell Team

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



Introduction to Reading Scientific Articles

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Fall 2020

Material is largely based on Dr. Meyer's Recommendations

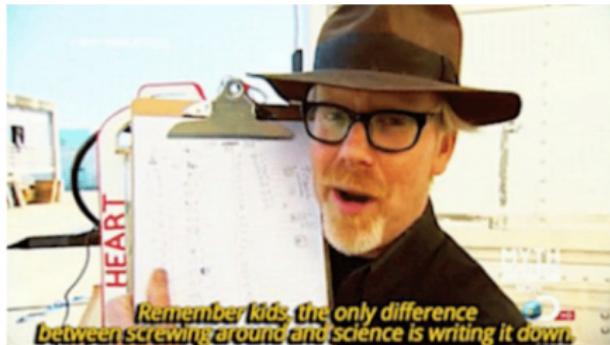


Purpose of a Scientific Paper

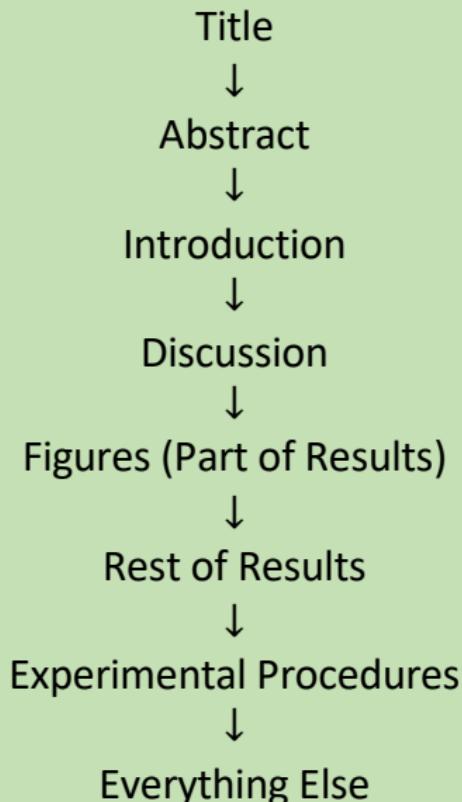
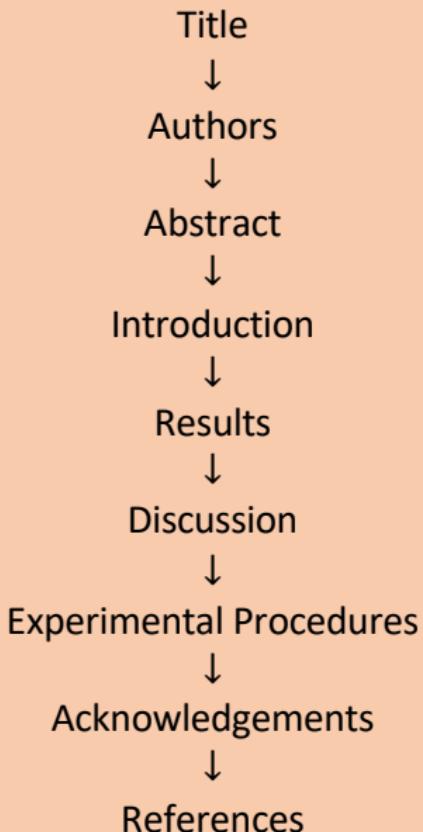
A **scientific paper** communicates what you have done to other scientists.

Allows other researchers to:

- accurately **replicate** your experiments
- use conclusions from your research as a **basis for future experimentation**



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



Title

The **title** concisely explains the information provided by the article.



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 ³, 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



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 Tweedie¹ and Robert J. Smith²

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

Snakes on a Spaceship—An Overview of Python in Heliosysics

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

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**



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**



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

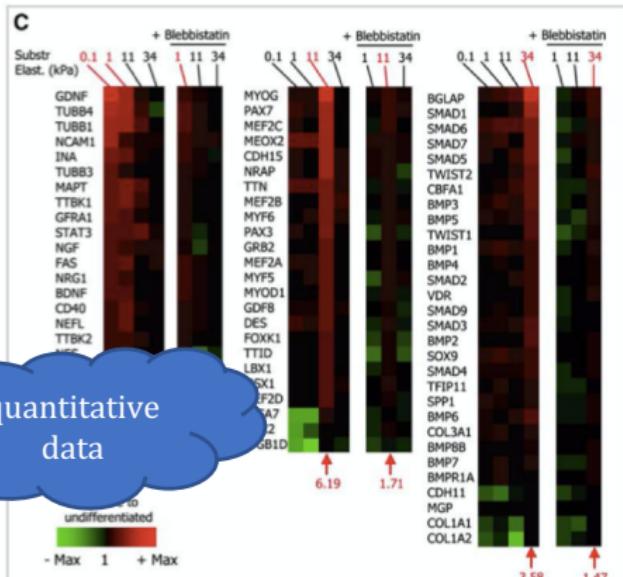
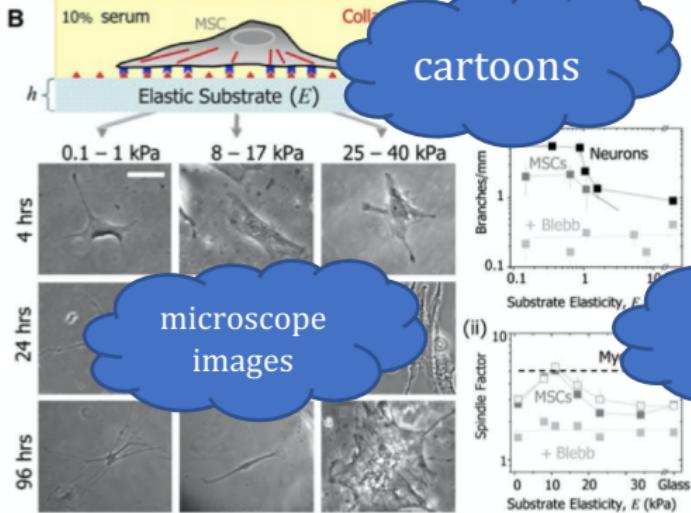


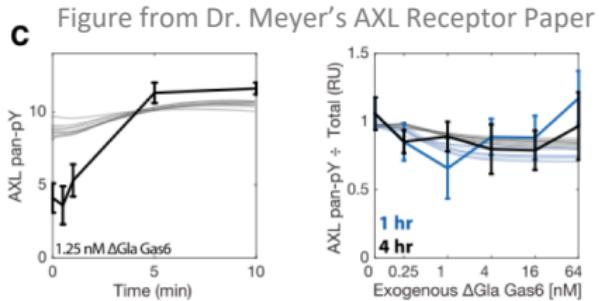
Figure 1. Tissue Elasticity and Differentiation of Native MSCs

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

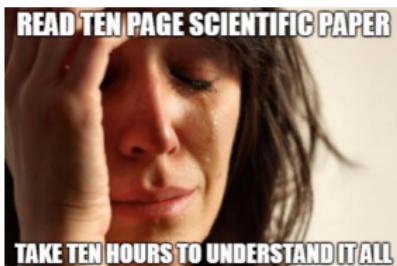
- Read the results **second to last**
- Write the results **second**



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**



READ TEN PAGE SCIENTIFIC PAPER

TAKE TEN HOURS TO UNDERSTAND IT ALL

<https://mindthegraph.com/blog/read-scientific-papers/#X6lGr59h1CJ>

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 inquiries about the article

Acknowledgments

- **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

What you write:

"Thanks to the Grant Funding Agency for supporting this work. This work was supported under grant N00014-98-7994."

What you actually want to say:

"None of the money was actually used for this paper but we needed to say this in order to get more \$\$ from them."

- **References**

- Useful when researching a specific topic discussed in the paper



Research is spending 6 hours reading 35 papers, so you can write one sentence containing 2 references.

Background: SARS-CoV-2

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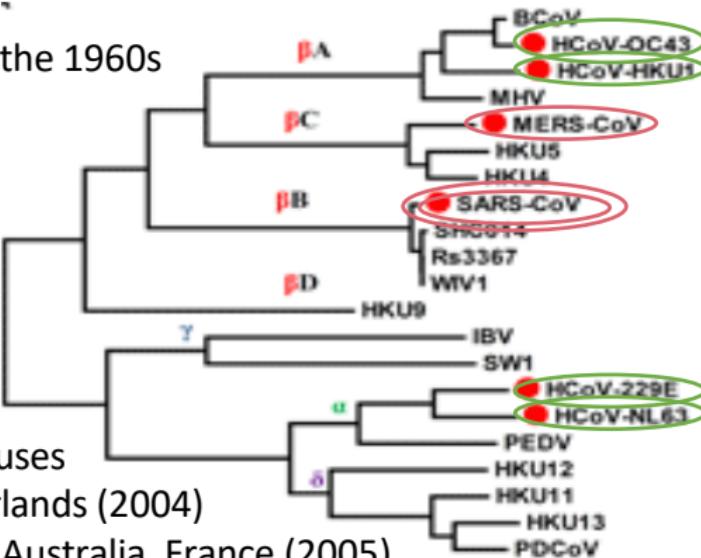
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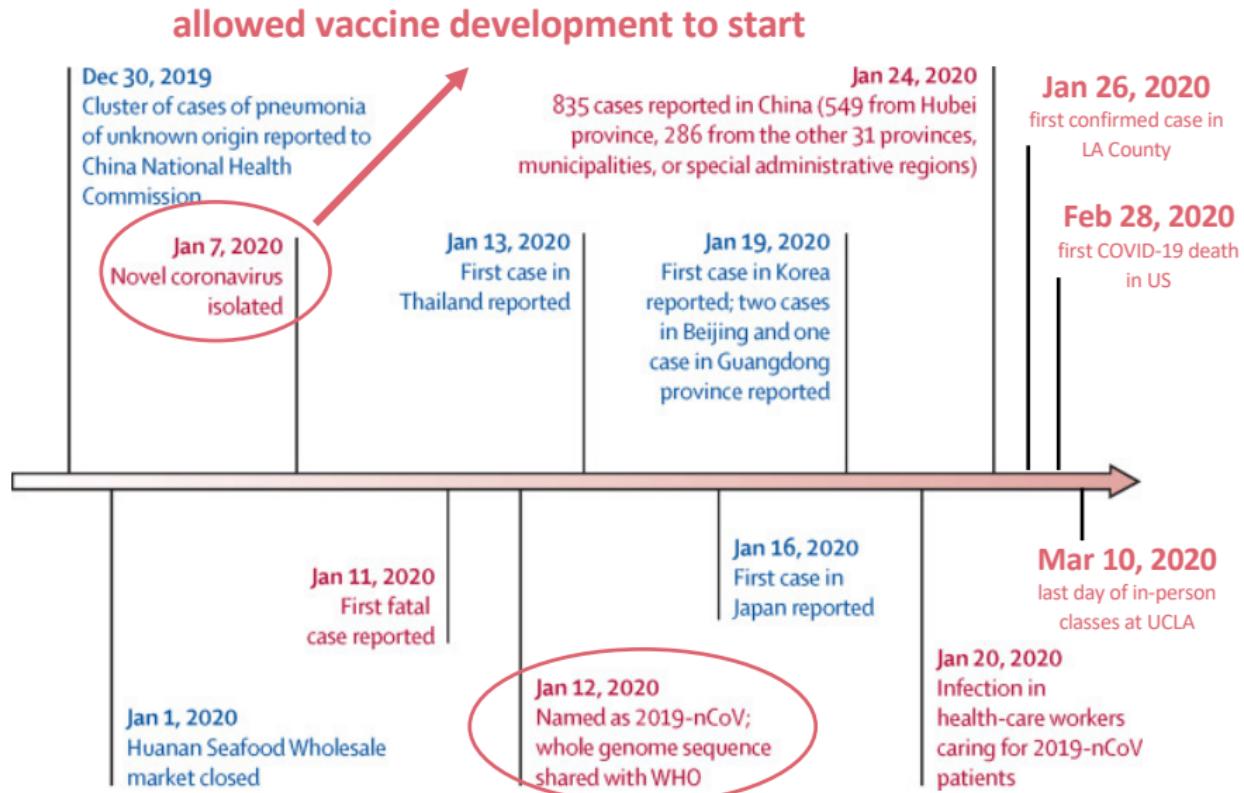


Human History with Coronavirus

- 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)

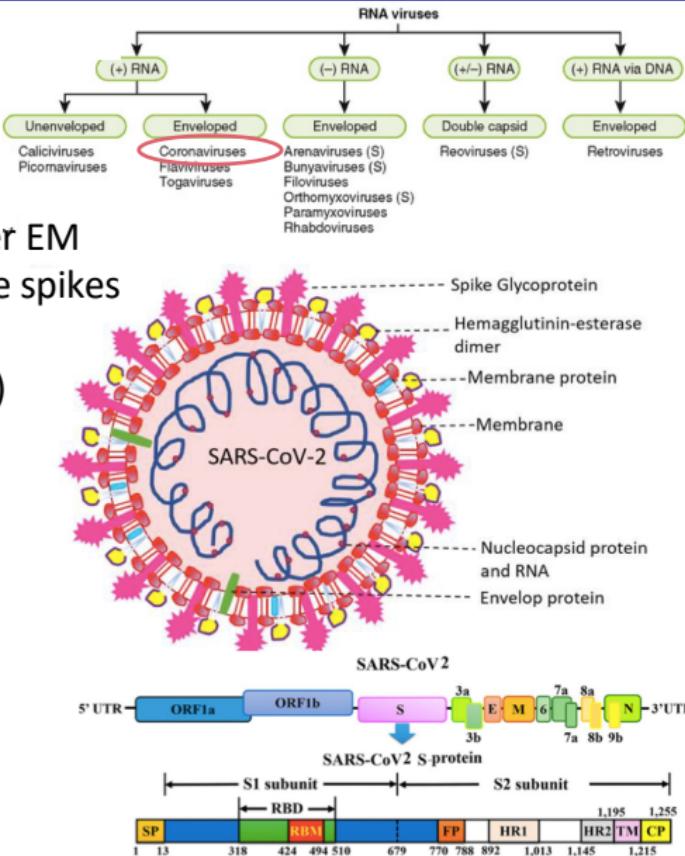


Early Timeline of SARS-CoV-2



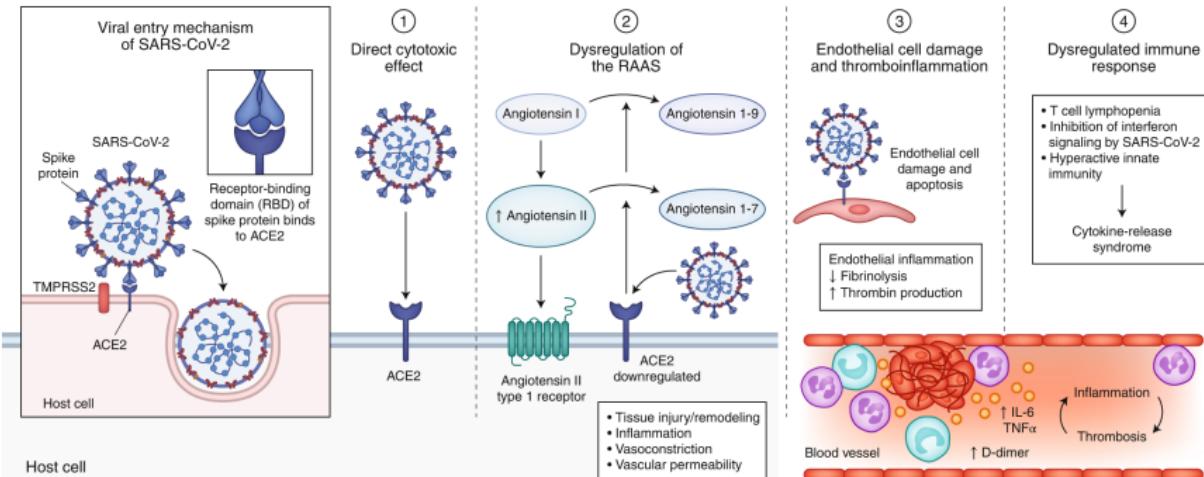
Structure of SARS-CoV-2

- 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



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

Testing for SARS-CoV-2

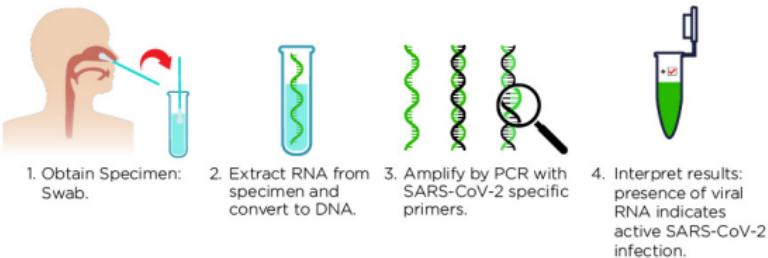
- Two main testing methods: Nucleic-Acid Based and Antibody Based

- Nucleic-Acid Based**

- Respiratory specimen
- Detects viral RNA
- Active infection
- Used for diagnosis

Molecular Tests (Nucleic Acid Detection)

Diagnose active SARS-CoV-2 infections

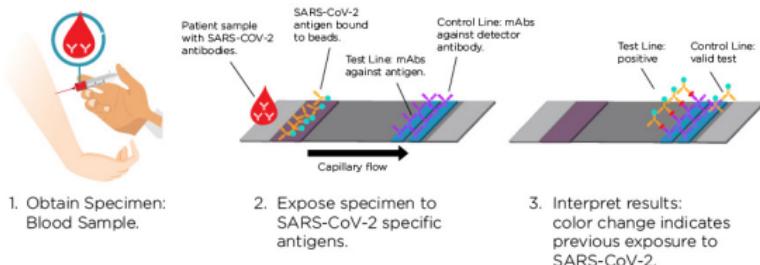


- Antibody Based**

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

Antibody Tests (Serology)

Detect immune response to SARS-CoV-2 exposure



Background: The Vaccine Development Process

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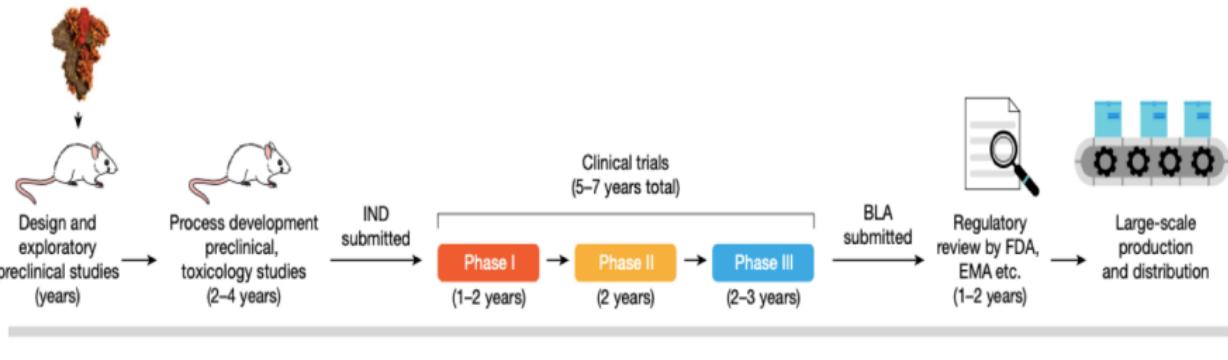
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Normal Vaccine Development

- 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)

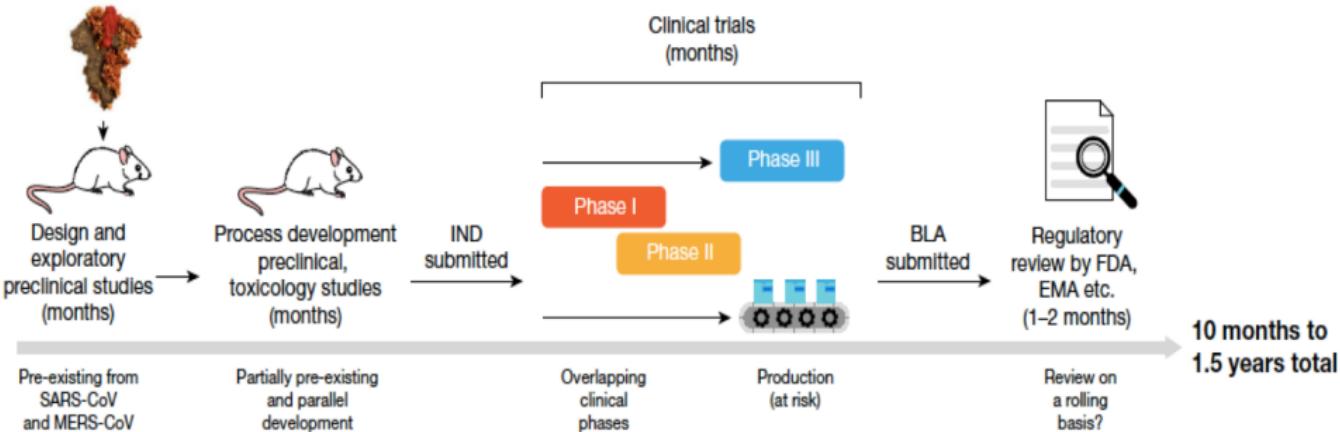
Traditional development



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 trial phases

SARS-CoV-2 vaccine development



Journal 1: SARS-CoV-2 Vaccines in Development

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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

Discussion Questions

- What was your main takeaway from this review article?
- What are the advantages and disadvantages of the three main types of vaccines in development?
- 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?