EUROScholars
European Undergraduate Research Opportunities

Synthesis and optimization of MTX-Loaded NP for the treatment of Gestational Trophoblastic Neoplasia

Divyasri Moulee, Rutgers University – New Brunswick
Supervisor: Marie Cohen, Doha Boukaoui, University of Geneva

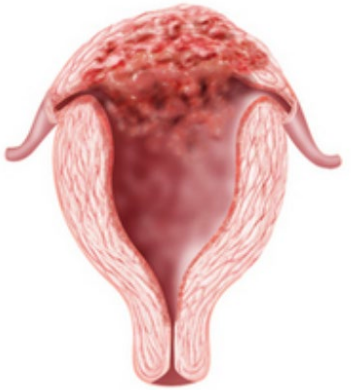
EUROScholars
European Undergraduate Research Opportunities

About Me

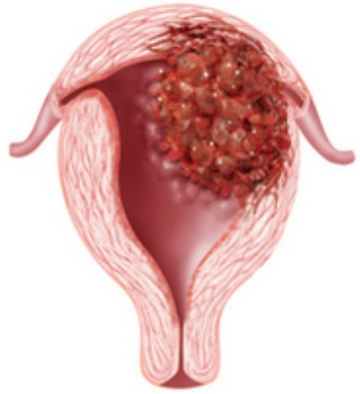
- Born in Chennai, India
- Majoring in Biochemistry, minor in Mathematics
- Involved at Dr KiBum Lee's Lab at Rutgers University
- Biochemistry Representative at SEBS Governing Council, and Assistant Coach at Dream Cricket Academy

Gestational Trophoblastic Neoplasia (GTN)

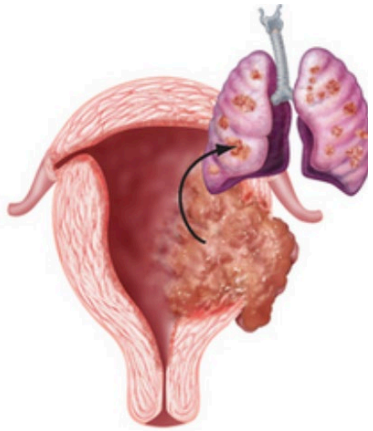
- Group of malignant tumors from placental cells.
- Tumors are classified into
  - Malignant Invasive Mole [MIM]
  - Epithelioid Trophoblastic Tumor [ETT]
  - Placental Site Trophoblastic Tumor [PSTT]
  - Choriocarcinoma [CC]
- The origin and particular function of the cells dictates the type of GTN
- The cell lines used in this project are JEG3 and BeWo cells, a type of choriocarcinoma cells



Placental site trophoblastic tumor



Invasive mole



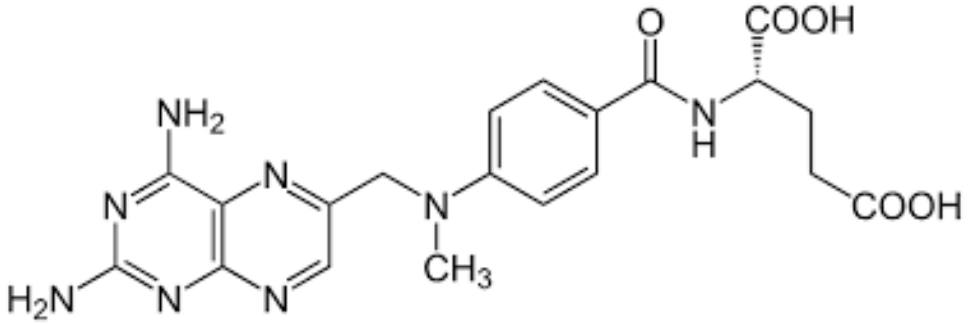
Choriocarcinoma

Current Treatment Options

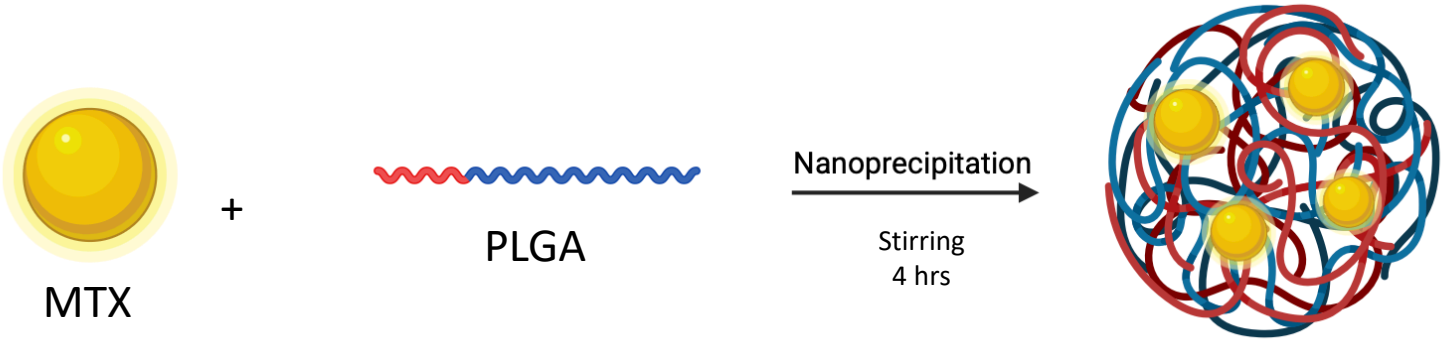
- Low-Risk GTNs
  - MTX – Single agent chemotherapy
  - Polychemotherapy
- High-Risk GTNs
  - Surgery and polychemotherapy
  - Salvage therapy: platinum salts and taxol

But these options are highly toxic, have side affects including altering fertility.

Methotrexate - MTX

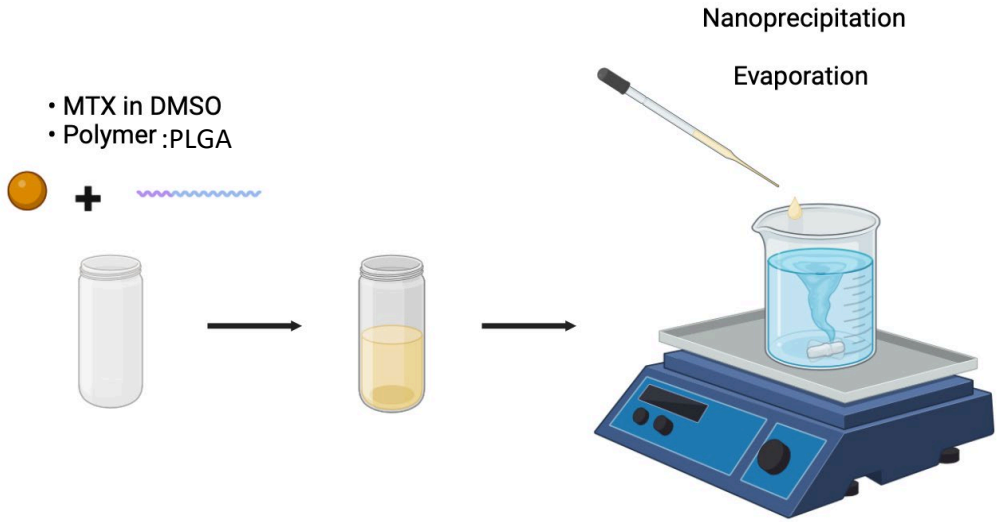


- Methotrexate inhibits the enzyme dihydrofolate reductase, which inhibit tumor cell DNA and RNA synthesis, therefore there are fewer tumor cells.
- Since MTX is restricted in our body
  - Due to its hydrophobic nature and the biodistribution in our bodies.
- To tackle this issue, MTX can be loaded into various nanocarriers, such as bio-polymers ex. PLGA.
  - This way, the PLGA-loaded NP improves efficiency of the drug on GTN and reduce any adverse effects of MTX.

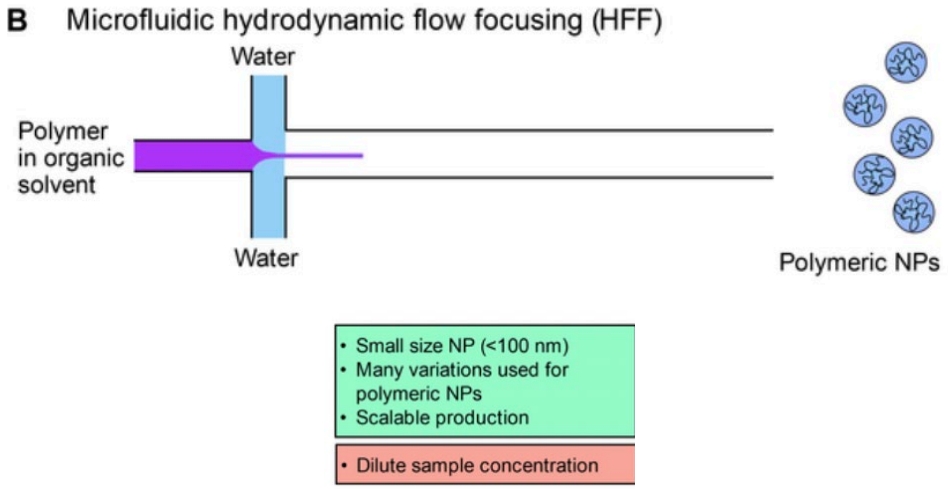


Synthesis of the Nanoparticles

- Nanoprecipitation



- Microfluidics



NPs were characterized by measuring the size using Dynamic Light Scattering (DLS) and Scanning Electron Microscopy (SEM). The encapsulation efficiency was measured using spectrophotometry and UPLC.

Nanoparticle Characterization – Size, PDI and Encapsulation Efficiency

	Size	Polydispersity Index (uniformity)	Encapsulation Efficiency
Nanoparticles	174.75 nm	0.205	53.9%

Size remained less than 200 nm for each batch of nanoparticles synthesized and the encapsulation of MTX was also high

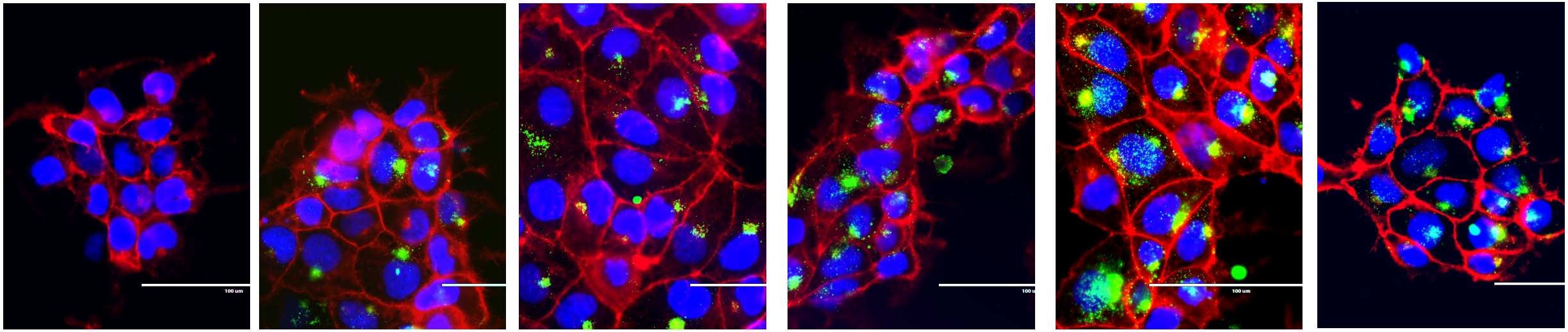
Nanoparticle Characterization – Stability Tests

Number of Days	Size – Day 1	Size - Day 7	Size - Day 14	Size - Day 21
Nanoparticles	168.5 nm	162.8 nm	167.3 nm	180.2 nm

The size of the nanoparticles remained less than 200 nm even after 3 weeks

Cellular Uptake of NPs

- Fluorescent NPs to BeWo at various time intervals



0 mins | 15 mins | 30 mins | 60 mins | 120 mins | 240 mins

- Staining: Blue – DAPI, Red – Phalloidin, and Green - GFP

Key Takeaways

- Nanoparticle uptake begins as early as 15 minutes in JEG3 and BeWo cell lines
- Generated stable MTX-NPs with an encapsulation efficiency of around 60%
  - Size of the NPs remained less than 180 nm after days, indicating stability and small size

Citations

- Cronstein B. N. (1997). The mechanism of action of methotrexate. Rheumatic diseases clinics of North America, 23(4), 739–755. https://doi.org/10.1016/s0889-857x(05)70358-6
- Lurain J. R. (2010). Gestational trophoblastic disease I: epidemiology, pathology, clinical presentation and diagnosis of gestational trophoblastic disease, and management of hydatidiform mole. *American journal of obstetrics and gynecology*, *203*(6), 531–539. https://doi.org/10.1016/j.ajog.2010.06.073
- Maleki et al. Int J Med Nano Res 2017, Methotrexate-Loaded PLGA Nanoparticles: Preparation, Characterization and their Cytotoxicity Effect on Human Glioblastoma U87MG Cells
- McGrath, S., Short, D., Harvey, R., Schmid, P., Savage, P. M., & Seckl, M. J. (2010). The management and outcome of women with post-hydatidiform mole 'low-risk' gestational trophoblastic neoplasia, but hCG levels in excess of 100 000 IU l(-1). *British journal of cancer*, *102*(5), 810–814. https://doi.org/10.1038/sj.bjc.6605529
- Zai Akma (2020, June 6). *Gestational trophoblastic disease*. Dr Zai's Medical Notes. https://mednote.home.blog/2020/06/06/gestational-trophoblastic-disease/