2019 CLASS OF 1971 FELLOWSHIP RECIPIENT

SEPTEMBER 3, 2019

BRANFORD COLLEGE

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STUDENT	**CLASS YR**
Alon Millet	20’
Arielle Soldatenko	21’

Alon Millet

Bio:

Alon Millet is a molecular, cellular, and developmental biology major in Branford College. Alon has been engaged in biology research since his freshman year of high school, but at Yale his interests crystallized around the immune system and the diverse ways that cancer and pathogens subvert it. Alon started his research at Yale under Dr. Akiko Iwasaki studying viral immunity, publishing a paper in *Science Immunology* before transitioning to the lab of Dr. Nikhil Joshi to pursue his interests in cancer immunology. Through his research, Alon plans to earn both his BS and his MS in four years through his major's combined BS/MS program. Outside of the lab, Alon serves as both a campus tour guide and a science tour guide, leading visitors and prospective students throughout campus – and the Branford courtyard when possible! – and peer tutors all four modules of the introductory biology sequence.

Summary:

Alon spent the past summer in the lab of Dr. Nikhil Joshi at the Anlyan Center, the primary center for immunology research at Yale, continuing to build towards his master's thesis. Alon's research concerns itself with immunotherapy, an exciting paradigm shift in cancer treatment that seeks to pit the body's own immune system against the tumor. However, for reasons that are not yet well understood, immunotherapy is very successful in a small subset of cancers such as melanoma and non-small cell lung cancer, but many others respond poorly to it. Historically, questions in this field have been challenging to address because of a lack of good models that faithfully recapitulate all aspects of the biology of the system. Mice, for instance, have fully functional immune systems that can correctly respond to tumors, but conventional mouse cancer models lack neoantigens and thus do not produce any immune response, whereas cell culture allows for immunogenicity through irradiation but cannot mimic the immune system. To solve this major need, Alon aims to produce a novel model of cancer (specifically pancreatic ductal adenocarcinoma, or PDAC, a classical example of a cancer that responds poorly to immunotherapy) by combining the Joshi lab's signature NINJA system, an inducible neoantigen genetic switch, with organoid culture, a means of growing cells in 3D suspension such that they form fully functional mini-organs.

So far, Alon has successfully produced these systems and shown that they correctly model both the cancer biology and the immunobiology. This summer, Alon principally focused on generating a broad CRISPR knockout screen against a set of genes canonically associated with poorer immunotherapeutic outcomes. Using the funds provided by the Class of 1971 Fellowship, Alon was able to generate a multiplexed CRISPR library and validate many of the guides through HT-seq, producing a number of knockout cell lines that were reincorporated into the NINJA-organoid model to identify which genes might play a role in damping the immune response against the tumor – though specific data remains confidential. Alon used a range of modern techniques in molecular biology in pursuit of this goal, including western blotting, high-content imaging, immunohistochemistry, diSPI microscopy, and major tools in genetic manipulation and cloning. Along the way, Alon also reverse engineered an essential commercial product, the QIAGEN Maxiprep kit, and optimized it for use in the Joshi lab, saving the lab and the department thousands of dollars a month in purchasing expenses.

Alon wishes to communicate his gratitude to the funding sources of the Class of 1971 Fellowship – their generosity and commitment to science at Yale and at Branford were essential in allowing him to make major advances towards his master's thesis this summer and to progress further as an immunologist.

Arielle Soldatenko

Bio:

Arielle Soldatenko is a Molecular, Cellular and Developmental Biology in Branford College. She has been involved in immunology research studying red blood cell transfusion alloimmunization in Dr. Stephanie C. Eisenbarth's lab at the Yale School of Medicine since her sophomore year. Outside of the lab, Arielle is co-President of MedSci, an organization of undergraduate volunteers who teach health and science lessons at New Haven elementary schools. She is also Chief of Staff for Yale Model Congress where she recruits and trains Yale students to moderate congressional style debate for high school students and helps run a four-day congressional simulation conference. Arielle also volunteers with the Hypertension Awareness and Prevention Project at Yale to provide free blood pressure readings and education on hypertension to the community. Her hobbies include taking spin classes, reading, and spending time with her friends.

Summary:

Arielle spent her summer conducting research in Dr. Stephanie C. Eisenbarth's lab at the Yale School of Medicine thanks to the generous support of the Class of 1971 Fellowship. Arielle improved her techniques and learned new skills important to immunology and translational research including tissue culture, ELISA, crossmatch, animal handling, immunofluorescence, and flow cytometry. She studied the innate immune pathways that regulate alloimmunization as a first step toward understanding and preventing red blood cell alloimmunization. While blood typing is used to minimize the risk of negative transfusion reactions, poorly characterized non-ABO blood antigens also cause alloimmunization, which cannot be prevented. Patients who require long-term blood transfusions, often those with hematological and bone marrow disorders, are at increased risk of red blood cell alloimmunity. If a discrete innate immune receptor were to be identified as responsible for initiation of red blood cell alloantibody production, this receptor could be inhibited with a soluble ligand before transfusion into patients. Using the funds received from the Class of 1971 Fellowship, Arielle used her animal handling skills to begin breeding a line of mice that lack functional Toll-like receptor 5 (TLR5) to explore if it participates in alloimmunization since no alloimmune response is observed when all TLR dependent signaling is blocked. She plans to conduct transfusion experiments with these

mice during the upcoming semester. She also explored dendritic cell specific loss of all TLR signaling using crossmatch, ELISA, and flow cytometry to determine if dendritic cells in particular are responsible for priming alloimmunity. She plans to continue investigating this question using a CD11c Cre MyD88 floxed mouse model during the upcoming semester. Arielle is very grateful for the opportunities provided to her by the Class of 1971 Fellowship, which allowed her to develop her research skills over the summer.