

Drug Delivery for Macrophage Immunotherapy

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Project Description: Macrophages are a tissue-resident cell of the innate immune system. They are involved in clearing cellular debris (apoptotic cells, tumor cells, pathogens) and maintaining tissue homeostasis. Early-phase clinical evidence suggests that macrophages could be useful as a cell-based therapy in a number of conditions including metastatic cancer, stroke, and brain injury. However, a consistent shortcoming of these investigations is the inability to influence the phenotype/behavior of the cell once it is injected. In the **Clegg Lab at OU**, we invent hydrogel, polymeric, and composite drug delivery systems that deliver pro- or anti-inflammatory cargo to macrophages *in vivo*. We have invented materials that sustain the release of drugs, which have a typical half-life of minutes to hours, for up to 1 month. By co-delivering these drug-delivering materials with donor macrophages, we can uniquely drive a therapeutic phenotype in the body. We are currently investigating the efficacy of these drug delivering material + donor macrophage therapies in the treatment of cancer and brain injury. The **central hypothesis** of the proposed project is that sustained delivery of anti-inflammatory cargo will sustain a therapeutic phenotype (tissue remodeling) of donor macrophages *in vivo*. This honors student project will involve the synthesis and characterization of an anti-inflammatory drug delivery systems, as well as the *in vitro* evaluation of the anti-inflammatory effect on human and mouse macrophages.

Student Role and Responsibilities: The undergraduate collaborators on this work will learn:

- Hydrogel and polymer synthesis
- Characterization of polymers and hydrogels using analytical techniques (FTIR, NMR, gravimetric analysis)
- Analysis of drug/pharmaceutical release from polymeric materials.
- Mammalian cell culture and sterile technique
- Fluorescence microscopy analysis of cell + material constructs.

Further, undergraduate students will have the opportunity to:

- Participate in lab group meetings with Dr. Clegg and his Ph.D. students
- Present their research in sub-group meetings with macrophage immunotherapy collaborators
- Complete a final thesis or poster presentation, if needed for their degree program.

In addition to the honors program, upon mutual agreement with Dr. Clegg, the participant can:

- Continue to work in the lab after the 10-week program for ~10 hours per week.
- Receive co-authorship on manuscripts or conference presentations for which the student has contributed writing, data analysis, or data collection.