1-1-2023

Manufacturing of Therapeutic T cells using Microbeads coated with Peptide Ligands

Kyung-Ho Roh
University of Alabama in Huntsville

RCEU 2023 Project Proposal

Project Title

Manufacturing of therapeutic T cells using microbeads coated with peptide ligands

Faculty Information

Name: Kyung-Ho Roh

Status: Associate Professor

Department/Program: Chemical and Materials Engineering

College: College of Engineering

Phone: 256-824-5292

UAH Email: kr0054@uah.edu

Proposal ID RCEU23-Roh-CHE-01

I. Project Description

Interests in immunotherapies using genetically engineered T cells have been rapidly growing due to their recent success in treatment of various cancers with unprecedented efficacies. The current manufacturing processes for the T cell therapeutics employ a combination of anti-CD3 and anti-CD28 antibodies to artificially activate the T cells so that they can proliferate in numbers. However, such artificial activation processes often exhaust the T cells or differentiate them to terminal effector phenotypes, which are detrimental for the successful engraftment and longevity of the engineered T cells in vivo when they are adoptively transferred into the patient. In our lab, we recently have discovered a novel peptide ligand against CD3 molecules on human T cells. In this RCEU project, we will develop a biohybrid structure of microbeads coated with this peptide ligands, and utilize them for T cell expansion. We hypothesize the T cells could be expanded in number without exhaustion, owing to the lower affinity of the novel peptide ligand toward CD3 compared to anti-CD3 antibody. We will test the phenotypes of the T cells using flow cytometry.

II. Student Duties, Contributions, and Outcomes

a. Specific Student Duties

The student will first perform a set of bioconjugation chemistries to modify the surface of commercial microbeads with custom-made peptides (Week 1). Next, the students will get trained for cell culture techniques using Jurkat T cells. Then the student will perform experiments to test the interaction between the peptide-modified microbeads and Jurkat cells by setting up and maintaining the cell culture at different cell-to-bead ratios (Week 2-4). Afterwards, the student will learn how to culture the human T cells isolated from peripheral blood mononuclear cells (Week 5), which will follow the last set of experiments by co-incubating the human T cells with the microbeads (Week 6-10). The outcome of each experiments will be obtained by characterizing the resulting T cells using flow cytometry.

b. Tangible Contributions by the Student to the Project (10% of Review)

Even if the fact that the peptide ligand can bind to human CD3 molecule has been verified previously, whether such binding for activation of primary human T cells has not been tested yet. The student will test this hypothesis by changing the testing parameters such as peptide densities and bead-to-cell ratio. Students will be involved in the entire process of the experiment, i.e. from the preparation of materials, cell culture, and the characterization of cell phenotypes.

c. Specific Outcomes Provided by the Project to the Student (30% of Review)

The student will learn the basic concept and practical procedure of cellular manufacturing, particularly about expansion and differentiation of the human T cells. The student will be trained for basic lab skills including pipetting and plating, preparation of cell culture media, aseptic techniques, bioconjugation chemistries, manipulation of magnetic microparticles, use of hemocytometer, cell culture techniques, optical microscopy, and flow cytometry. Students will get

trained on critical thinking as well as effective communication skills for science and engineering discussion.

III. Student Selection Criteria

This project is essentially open to students at all academic ranks and from any academic discipline. However, the preference will be given to a candidate who meets these criteria: i) strong motivation in biomedical research, ii) experience and willingness to learn wet laboratory experiments, iii) background trainings in chemistry, biology, chemical engineering or related fields.

IV. Project Mentorship *(30% of Review)*

Over the 10-week project, the student will have weekly meetings with the faculty member (PI). During the meeting time, the student will i) be given short lectures on the background principles of the project, ii) share the progress in the project, and iii) discuss how to prepare the final report and poster presentation. The mentorship for the practical experiment will be provided by a postdoc researcher, Dr. Pearlson Prashanth. The RCEU student will also participate in the biweekly group meetings. Towards the end of the project period, the student will be given a chance to present the data in front of the research group.