A proposal towards proposed research in computational biology

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1 Specific Aims

Chimeric Antigen Receptor (CAR) T cell therapy engineers a cancer patient's T cells to express one or more synthetic antibodies chosen to specifically target that patient's cancer. This approach has shown remarkable success with acute lymphoblastic leukemia (ALL) when targeting CD19. Recent work by Perna et al., (2017) sought to identify potential CAR targets for Acute Myeloid Leukemia (AML), with the goal of approaching the performance of ALL results. While they identified no single target which was as promising as CD19, they identified a strategy by which paired weaker targets may be selected to maximize selectivity, and offers several paired targets of interest. The Wong Lab at Boston University seeks to extend this work by identifying more complicated combinatorial pairings of co-expressed targets which preserve the specificity of the effects, but allow the use of more potent but otherwise less specific antigens. In this work, we propose to design a target selection algorithm to select candidate sets of four targets to allow the use of higher AML-affinity candidates which were excluded by Perna et al. for their off-target effects by coupling them with AML-specific co-expressed sites.

To this end, we propose the following Specific Aims:

1. Preparation of Data Sources

   - proteomics data: huge.

   - transcriptomics data: even more huge.

2. Target Selection Algorithm

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2 Project Description

2.1 Significance

CAR really works against AML and it needs to work against other cancers. So far it works best when there's a rockstar target like CD19; the most promising way this approach generalizes is if multiple targets can be combined.

2.2 Innovation

2.3 Research Strategy

2.3.1 Background

2.3.2 Aim 1...n

2.3.3 Resources

- datasets with links
- wong's grad student
- graham has cluster access if we need to flip big data

2.3.4 Timeline

2.3.5 Collaboration Plan

- graham and kestas code
- rachel and kat: bio
- we have a grad student in wong's lab who wants to help, who are they
-

References

Perna, F., S. H. Berman, R. K. Soni, J. Mansilla-Soto, J. Eyquem, M. Hamieh, R. C. Hendrickson, C. W. Brennan, and M. Sadelain (2017). "Integrating Proteomics and Transcriptomics for Systematic Combinatorial Chimeric Antigen Receptor Therapy of AML." In: *Cancer Cell* 32.4, 506–519.e5. ISSN: 15356108. DOI: 10.1016/j.ccell.2017.09.004.

BIOGRAPHICAL SKETCH
Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES**.

NAME: Voysey, Graham E.

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POSITION TITLE: Research Engineer

EDUCATION/TRAINING (*Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.*)

INSTITUTION AND LOCATION	DEGREE (*if applicable*)	Completion Date MM/YYYY	FIELD OF STUDY
Boston University	B.S.	09/2002	Biomedical Engineering
Boston University	M.S.	08/2016	Biomedical Engineering

A. Positions and Honors

Positions and Employment

2006–2010	Research Engineer, InfoSciTex Corp, Waltham, MA
2010–	Research Engineer, Boston University, Boston, MA
2016–	Research Engineer, Neurala Inc, Boston, MA

Honors

2016	Boston University Clinical and Translational Institute Mini-Sabbatical

B. Contribution to Science

C. Research Support

Ongoing Research Support

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.

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NAME: Elkind, Katherine

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INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Gettysburg College	BA	05/2011	Spanish Linguistics
Boston University	MS	01/2018	Electrical and Computer Engineering

B. Positions and Honors

Positions and Employment
2016 -   Intern, STAR Analytical Services, Lexington, MA
2017 -   Research Assistant, CIDAR Lab, Boston University, Boston, MA
2017   Teaching Assistant, Department of Electrical and Computer Engineering, Boston
                   University, Boston, MA
2011 - 2014   Administrator, Vamos Spanish Academy, Buenos Aires, Argentina

C. Contribution to Science

1. My internship with STAR Analytical Services has focused on signal processing, primarily of acoustic and speech signals. I've written code to aid with the blind separation of multiple source signals. These software would be employed with hearing aids in order to allow hearing aid users to choose what sounds they wish to listen to in a noisy environment, rather than only being able to turn up the volume and amplify every sound in a noisy environment. I've acted as an assistant to the primary investigators.

2. My experience as a Research Assistant with CIDAR Lab has focused on CAD Tools for Synthetic Biology. My project development has focused on front-end design of a tool and workflow for the design and verification of genetic logic circuits. This software allows non-technical users to take advantage of computer automation so that they can design the best genetic circuits to achieve their goals. I've been the primary developer for the design prototypes.