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Selection of Novel Peptide Ligands Specific to Human CD40 using Phage Display Peptide Libraries

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UAH RCEU 2020 INITIAL PROPOSAL

Title Page

Project Title: Selection of novel peptide ligands specific to human CD40 using phage display peptide libraries

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Project Description

Vaccination has been protecting humankind from so many fatal infections, which is the ultimate example of "immunoengineering". As a canonical result of vaccination, specialized immunological molecules called antibodies (also called immunoglobulin) are created by B cells in our bodies. For this, the B cells need to be activated by complex interactions with other critical immune cell types including the T cells. The interaction between the B cell and T cell is mediated by many molecular-molecular interactions, and one of the most critical interactions originates from the specific binding of CD40L on T cells to CD40 on B cells. It has been previously demonstrated that the soluble form of CD40L molecule can be used as a protein therapeutic for enhancement of B cell functions in patients suffering from immunodeficiencies for various reasons.

In this RCEU project, the student will employ a mixture of numerous peptide ligands (~10^9 kinds) expressed on bacteriophages (so called, phage display peptide library) to select a small number of potential ligands that can specifically bind to CD40 molecules. The selection procedure is called "biopanning". The student will be trained for the relevant laboratory techniques and will be responsible for performing at least 3 rounds of biopanning experiments independently. As a critical outcome, the student will identify the amino acid sequences of a small set of peptide ligands that are selected for specific binding to CD40, which could be further developed in various B cell engineering applications.

Student Duties, Contributions, and Outcomes

Specific Duties: The student will design his/her own biopanning experiment and perform the biopanning experiments independently. The biopanning procedure includes i) modification of the surface of magnetic microparticles with recombinant CD40 molecules; ii) incubation with the phage display library; iii) washing; iv) eluting the selected phages; v) infection of bacterial cells with the selected phages; vi) expansion of phages; vii) isolation of expanded phages; and viii) repeat for the next round. During the 10 week-project, the student will complete at least 3 rounds of biopanning to identify the resulting set of peptide ligands that are specific to the target molecule CD40. After each round of biopanning, the clonal enrichment data will be quantified, analyzed, and recorded for the final report. After the final round of biopanning, the DNA sequencing will be performed for 20 resulting phage clones.

Tangible Contributions: The outcomes of this project will be targeted for publication in the UAH undergraduate research journal, *Perpetua*. Once the resulting peptides are further developed in conjunction with other biomaterials platforms for B cell engineering projects, the student will participate in writing a publication of scientific journal article as a co-author.

Specific Outcomes: The student will learn the basic concept and practical procedure of chemical directed evolution, in particular the use of phage display peptide libraries. The student will be trained for basic lab skills including pipetting and plating, preparation of agar plates, basic bacterial cell culture, isolation of plasmids, purification of phage, and manipulation of magnetic microparticles.

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 in wet laboratory experiments, iii) background trainings in chemistry, biology, chemical engineering or related fields.

Faculty Mentorship

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. The mentorship for the practical experiment will be also provided by a 3rd year PhD student who is using the phage display technology for his PhD thesis research (Mr. Armin Ahmadi). The 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 group.

Proposed time line of the project: