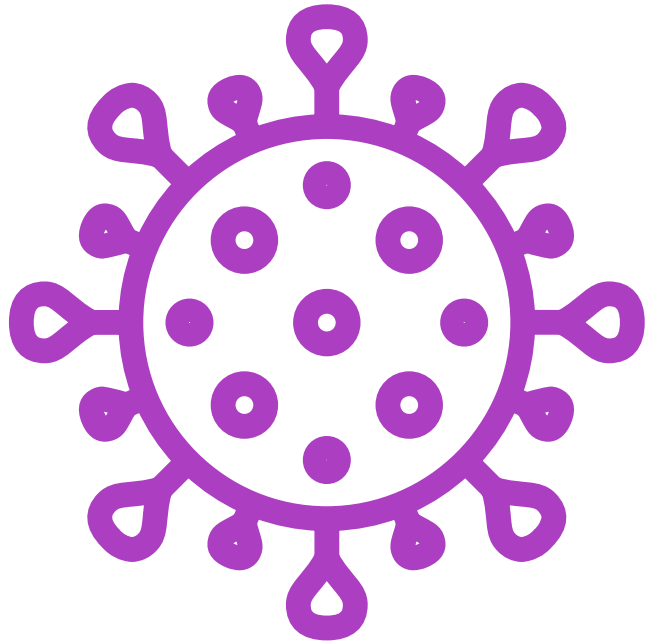
FINAL PROJECT

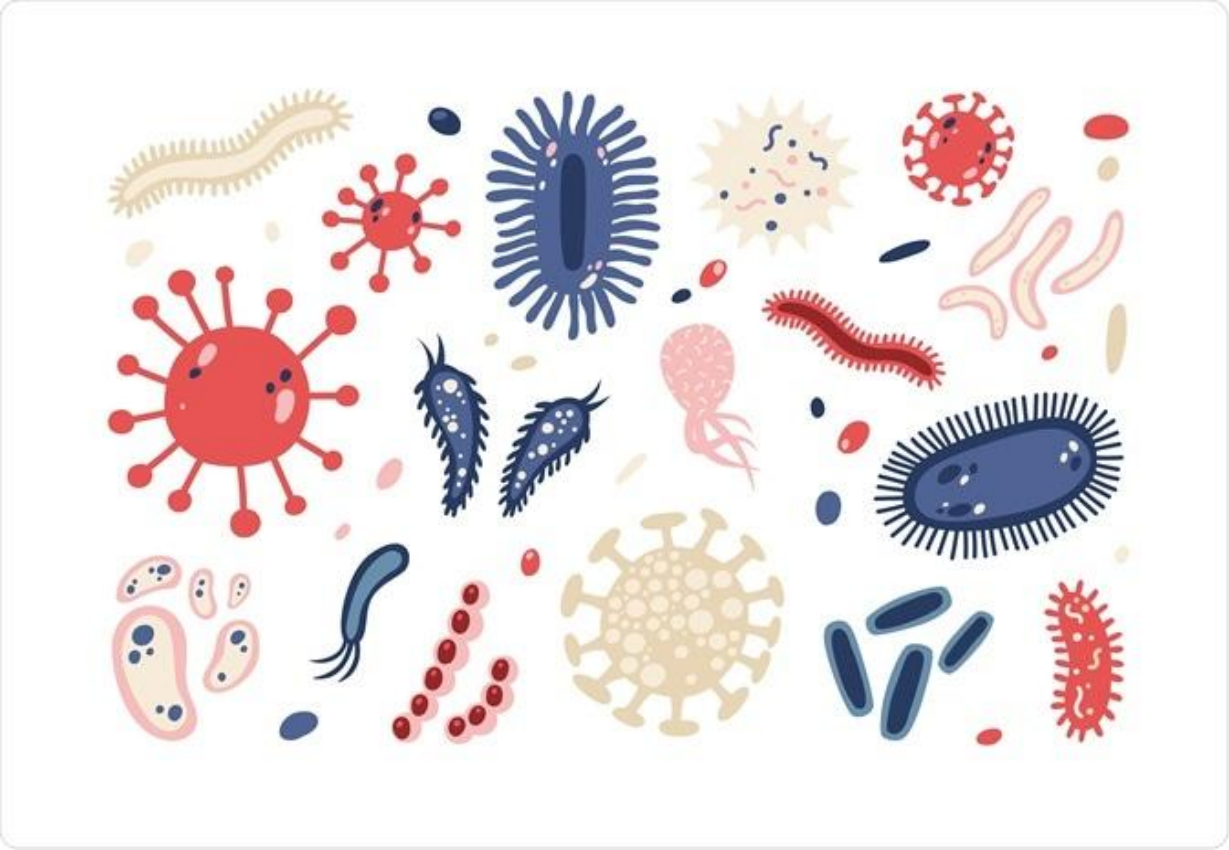
TOPICS IN BIOLOGY:

PATHOGENS AMONG US



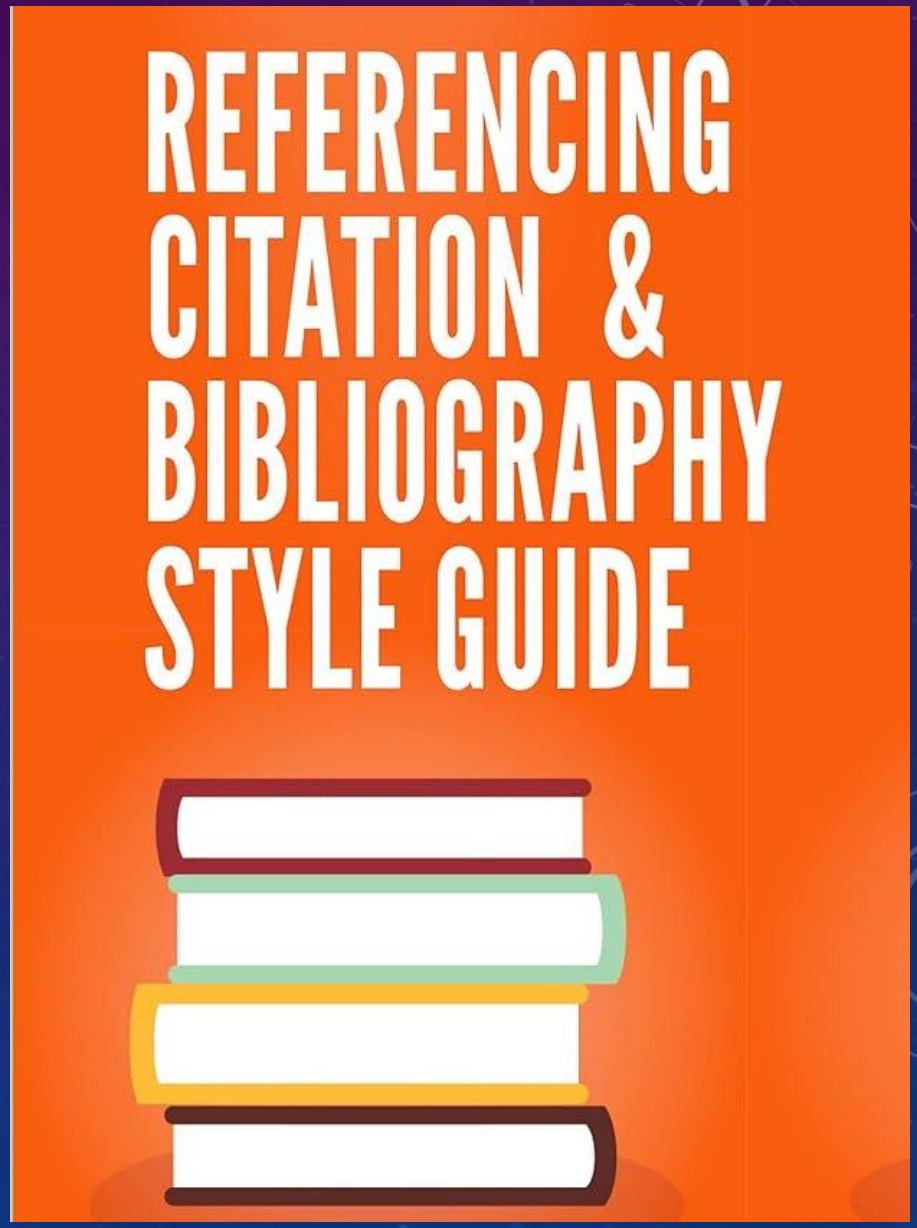
TOPIC

- How microbes play a role in your life
  - Includes all microbes not just microorganisms
- Choice of what you want your project format to be
  - Examples:
  - Research paper, video essay, powerpoint and lecture, poster, etc.



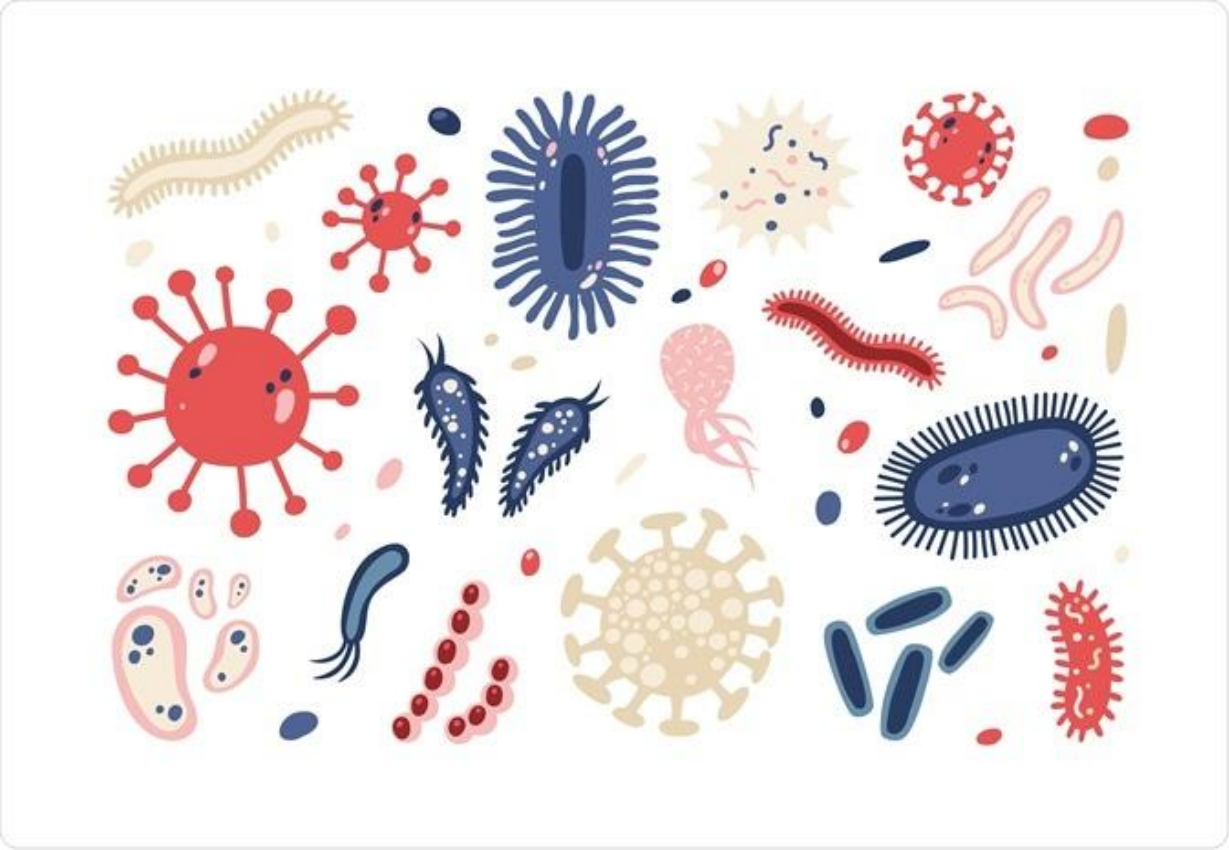
SOURCES

- Five scientific sources minimum
  - For projects outside of a research paper include a separate page with your full citations and annotated bibliography
- APA 7th edition citations
- In-text citations also needed



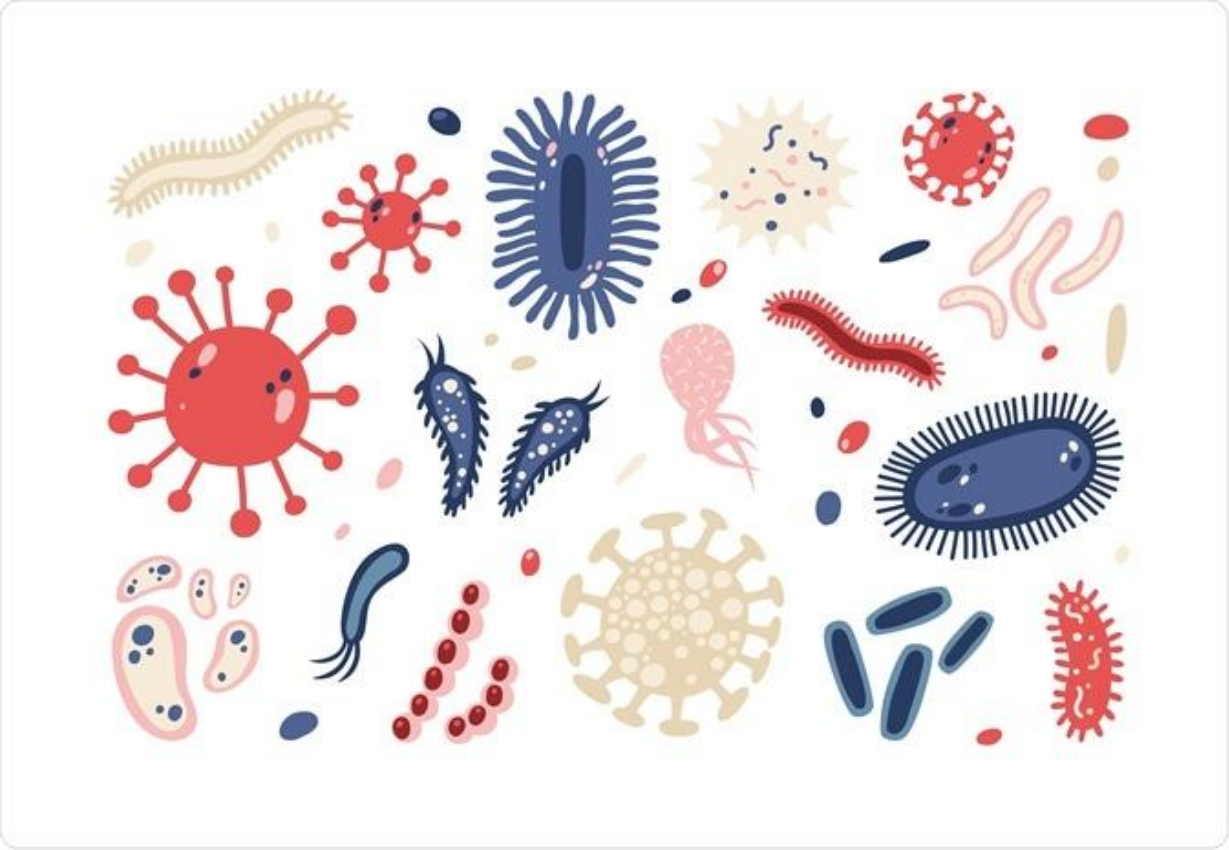
NECESSARY INCLUSIONS

- Scientific name of microbe(s)
- How those microbes directly impact life
  - Example:
  - *Penicillium camemberti* is utilized to make camembert cheese, camembert cheese is very popular



NECESSARY INCLUSIONS

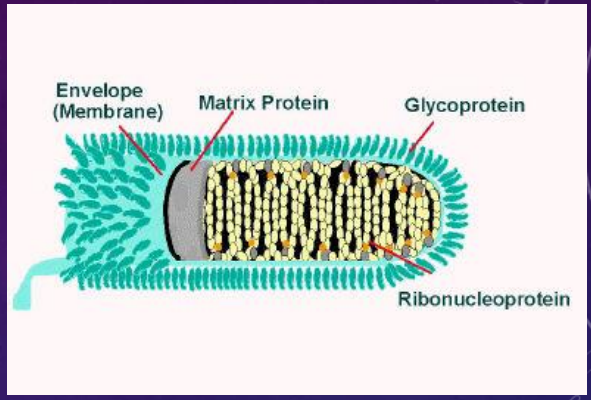
- Discussion of mechanism used in the microbe's impact
  - If a pathogen discuss pathogenesis and how the disease impacts the organism it is infecting
  - If not a pathogen, discuss the metabolic system being used to make the product

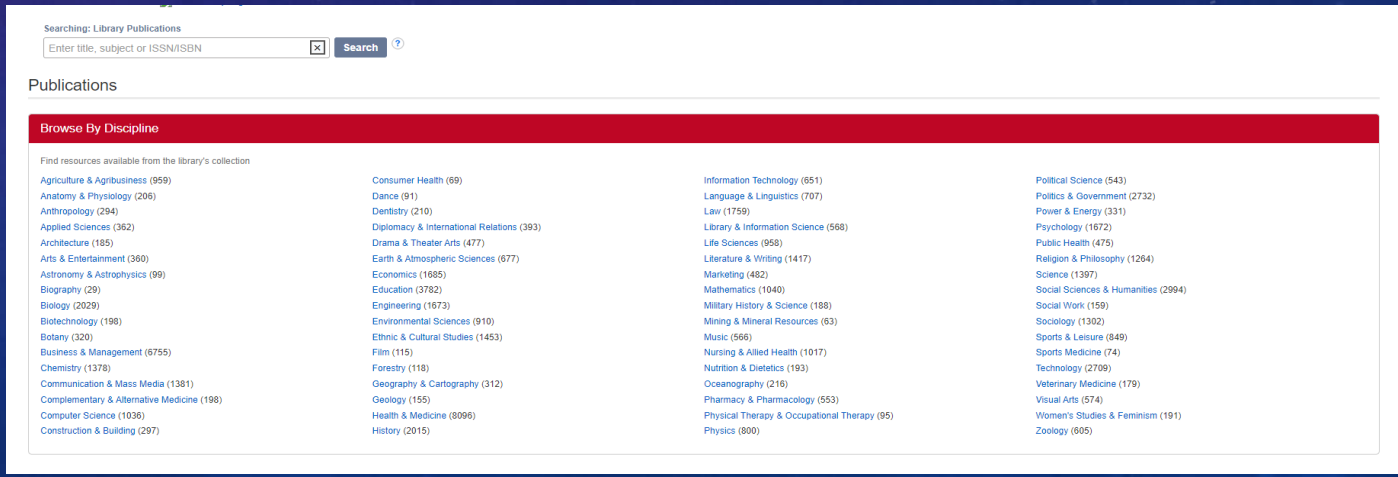


INTRODUCTION TO LITERATURE SEARCH

HOW TO START

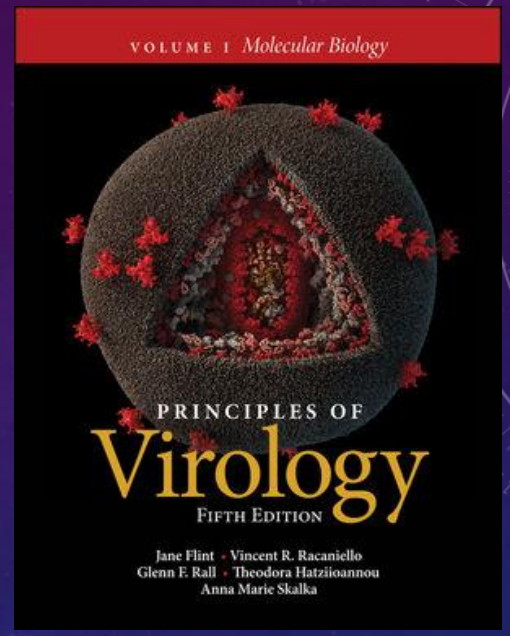
- Determine your topic.
  - Rabies / The Rabies Virus
- Choose your starting search site.
  - ScienceDirect
  - FSC Library Databases
    - Publication Search

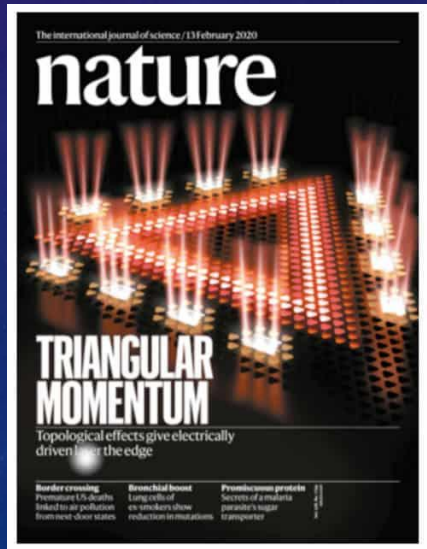




WHAT COUNTS?

- Peer Reviewed Literature
  - Textbooks
  - Articles
    - Research/Primary Source
    - Review





WHAT COUNTS?

- Research/Primary Source
  - Novel work
  - Methods and results focused
  - A novel mRNA rabies vaccine as a promising candidate for rabies post-exposure prophylaxis protects animals from different rabies viruses

Microbial Pathogenesis 185 (2023) 106425

Contents lists available at ScienceDirect

Microbial Pathogenesis

journal homepage: www.elsevier.com/locate/micpath

A novel mRNA rabies vaccine as a promising candidate for rabies post-exposure prophylaxis protects animals from different rabies viruses

Peng-Cheng Yu [a], Mo Dan [b,c], Ying He [a], Sheng-Li Meng [d], Han-Yu Yang [b,c], Xiaoye Su [b,c], Ya-Juan Wang [b,c], Lu Lv [b,c], Yu-Fei Sun [b,c], Xiao-Yan Tao [a], Qian Liu [a], Shu-qing Liu [a], Sheng-Li Bi [a,*], Wu-Yang Zhu [a,**]

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ARTICLE INFO

Keywords:
Rabies vaccine
RABV
RVNA
Immunogenicity
Protective capacity

ABSTRACT

Rabies, caused by the rabies virus (RABV), is the most fatal zoonotic disease. It is a neglected tropical disease which remains a major public health problem, causing approximately 59,000 deaths worldwide annually. Despite the existence of effective vaccines, the high incidence of human rabies is mainly linked to tedious vaccine immunisation procedures and the overall high cost of post-exposure prophylaxis. Therefore, it is necessary to develop an effective vaccine that has a simple procedure and is affordable to prevent rabies infection in humans. RABV belongs to the genus *Lyssavirus* and family *Rhabdoviridae*. Previous phylogenetic analyses have identified seven major clades of RABV in China (China I–VII), confirmed by analysing nucleotide sequences from both the G and N proteins.

This study evaluated the immunogenicity and protective capacity of SYS6008, an mRNA rabies vaccine expressing rabies virus glycoprotein, in mice and cynomolgus macaques.

We demonstrated that SYS6008 induced sufficient levels of rabies neutralising antibody (RVNA) in mice. In addition, SYS6008 elicited strong and durable RVNA responses in vaccinated cynomolgus macaques. In the pre-exposure prophylaxis murine model, one or two injections of SYS6008 at 1/10 or 1/30 of dosage provided protection against a challenge with a 30-fold LD_{50} of rabies virus (China I and II clades). We also demonstrated that in the post-exposure prophylaxis murine model, which was exposed to lethal rabies virus (China I–VII clades) before vaccination, one or two injections of SYS6008 at both 1/10 and 1/30 dosages provided better protection against rabies virus challenge than the immunization by five injections of commercial vaccines at the same dosage. In addition, we proved that SYS6008-induced RVNAs could neutralise RABV from the China I–VII clades. Finally, 1/10 of the dosage of SYS6008 was able to stimulate significant RABV-G specificity in the T cell response. Furthermore, we found that SYS6008 induced high cellular immunity, including RABV-G-specific T cell responses and memory B cells.

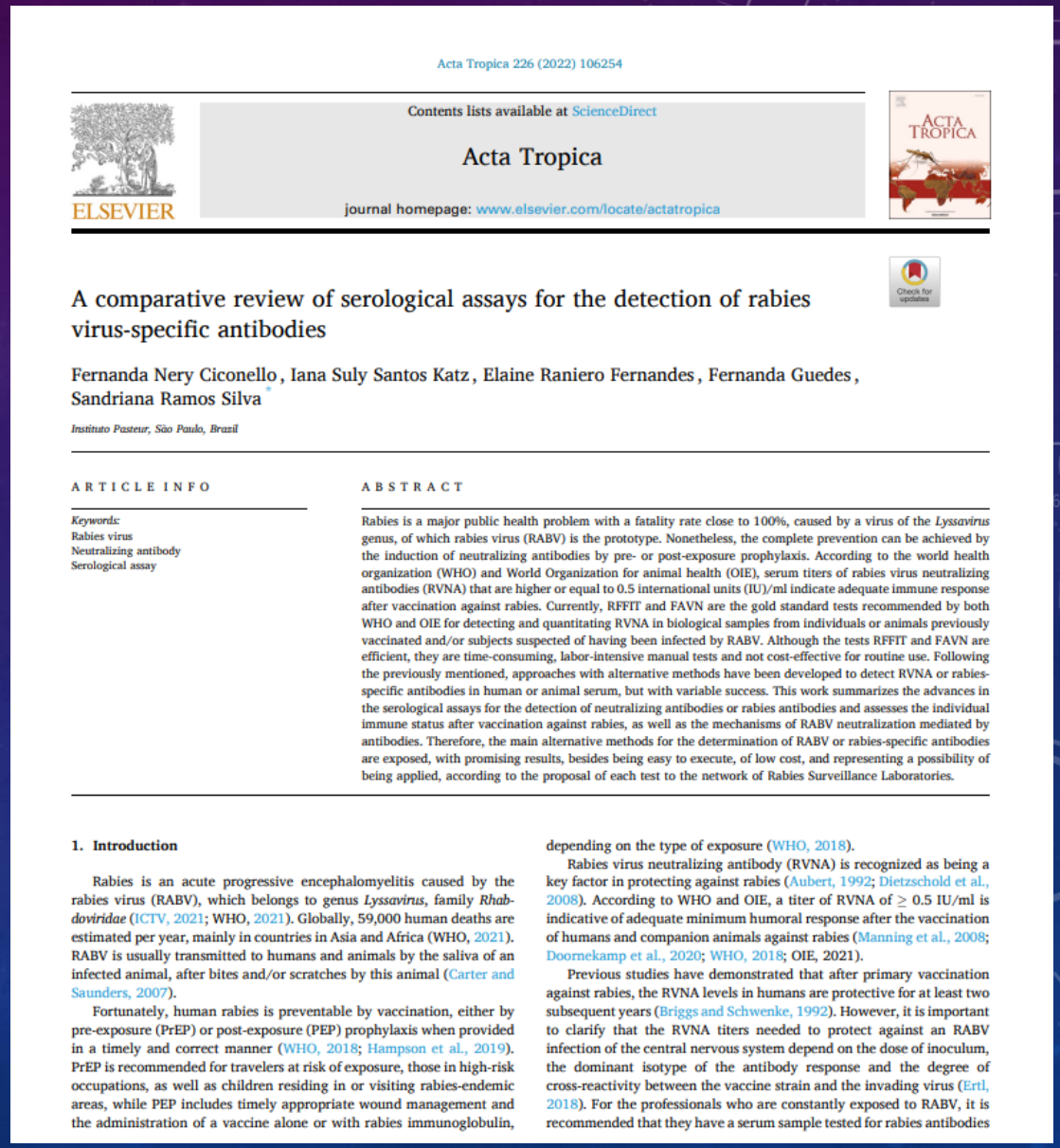
Our results imply that the SYS6008 rabies vaccine, with a much simpler vaccination procedure, better immunogenicity, and enhanced protective capacity, could be a candidate vaccine for post-exposure prophylaxis of rabies infections.

1. Introduction

Rabies is the most lethal zoonotic disease, which is caused by the rabies virus (RABV) that belongs to the genus *Lyssavirus* and family *Rhabdoviridae* [1,2]. As a neglected tropical disease (NTD), rabies is a serious global public health problem, with 99 % of rabies-related deaths occurring in low- and middle-income countries where dog-mediated

WHAT COUNTS?

- Review
  - Compilation/Analysis
  - Drawing new conclusions
  - A comparative review of serological assays for the detection of rabies virus-specific antibodies



Acta Tropica 226 (2022) 106254

Contents lists available at ScienceDirect

Acta Tropica

journal homepage: www.elsevier.com/locate/actatropica

A comparative review of serological assays for the detection of rabies virus-specific antibodies

Fernanda Nery Ciconello, Iana Suly Santos Katz, Elaine Raniero Fernandes, Fernanda Guedes, Sandriana Ramos Silva *

Instituto Pasteur, São Paulo, Brazil

ARTICLE INFO

Keywords:
Rabies virus
Neutralizing antibody
Serological assay

ABSTRACT

Rabies is a major public health problem with a fatality rate close to 100%, caused by a virus of the *Lyssavirus* genus, of which rabies virus (RABV) is the prototype. Nonetheless, the complete prevention can be achieved by the induction of neutralizing antibodies by pre- or post-exposure prophylaxis. According to the world health organization (WHO) and World Organization for animal health (OIE), serum titers of rabies virus neutralizing antibodies (RVNA) that are higher or equal to 0.5 international units (IU)/ml indicate adequate immune response after vaccination against rabies. Currently, RFFIT and FAVN are the gold standard tests recommended by both WHO and OIE for detecting and quantitating RVNA in biological samples from individuals or animals previously vaccinated and/or subjects suspected of having been infected by RABV. Although the tests RFFIT and FAVN are efficient, they are time-consuming, labor-intensive manual tests and not cost-effective for routine use. Following the previously mentioned, approaches with alternative methods have been developed to detect RVNA or rabies-specific antibodies in human or animal serum, but with variable success. This work summarizes the advances in the serological assays for the detection of neutralizing antibodies or rabies antibodies and assesses the individual immune status after vaccination against rabies, as well as the mechanisms of RABV neutralization mediated by antibodies. Therefore, the main alternative methods for the determination of RABV or rabies-specific antibodies are exposed, with promising results, besides being easy to execute, of low cost, and representing a possibility of being applied, according to the proposal of each test to the network of Rabies Surveillance Laboratories.

1. Introduction

Rabies is an acute progressive encephalomyelitis caused by the rabies virus (RABV), which belongs to genus *Lyssavirus*, family *Rhabdoviridae* (ICTV, 2021; WHO, 2021). Globally, 59,000 human deaths are estimated per year, mainly in countries in Asia and Africa (WHO, 2021). RABV is usually transmitted to humans and animals by the saliva of an infected animal, after bites and/or scratches by this animal (Carter and Saunders, 2007).

Fortunately, human rabies is preventable by vaccination, either by pre-exposure (PrEP) or post-exposure (PEP) prophylaxis when provided in a timely and correct manner (WHO, 2018; Hampson et al., 2019). PrEP is recommended for travelers at risk of exposure, those in high-risk occupations, as well as children residing in or visiting rabies-endemic areas, while PEP includes timely appropriate wound management and the administration of a vaccine alone or with rabies immunoglobulin, depending on the type of exposure (WHO, 2018).

Rabies virus neutralizing antibody (RVNA) is recognized as being a key factor in protecting against rabies (Aubert, 1992; Dietzschold et al., 2008). According to WHO and OIE, a titer of RVNA of $\geq$ 0.5 IU/ml is indicative of adequate minimum humoral response after the vaccination of humans and companion animals against rabies (Manning et al., 2008; Doornekamp et al., 2020; WHO, 2018; OIE, 2021).

Previous studies have demonstrated that after primary vaccination against rabies, the RVNA levels in humans are protective for at least two subsequent years (Briggs and Schwenke, 1992). However, it is important to clarify that the RVNA titers needed to protect against an RABV infection of the central nervous system depend on the dose of inoculum, the dominant isotype of the antibody response and the degree of cross-reactivity between the vaccine strain and the invading virus (Ertl, 2018). For the professionals who are constantly exposed to RABV, it is recommended that they have a serum sample tested for rabies antibodies

WHAT DOES NOT COUNT?

- Search Engines
- Non-peer reviewed cites / documents
  - WebMD
  - Blog posts
  - Wikipedia*

WHAT DOES NOT COUNT?

- Wikipedia
  - Cite their sources at the end of articles
  - Good way to start if you are stuck

References

1. ^ a b c d e f g h i j k l m n o p q r s t u "Rabies Fact Sheet N°99". *World Health Organization*. July 2013. Archived from the original on 1 April 2014. Retrieved 28 February 2014.
2. ^ "Rabies – Symptoms and causes". *Mayo Clinic*. Retrieved 9 April 2018.
3. ^ "Rabies". *Mayo Clinic*. Retrieved 5 October 2023.
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5. ^ "Rabies diagnosis and treatment=27 June 2023". *Mayo clinic*.
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9. ^ "Animal bites and rabies". *Johns Hopkins Medicine*. 27 February 2020.
10. ^ a b c d Cotran RS, Kumar V, Fausto N (2005). *Robbins and Cotran Pathologic Basis of Disease* (7th ed.). Elsevier/Saunders. p. 1375. ISBN 978-0-7216-0187-8.

REFERENCE CITATIONS

- Full reference
- Different styles
  - MLA
  - Chicago
  - **APA**
  - Nature

REFERENCE CITATIONS

- APA
  - (Ciconello et al., 2021)
  - Ciconello, F.N., Katz, S.I.S., Fernandes, E.R., Guedes, F., & Silva, S.R. (2021). A comparative review of serological assays for the detection of rabies virus-specific antibodies. *Acta Tropica, 226*(2022), 106254-106257. https://www.sciencedirect.com/science/article/pii/S0001706X21004320
- Nature
  - Subscript number in order of appearance
  - Ciconello, F.N., Katz, S.I.S., Fernandes, E.R., Guedes, F., & Silva, S.R. (2021). A comparative review of serological assays for the detection of rabies virus-specific antibodies. *Acta Tropica, **226.*** https://www.sciencedirect.com/science/article/pii/S0001706X21004320 (2022)

LITERATURE SEARCH HOMEWORK

- Choose a disease / microbe (bacteria, virus)
- Find one peer-reviewed scientific source related to your chosen topic
- Complete the Canvas Literature Search assignment by Friday, Sept. 5th