Development of PDL1-Targeted Methotrexate-Loaded Nanoparticles for Treatment of Gestational Neoplasia

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About Me

- Molecular Biology Major; Chemistry and Medical Physics Minor

- Involved in the DU Undergraduate Research Journal, University Honors Program, and Phi Beta Kappa

- Intended to pursue a PhD in molecular biology/biochemistry

- Hobbies: Skiing, Golf, Hiking, Florist, and Gardening

# What is Gestational Trophoblastic Neoplasia?

- A group of rare cancers that arise from abnormal placental tissues

- Cancers arise from hydatidiform moles, miscarriages, ectopic pregnancies, or after various stages of pregnancy

- Cancers include invasive mole, choriocarcinoma, placental site trophoblastic tumor, and epithelioid trophoblastic tumor

Current Treatment Options for Malignant Gestational Trophoblastic Neoplasia

- Chemotherapy (methotrexate)

- 25-69% of patients undergo methotrexate resistance, making methotrexate treatment ineffective

- Alternative drug treatments are effective, but highly toxic and often result in sacrificing fertility

New Treatment Approaches

- Nanoparticles

  - Increases bioavailability of hydrophobic drugs

  - Reduces administered doses

  - Increases response of treatment

- Immunotherapy

  - PD-L1 is a ligand expressed by trophoblasts

 - Blocking PD1-PDL1 interaction allows activation of the immune system
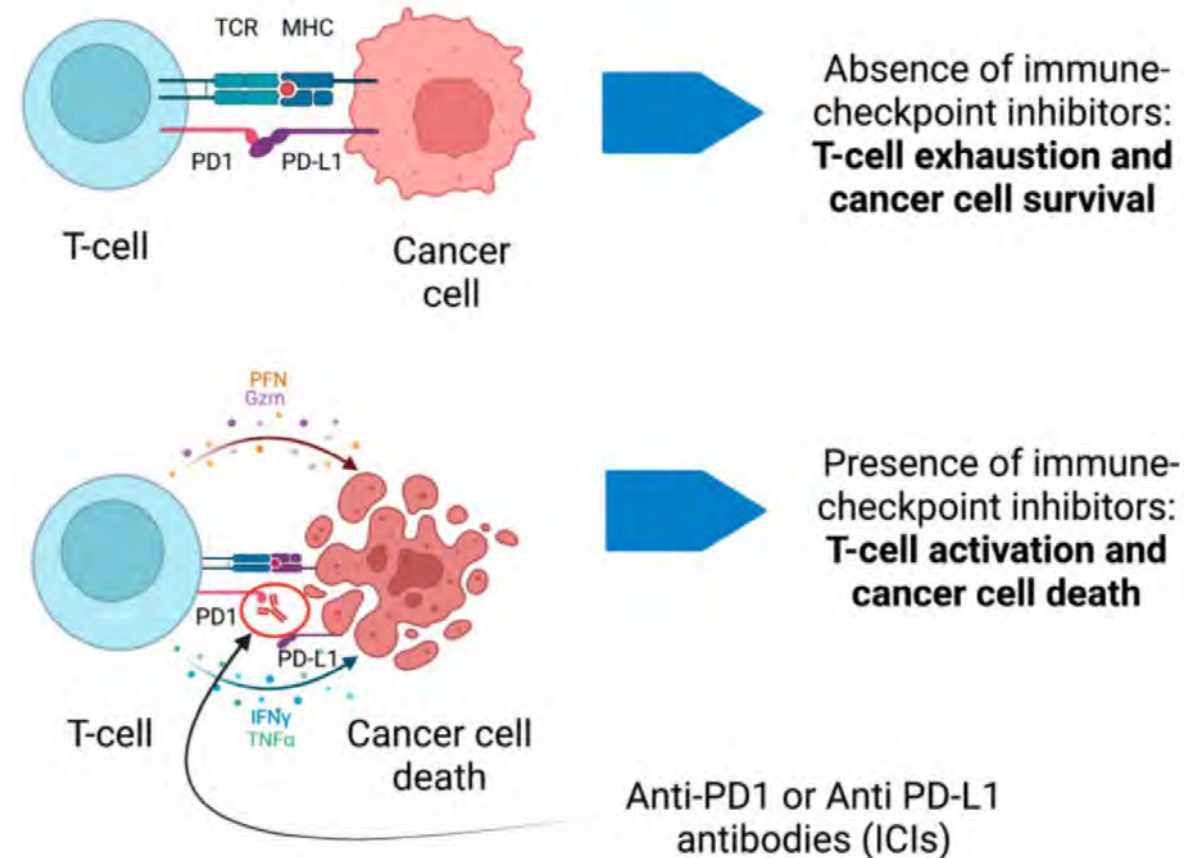
PDL1-Targeted Methotrexate Nanoparticles

We aim to:

- Load nanoparticles with chemotherapy drug (methotrexate)
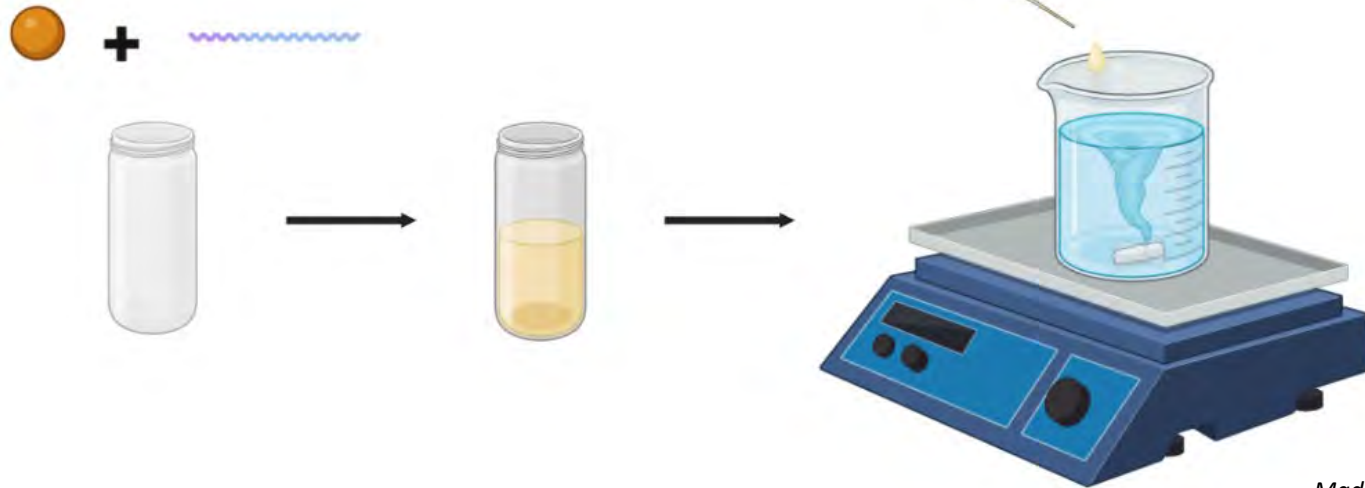
- Graft an antibody (anti-PDL1) to nanoparticles

Overall Goal:

- Deliver methotrexate directly to cancerous trophoblasts and reverse the immune tolerance of cancerous trophoblasts by using an antibody to target PDL1 on cell surface and block immune checkpoints
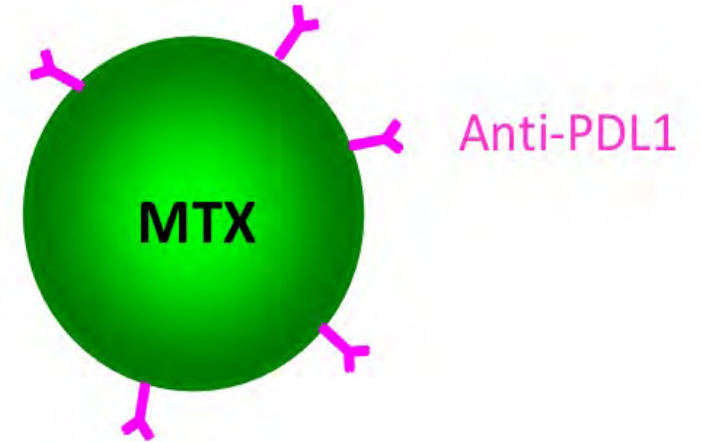
- Nanoprecipitation

  - Polymer
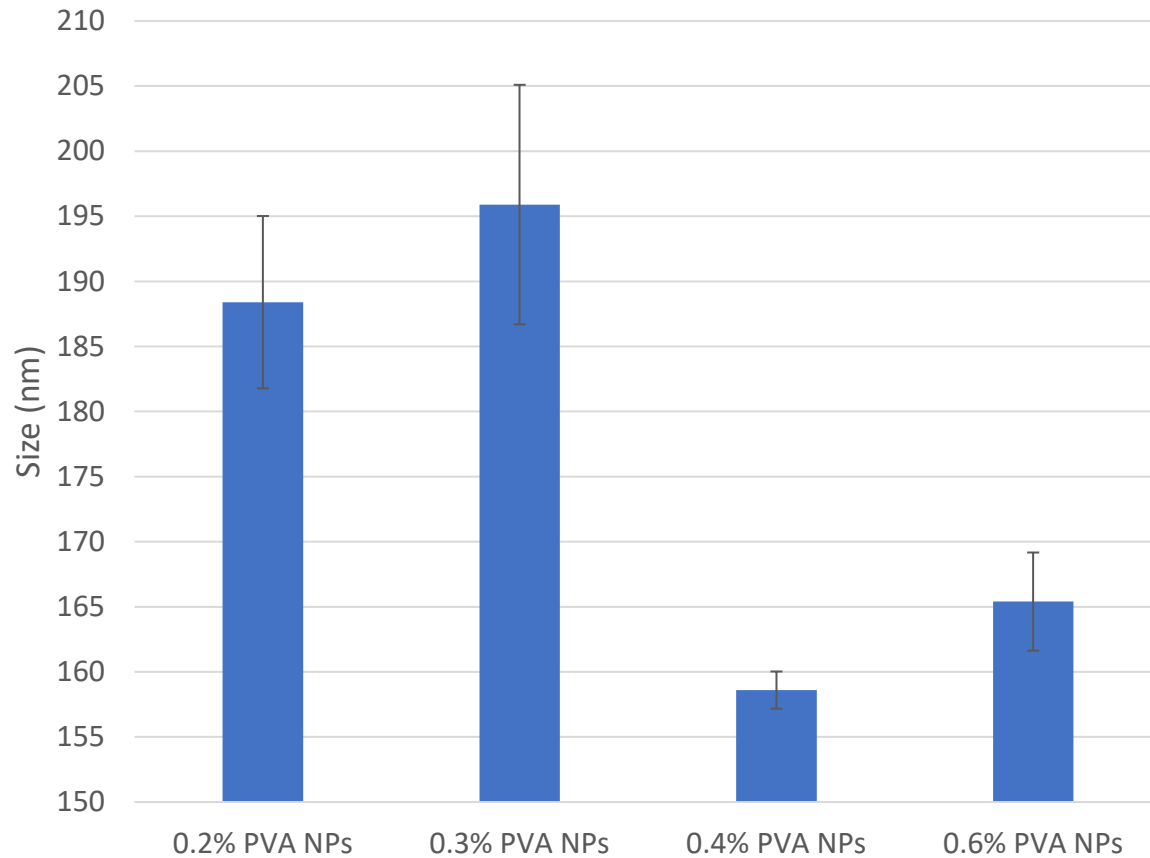 - Methotrexate in 13% DMSO + Acetone

Evaporation

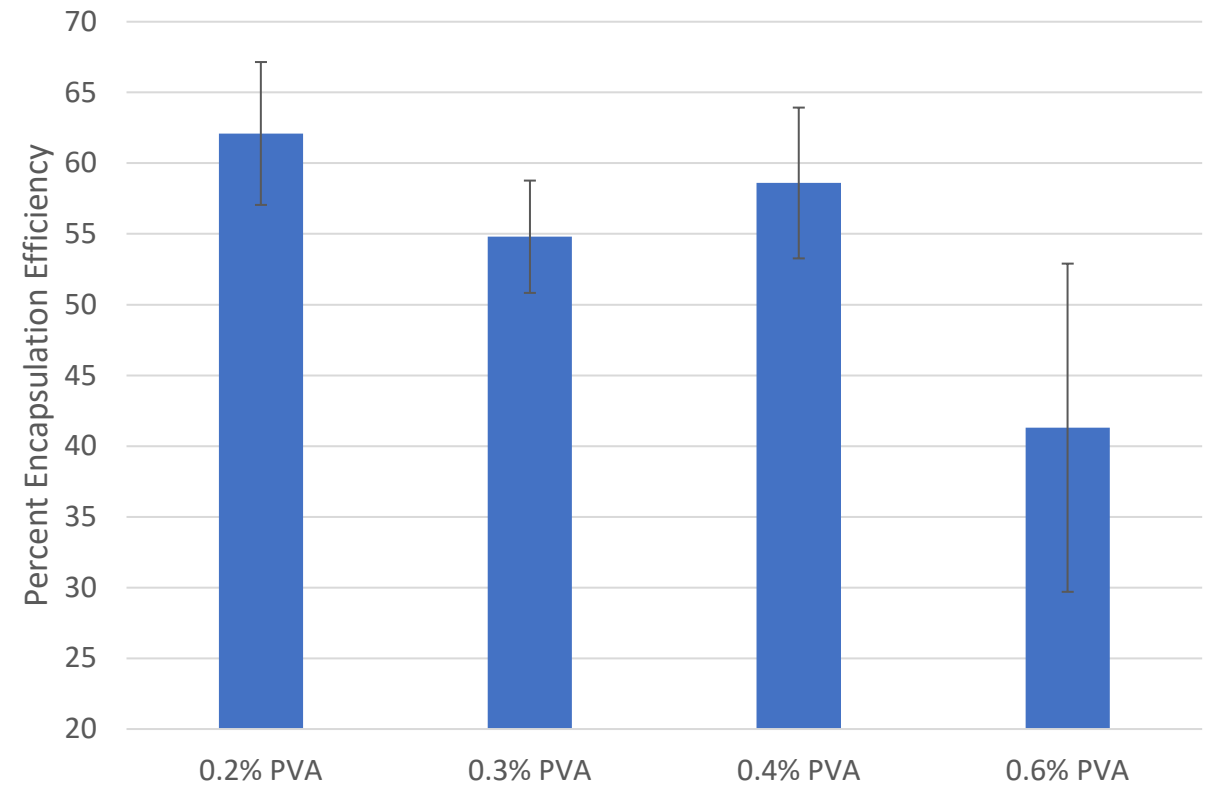*Made with BioRender*

- Characterization:

  - Dynamic Light Scattering, Dosage/Stability Assays, Lyophilization, and more techniques are used to determine the size and stability of nanoparticles

Optimizing Nanoprecipitation

Average Sizes of Nanoparticles After Washing

Average Encapsulation Efficiencies Per PVA Condition

Polyvinyl Alcohol (PVA) stabilizes nanoparticles

Key Takeaways

- Size

  - Increasing PVA concentration will decrease the nanoparticle size

    - Larger nanoparticles are targeted by macrophages for phagocytosis and have reduced retention

- Encapsulation Efficiency

  - Amount of methotrexate loaded into the nanoparticle compared to the total amount available

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