Title: Toxoplasmosis vaccine: advantages and challenges

Presenter: Dr. Reza Saberi

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Introduction

Toxoplasmosis is a zoonotic disease caused by the parasite *T. gondii*

An effective vaccine can significantly benefit both **medical** and **veterinary** fields.

Human Vaccine Necessity:

- Reduce infection rates and mortality.

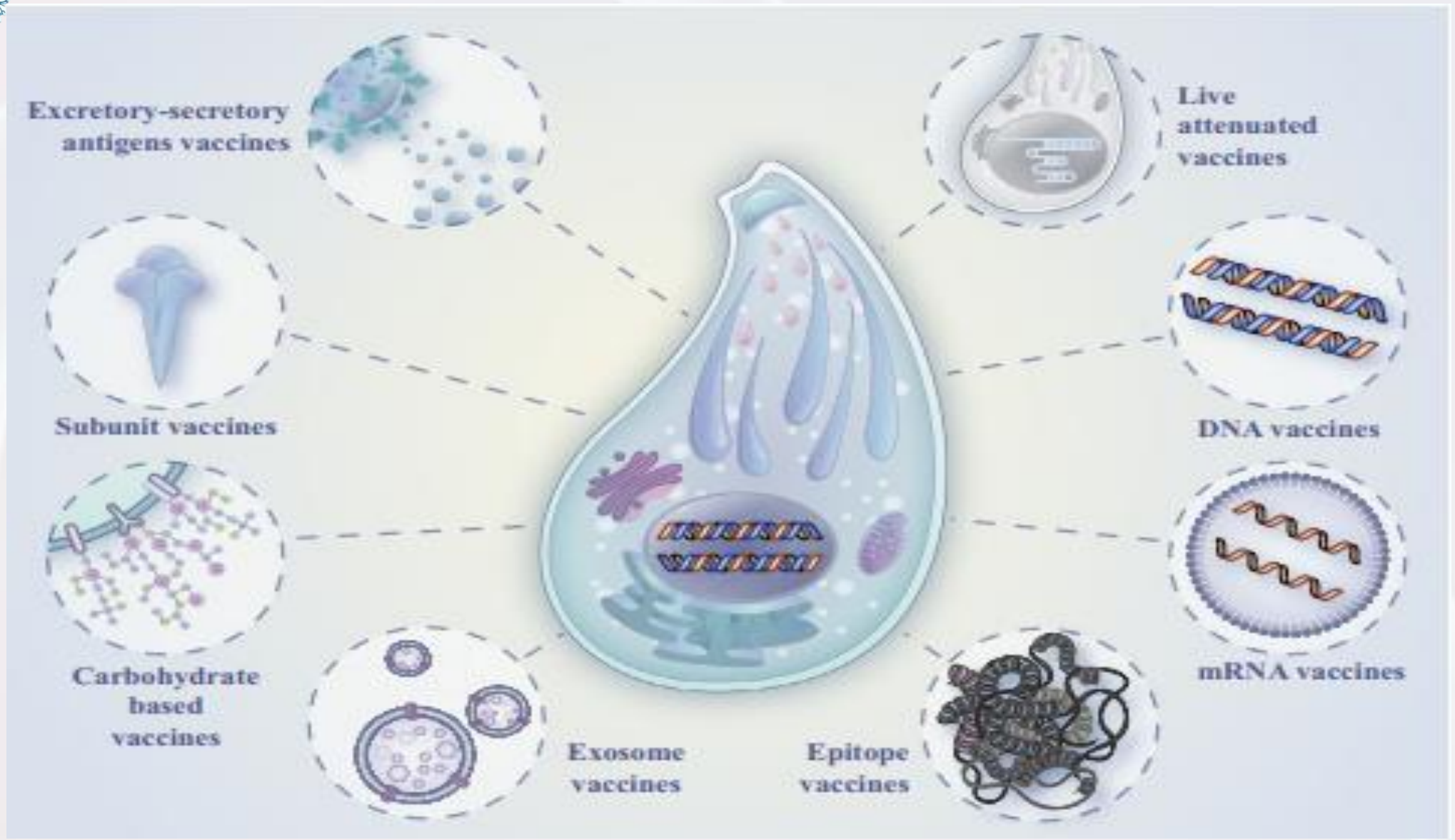
- Reduce the burden of chronic cases requiring long-term care.

Benefits of Animal Vaccines:

- Enhance reproductive health in livestock.

- Minimize health risks associated with consuming contaminated meats.

Types of Vaccines for Toxoplasmosis.



Types of Vaccines for Toxoplasmosis.

1. Vaccines based on excretory-secretory

- Antigens Excretory-secretory antigens (ESA) produced by tachyzoites account for most circulating antigens in the serum and cerebrospinal fluid of the host.
- ESA immunization can improve animal survival rates by reducing parasitemia of highly virulent strains and controlling infections.
- Subcutaneous injection of ESA reduced the formation of tissue cysts in pigs after *T. gondii* infection compared to the control group.

Types of Vaccines for Toxoplasmosis.

2. Live Attenuated Vaccines (Toxovax®)

- Derived from the S48 strain of *T. gondii*.

- Provides protection for up to 18 months against abortion due to *T. gondii* infection.

- Induces immune response in sheep to prevent abortion and limit parasite spread.

- Inoculated ewes develop antibodies that help control the parasite upon exposure.

Toxovax®

Limitations:

- Limitations include a short shelf life and the potential for reversion to virulence.
- Does not prevent transmission to humans.
- The effect on reducing tissue cysts in contaminated meat is unclear and requires further research.

T-263 Strain

- T-263 Strain: This strain does not form cysts in intermediate hosts and has shown an 80% reduction in oocyst formation in cats post-infection.

However, it was **never commercially** released despite its promising results.

Types of Vaccines for Toxoplasmosis.

3. Inactivated Vaccines

These vaccines use killed parasites to induce an immune response.

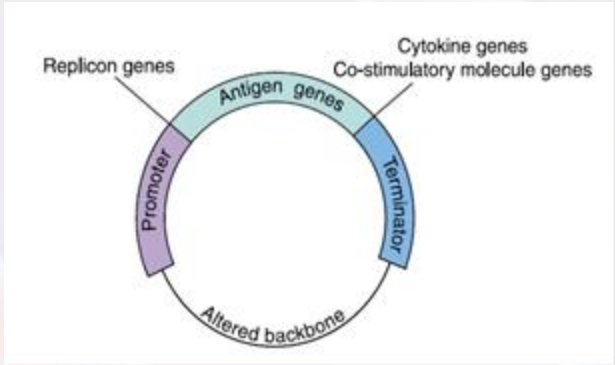
However, they have generally shown limited success compared to live attenuated vaccines.

Types of Vaccines for Toxoplasmosis.

4. DNA Vaccines

These vaccines involve introducing plasmid DNA encoding *T. gondii* antigens into the host, prompting an immune response.

Various studies have shown promising results in animal models, but they are still largely experimental.



Advantages:

Safety and Stability: non-infectious and do not require cold-chain storage.

Cost-Effectiveness.

Flexibility: designed and modified based on emerging strains or new research findings.

Challenges:

Weak Immune Responses: strong immune responses in animal models, weaker responses in higher primates and humans.

Safety: the risk of plasmid integration into the host genome is low, it remains a concern.

Types of Vaccines for Toxoplasmosis.

5. Subunit Vaccines

These contain purified proteins or peptides derived from the parasite to stimulate an immune response without using live pathogens.

	Key Antigens and Candidates
	HSP 70
	GRA1, GRA2, GRA4, GRA5,GRA6
Systematic review studies	ROP1, **ROP2**, ROP4, **ROP9**, **ROP16**, ROP18
	MIC1, **MIC3, MIC4, MIC13**
	SAG1, SAG2, SAG3

Advantages:

Safety: lower risk of infection compared to live attenuated vaccines.

Targeted Immune Response: target specific stages of the parasite or immune pathways.

Challenges:

Immunogenicity: Require adjuvants to boost their effectiveness,.

Complexity of Antigen Selection.

Types of Vaccines for Toxoplasmosis.

6. Epitope-based Vaccines

These vaccines focus on specific epitopes (the parts of antigens recognized by the immune system) and can be designed to minimize risks associated with traditional vaccines.

They are still under development but offer a promising avenue for future research.

1. **Multi-Epitope Constructs**: Recent studies have designed multi-epitope vaccines incorporating B- and T-cell epitopes from various *T. gondii* proteins, such as ROP2, MIC3, and GRA7.
2. **Immunoinformatics** Approaches: Advanced computational methods have been employed to predict the most effective epitopes. For instance, a study identified 14 linear B-cell epitopes and multiple T-cell epitopes from T. gondii membrane proteins, ensuring broad population coverage for potential vaccine candidates[3][4].

3. **Chimeric Antigens**: Some vaccine designs utilize chimeric antigens that combine multiple epitopes linked by flexible linkers.

Efficacy and Immune Response

Induction of Immune Responses: Epitope-based vaccines have shown the ability to induce both humoral (antibody-mediated) and cellular immune responses.

For example, a candidate vaccine called TgVax452 demonstrated significant activation of specific antibodies and cytokines in preclinical models.

Stability and Safety: The designed vaccine constructs have been evaluated for stability and safety using molecular dynamics simulations and immunogenicity assessments.

These evaluations suggest that the epitope-based vaccines are non-toxic and capable of triggering primary immune responses effectively.

Challenges Ahead

Several challenges remain in developing epitope-based vaccines for toxoplasmosis:

1. **Validation of Efficacy: Most candidate vaccines require extensive laboratory testing to confirm their effectiveness in vivo, as current studies primarily rely on computational predictions.**
2. **Complexity of the Parasite: The intricate life cycle of T. gondii poses challenges in ensuring comprehensive protection across different stages of infection, necessitating a focus on stage-specific antigens.**

Types of Vaccines for Toxoplasmosis.

7. mRNA Vaccines

mRNA vaccines work by introducing a piece of genetic material that instructs cells to produce a specific protein from the pathogen, thereby eliciting an immune response.

mRNA Vaccines

- Self-amplifying RNA vaccines, such as **RREP-NTPase-II**, can induce robust immune responses in mice.
- These vaccines led to high levels of IgG antibody production and increased levels of IFN-γ, contributing to significant reductions in parasite load in the brain.
- Novel mRNA vaccines like **TGGT1_216200 and TGGT1_278620**, both delivered via lipid nanoparticles (LNP).

Challenges and Future Directions

Currently, there are no approved mRNA vaccines specifically for human use against toxoplasmosis, although several candidates are under investigation.

The complexity of *T. gondii* 's life cycle and its ability to evade immune responses complicate vaccine development.

Types of Vaccines for Toxoplasmosis.

8. Nanoparticle Vaccines

Utilize nanoparticles to deliver antigens more effectively and enhance the immune response.

This approach is still experimental but shows potential for improving vaccine efficacy against *T. gondii*.

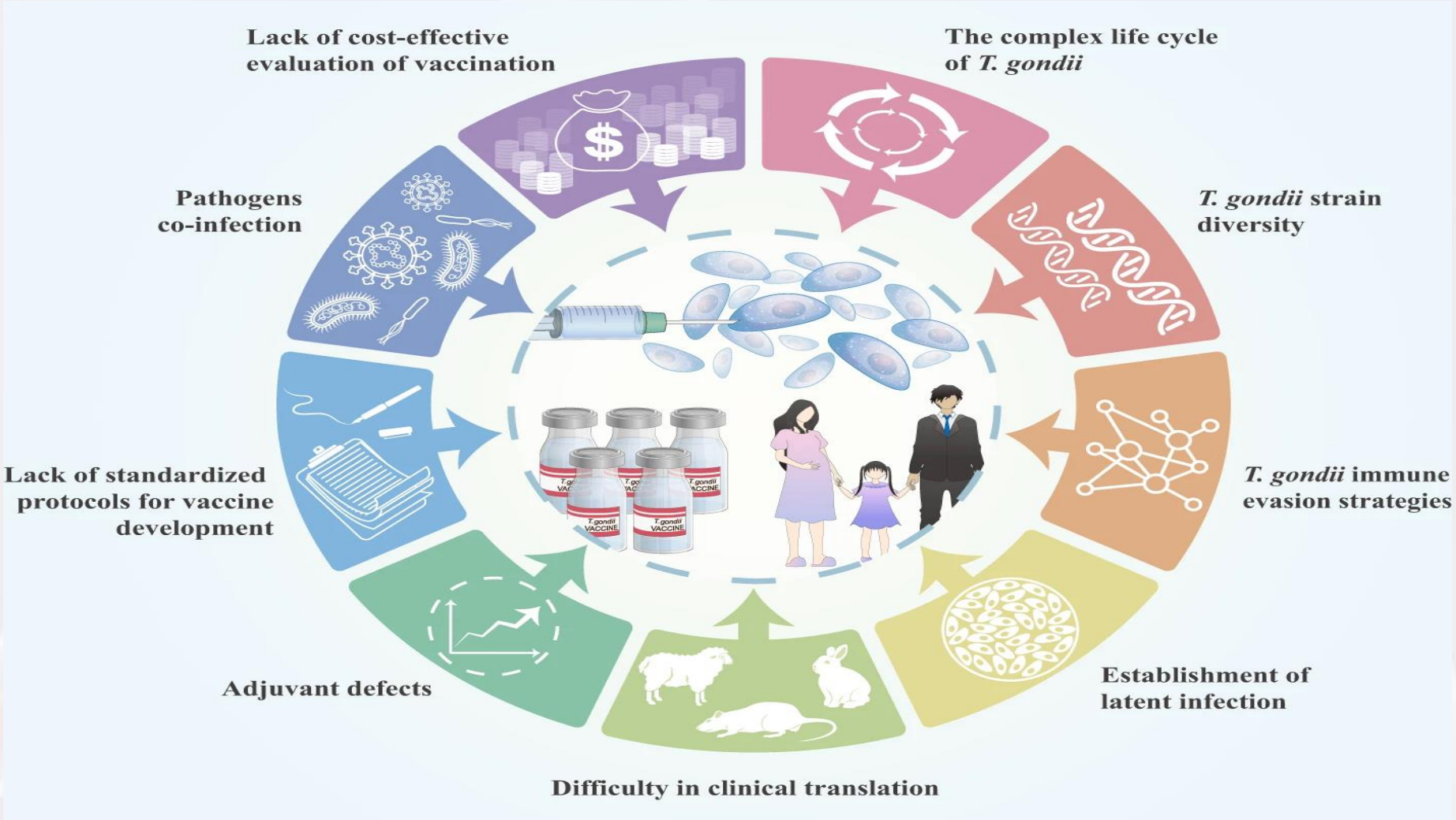
1. **Polymeric Nanoparticles:** These are often made from biodegradable materials and can encapsulate antigens effectively.

2. **Lipid Nanoparticles (LNPs):** LNPs have been used to deliver mRNA vaccines targeting T. gondii antigens.

3. **Self-Assembling Protein Nanoparticles:** These nanoparticles can present multiple epitopes simultaneously, promoting robust T cell activation.

They have been shown to activate both CD4+ and CD8+ T cells, which are crucial for effective immunity against the parasite.

Conclusion…


Lack of cost-effective evaluation of vaccination
The complex life cycle of T. gondii
Pathogens co-infection
T. gondii strain diversity
Lack of standardized protocols for vaccine development
T. gondii immune evasion strategies
Adjuvant defects
Establishment of latent infection
Difficulty in clinical translation

Thank you for your attention