Parasitic Pathogenesis of *Toxoplasma gondii*

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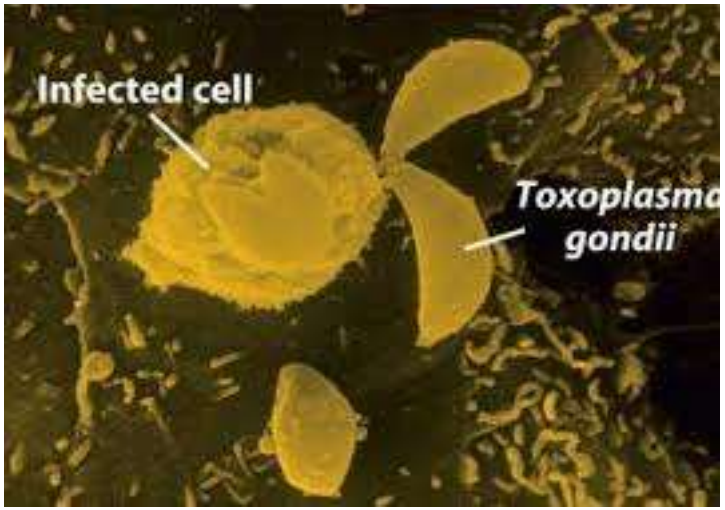
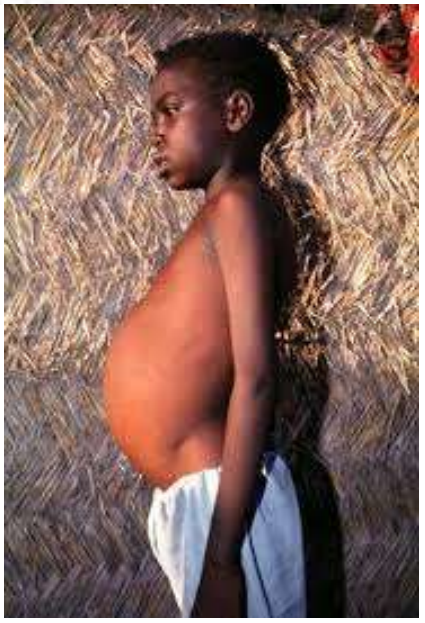
Background on *T. gondii*

- Protozoan parasite
- Infects warm blooded animals via:
  - Undercooked meat
  - Food or water contaminated with cat feces
  - Blood transfusion
  - Organ transplantation
  - Transplacentally from mother to fetus
- **Chronic infection** with cysts typically found in skeletal muscle, myocardium, brain, and eyes
- Two life stages:
  - Tachyzoite
    - Fast growing, disseminating, acute stage
  - Bradyzoite
    - Slow growing, cyst forming, chronic stage

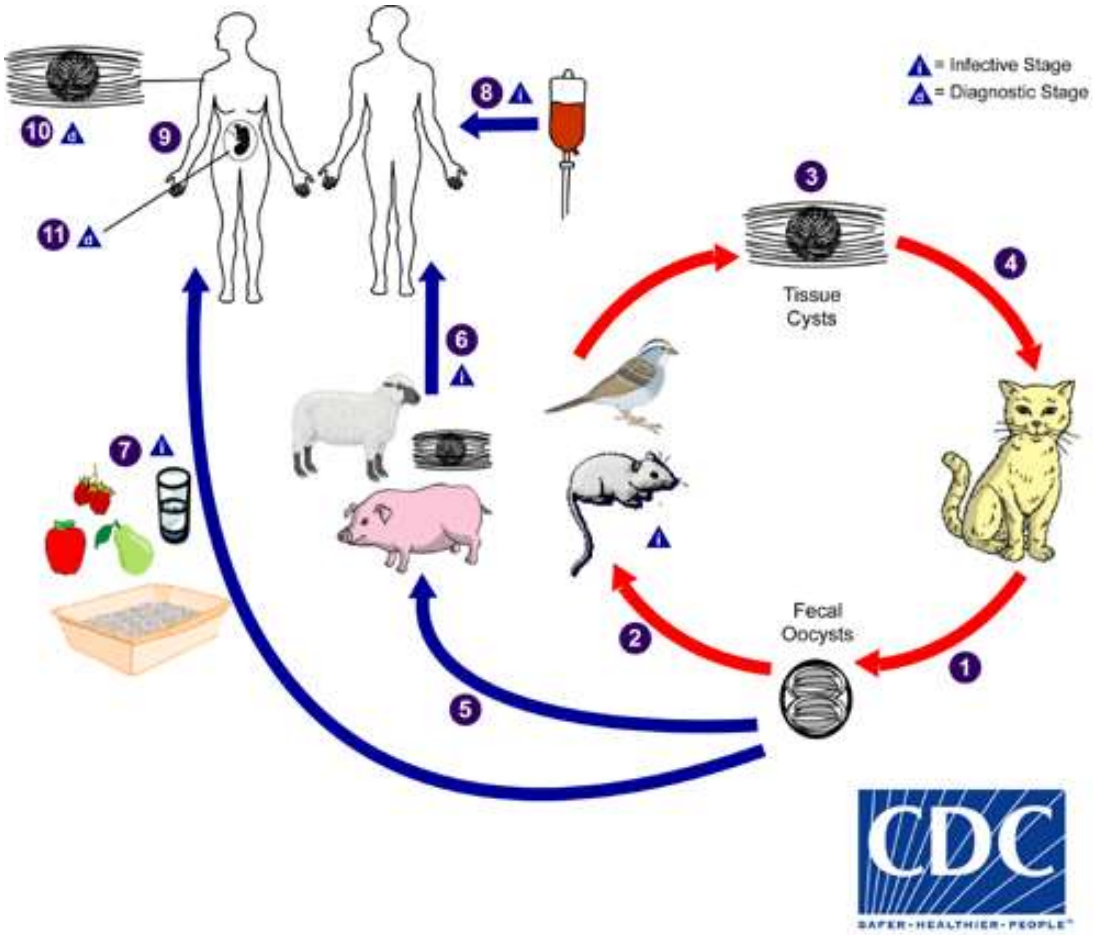


Background on *T. gondii*

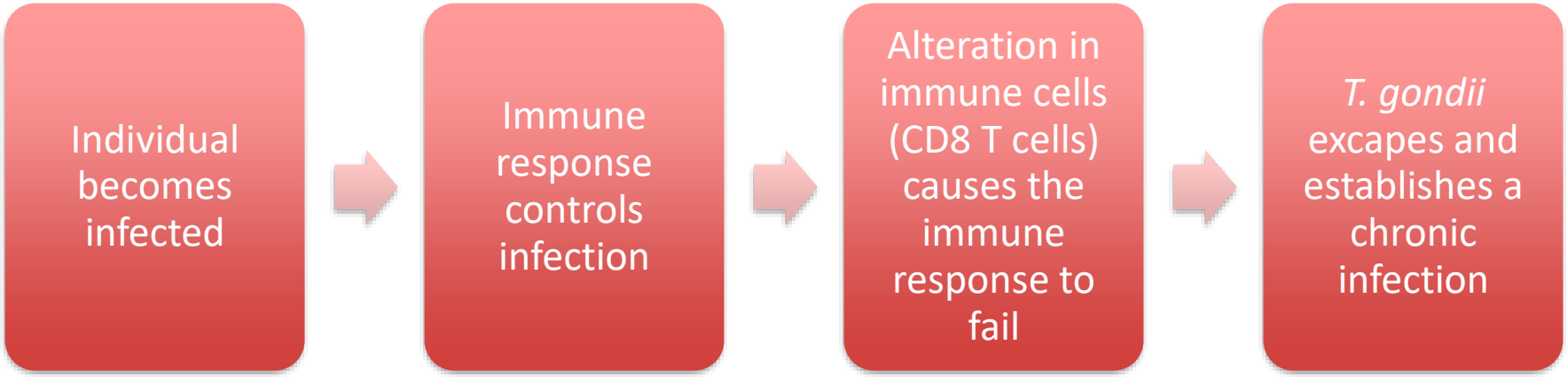
- Worldwide epidemic
  - > 60 million people infected in the U.S.
- Symptoms
  - Most people unaware of infection
  - Swollen lymph nodes
  - Muscle aches
  - Brain damage: seizures, encephalitis, brain lesions, etc.
  - Lung problems
  - Blurred vision
  - Stillbirth or miscarriage
- Immunologically compromised individuals are at greatest risk
  - Infants
  - Individuals with AIDS



Background on *T. gondii*



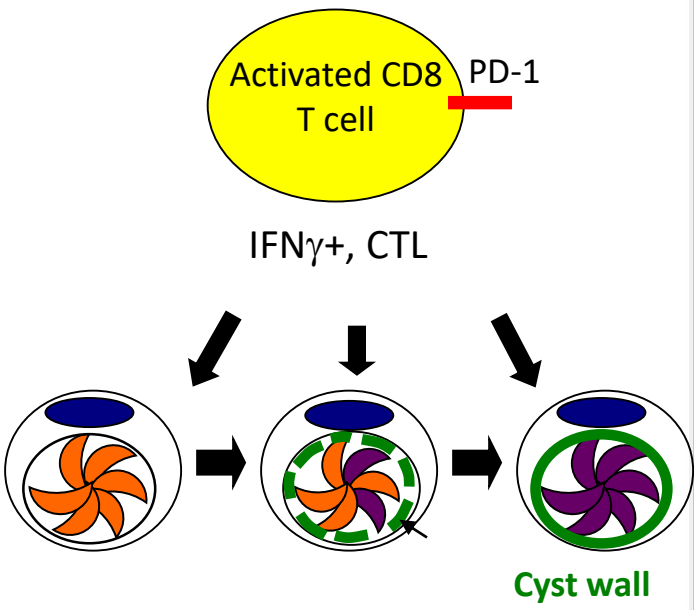
T. gondii Establishes a Chronic Infection



Loss of CD8 T Cells means loss of…

- Host defense against intracellular pathogens that live or produce in the cell's cytosol
- Immunological memory

What is happening to these CD8 T Cells?



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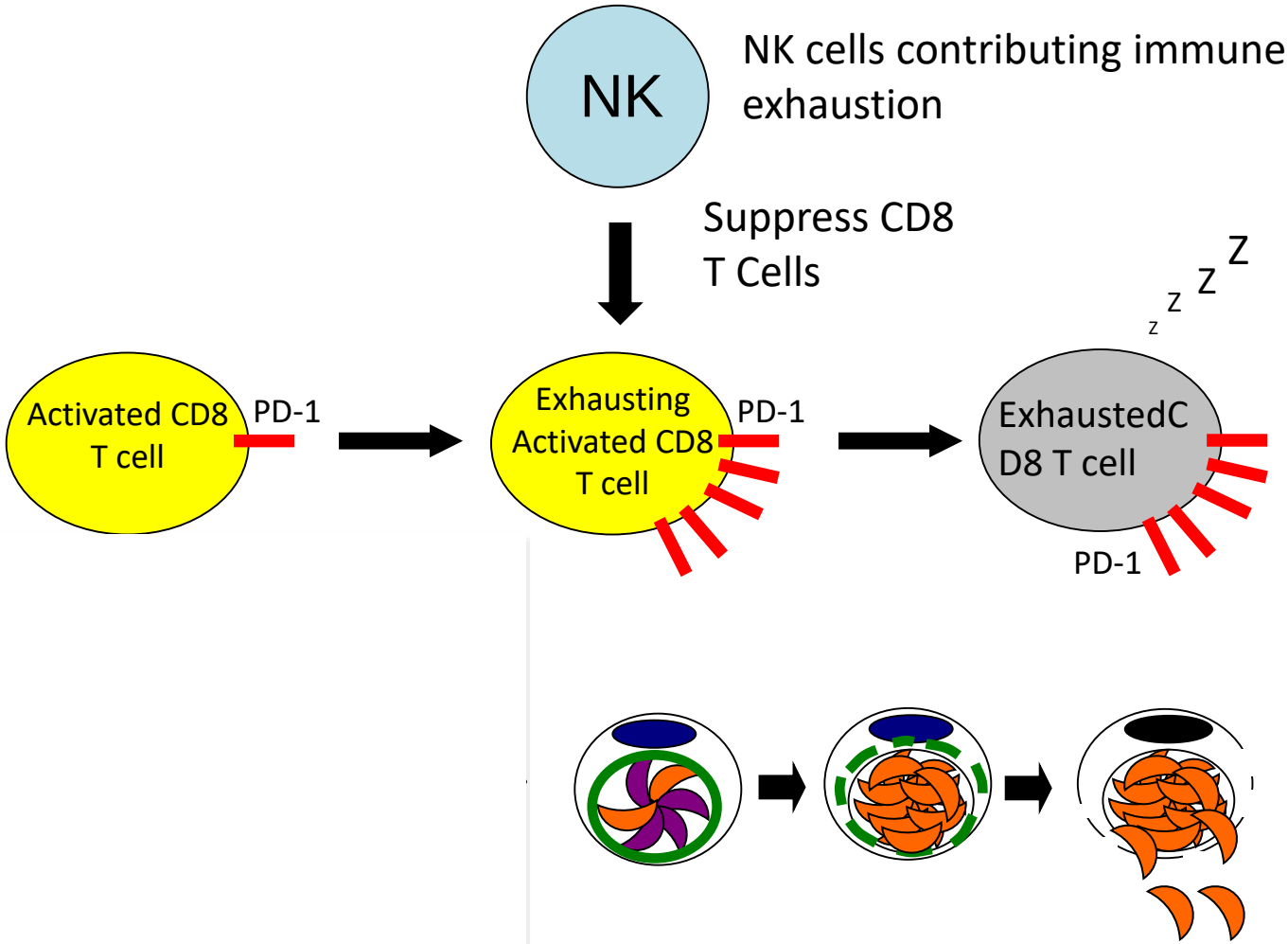
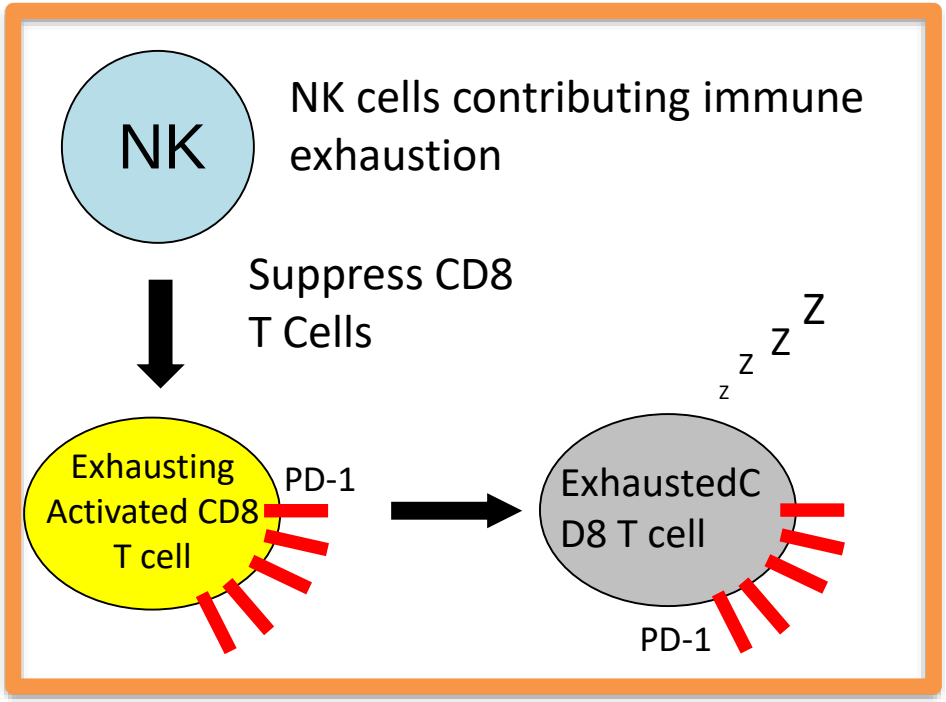


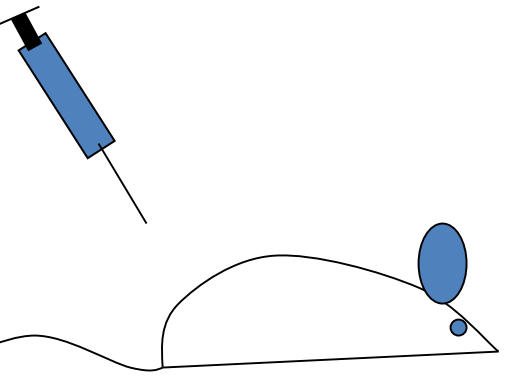
Experimental Focus

Specific Aim 1: Determine if NK cells suppress CDB T cell function, thereby promoting immune exhaustion.

Specific Aim 2: Define the mechanism by which NK cells contribute to immune exhaustion.

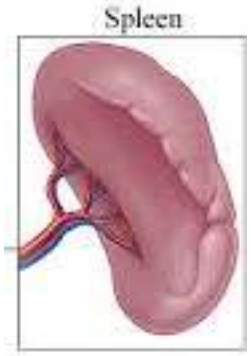


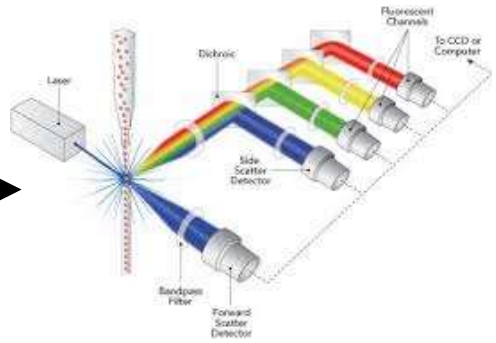
Experimental methods



Infected mice with
T. gondii

5 weeks post infection, administer NK cell blocking antibody for two weeks





Flow cytometry

Findings

After NK cell depletion:

- CD8 T- cells were at a higher number
- The overall health of the mice improved, increasing the life span

Hypotheses for NK mode of action

1. NK cells are suppressing CD8 T cell function by blocking IFNγ+, CTL
2. NK cells are indirectly suppressing CD8 T cells by blocking other immune cells (APCs)

3. NK cells are killing the CD8 T cells

Significance of this research

- Potential cure for the millions infected with *T. gondii*
- Applicable to other chronic infections
- Better medical treatment of cancerous growths, which NK cells help regulate

Acknowledgments

<u>UW Gigley Lab:</u>
Dr. Jason Gigley
Daria Ivanova
David Donley
Ryan Krempels
Steve Denton
Kaitlyn Weitzman
Sari Mayhue
David Stephenson
David Rach
Tyler Graham

<u>Funding</u>
INBRE

Questions?

Thank you for coming!!