Study of Nanoparticles for the Delivery of Tuberculosis Drugs

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Overview

- **Motivation:**
  - SQ641, SQ922 and SQ997 are promising anti-TB compounds
  - Advantages: inhibit formation of eubacteria cell wall
  - suppress mutation of TB
  - can work in combination with TB drugs currently on market
  - Drawback: low solubility in water inhibits *in vivo* delivery

- **Purpose:**
  - Attempt to encapsulate drug compounds within a nanoparticle (NP) suspension, resulting in increased uptake and more efficient release
Method

Using Flash Nano-precipitation process, make different formulations of NPs containing drug compounds, stabilized with PEG-PLA block copolymer

SQ997, SQ922, SQ641

PEG-PLA block copolymer

THF solvent

1:10 ratio Organic:H₂O

Dialysis

H₂O

Test NPs for stability over time, in vivo/in vitro uptake, toxicity
Results - Stability

10mg SQ922, 30mg polymer in 10ml THF
Results - Stability

5mg SQ997, 5mg polymer in 2.5ml THF

SQ641, the most potent compound, yielded the least stable NPs
Results - Uptake

In vivo: Issues with concentrating NP suspensions to level suitable for testing with bacteria

Methods: Freeze drying

Hydrogen bonding coacervation precipitation (HBCP) - form H-bonding networks between PEG and Citric acid
Results - Uptake

*In vitro*: Formation of magnetic lipid microparticles allows for quantifying amount of drug released from NPs

- Fractionate microparticles, isolating those larger than 10um in diameter
- Mix magnetic microparticles and drug-loaded NPs together in solution to allow loading of drug into microparticles
- Recover microparticles to determine release amount
Current work

Determine best method to concentrate NPs for *in vivo* studies
- precipitate, re-suspend particles in smaller volume water

Continue *in vitro* studies with different combinations of NP solutions, microparticle solutions; recent results indicate low amount of drug release

Ultimately, we hope this novel drug delivery system can quickly and efficiently kill off TB infection, resulting in less frequent dosing needed

Conclusions

While development of effective drugs is critical, delivery of active to infected sites in the body is just as important a consideration

Drugs not inherently soluble in blood can be coated with hydrophilic polymers in a manner that ensures stability and allows for targeting