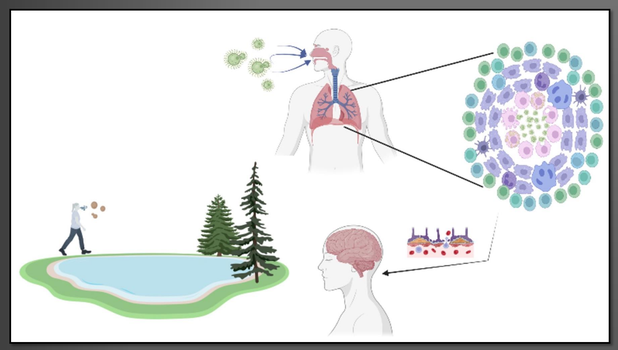
Evaluation of vaccine-mediated immune responses against *Cryptococcus neoformans*

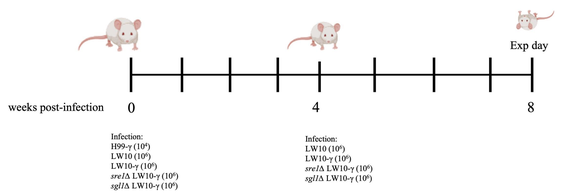
Christine Sayegh, Natalia Castro Lopez, Floyd L. Wormley, Jr.
Department of Biology, Texas Christian University, Fort Worth, TX, USA

Introduction

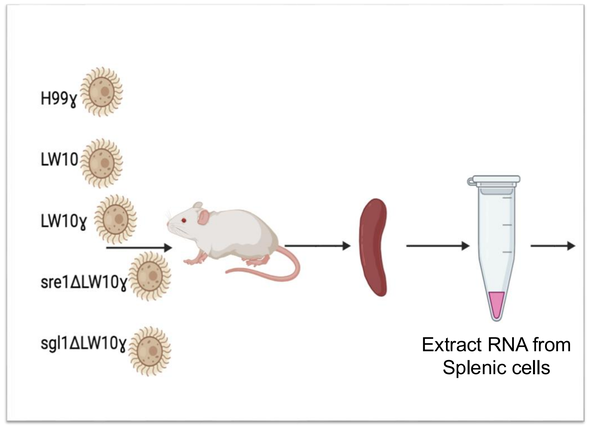
- ***Cryptococcus neoformans*** is a fungal pathogen that affects the lungs and CNS, especially in those with impaired T-cell function (e.g., AIDS, immunosuppression).
- **No current vaccines** and limited antifungal treatments available.
- Our lab developed **H99γ**, a strain of *C. neoformans* expressing mouse IFN-γ, which provides **protective immunity in mouse models**.
- **Goal**: Use H99γ variants to study the immune response and develop new therapeutic strategies.
- This study **evaluates the ability of new vaccine strains to induce protective immunity against *C. neoformans***.

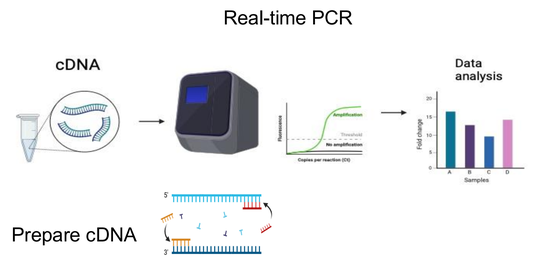


Experimental Methods

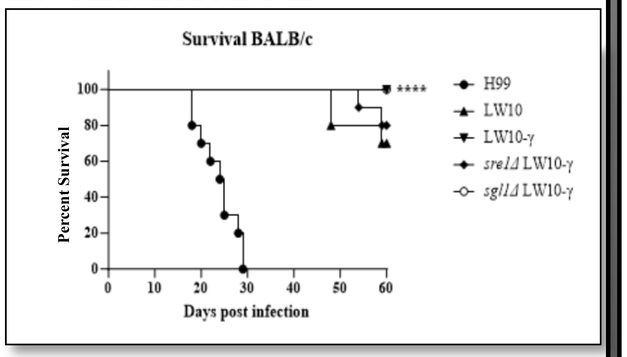


Experimental Methods

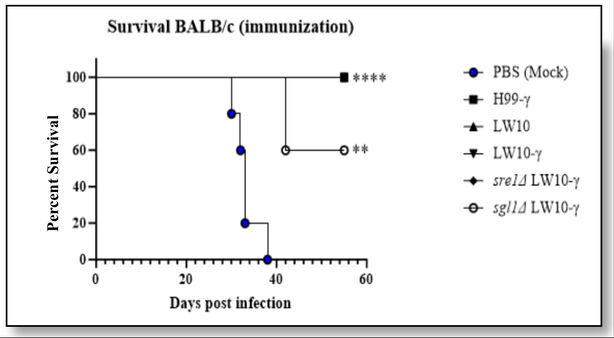




BALB/c mice infected with LW10γ KOs strains shows increased survival



Immunization with LW10γ KOs leads to an increased survival



IL-2 and NOS2 is downregulated in the lungs of immunized mice

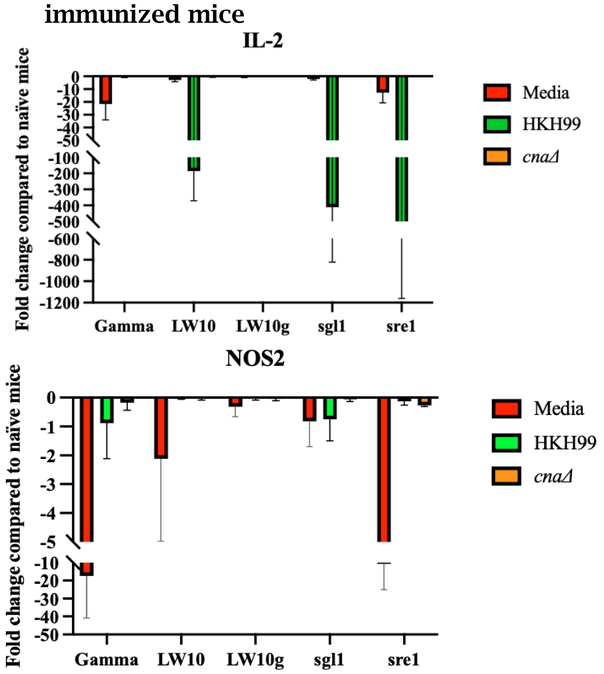


Figure 1. Leukocytes were isolated from the lungs after immunization and cultured with either HKH99, cnaΔ, or media alone for 24 hr, after which cells were taken to isolate RNA and perform qPCR. Real-time PCR analysis of each transcript was normalized to GAPDH. (A) IL-2, (B) NOS2 gene expression.

Findings and Future directions

Gene Expression Analysis:

- Measured IL-2 and NOS2 in lungs of mice immunized with LW10 strain variants.
- Lung cells exposed to HKH99 or *cnaΔ* post-isolation.
- IL-2 downregulated >5-fold in HKH99-exposed cells from LW10, LW10-γ-sgl1Δ, and LW10-γ-sre1Δ groups.
- NOS2 expression decreased in untreated lung cells.
- No increase in IL-2 or NOS2 observed.

Ongoing & Next Steps:

- Will analyze additional Th-1/Th-2 markers for links to survival and protection.
- Plan to examine macrophages and dendritic cells for targeted gene expression.
- Will assess genes linked to:
  - Protection: IFN-γ, TNF-α, STAT-1
  - Non-protection: ARG1, IL-4, IL-10

Future Work:

- Test top vaccine in CD4+ T-cell-deficient mice (immunocompromised model).
- If effective and safe, progress to clinical trials.

Acknowledgments

- We would like to thank Dr. Yeqi Li and Dr. Xiaorong Lin from UGA.
- This work was supported by Dr. Wormley's TCU start-up funds.