**Problem**

Annually, two million people die from active tuberculosis (TB). A fraction of the deaths is from the reactivation of a dormant form of tuberculosis called latent tuberculosis (LTB). In LTB, Mycobacterium tuberculosis (Mtbc) is encapsulated by structures called granulomas which are impenetrable to anti-TB drugs. There is an urgent need to design and develop novel therapeutics to effectively treat LTB infections.

**Goal**

Formulate a spray dried powder (SDP) that incorporates a live bacterial immunotherapeutic agent, bacillus Calmette–Guérin (BCG), with an anti-TB drug, isoniazid, loaded in nanoparticles (INH NP). We hypothesize that when the SDP is delivered by the pulmonary route it will disrupt the lung granulomas leading to the elimination of Mtbc from the LTB patient.

**Methods**

- **Nanoparticles Characterization**
  - **Figure 1**: The size and charge of the NPs before spray drying (BSD) and after spray drying (ASD) (n=6, Mean ± SD)
  - **Figure 2**: Different combinations of spray dried powders

- **Drug Loading Analysis (Indirect & Direct)**

- **Suspension of NP and BCG in Leucine**

- **Spray Dry (Büchi mini spray dryer)**

- **Characterize Spray Dried Powder Size (Aerosizer)**

- **Characterization of NP Size & Charge (Malvern Zetasizer)**

- **Nanoparticle Synthesis (emulsification/solvent evaporation)**

**Results**

- **Spray Dried Powder (SDP) Characterization**
  - SDP Yield (% w/w) 36.90
  - Avg. SDP Size (µm) 2.47 ± 0.05
  - Drug Loading (% wt INH/wt NP) 38.60 ± 2.70

**Conclusion**

- ✓ Our data shows that the BCG and INH loaded NPs, i.e. the combination of immuno- and chemotherapy, can successfully be incorporated in an inhalable dry powder and used as a potential delivery system in LTB patients
- ✓ This inhalable dry powder may serve as the next step in controlling and eradicating LTB infections caused by one of the most virulent bacterial pathogens
- ✓ Further studies are needed to evaluate the immunogenicity of BCG and the toxicity of INH NPs in animal models

**Future Studies**

- Characterize Spray Dried Powder Aerodynamic Diameter
- Characterize using Scanning Electron Microscopy
- Characterize using Confocal Microscopy