Riley S. Drake
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Relevant Experience

Visiting Student, Department of Health Sciences and Technology

Macrophages are the primary antigen presenting cells in most immunogenic solid tumors. The presence and phenotype of macrophages within the tumor has been shown to have a significant effect patient prognosis. Using recently refined single-cell RNA sequencing technology, I aim to describe the relationship between macrophage profile and patient prognosis.

Director of Materials, Vibrant Composites LLC

Designed materials and adhesives to be used in the layups of Printed Circuit MEMS (PC-MEMs) pop up assemblies. Tested prototypes and engineered appropriate circuitry.

Visiting Scientist, The Whitehead Institute for Biomedical Research
Visiting Scholar, The Broad Institute of MIT and Harvard

Cohosted in the labs of David Sabatini and Eric Lander, I worked to characterize the Biological Functions of cell-line specific essential genes. These essential genes were discovered by large gene screens: For each gene of interest, the forward (sense) and reverse (anti-sense) sequences were inserted using the CRISPr genome-editing system. At the endpoint of the experiment the remaining live cells are measured to determine the ratio of the number of genes containing the sense transcript to those containing the anti- sense transcript— this is known as the essentiality score. If the essentiality score is greater than 0.8, the gene being investigated is usually considered an essential gene and is thought to be important for the continued survival of that cell type. Interestingly, we found that gene essentiality varies greatly by cell type. In particular, some cancer cell lines rely on genes that are unimportant to non-cancerous cell lines, making them attractive therapeutic targets. Having identified some essential genes for Chronic Myeloid Leukemia which seemed non- essential to somatic cells, I characterized the (a) localization of the proteins produced by these essential genes using confocal microscopy (b) the molecules that interacted with proteins produced by the genes of interest using mass spectrometry.

Laboratory Assistant, Lauer Lab; Massachusetts General Hospital

Here, I began to investigate a possible link, first described by the Lucas Group in 2004, between chronic Hepatitis C infection and diminished proliferation and functionality of CD8 T-cells. To study this I examined the ability of CD8 cells in HCV+ samples challenged with cytomegalovirus (CMV), which typically only effects immunosupressed patients. I then compared the expression of known markers of CD8 functionality and proliferation in HCV+ and HCV- samples (both groups challenged with CMV) using 13-color flow cytometry. My results didn't consistently confirm the results reported by the Lucas group, demonstrating that further study of this phenomena is required.

Laboratory Assistant, Powell Lab; Johns Hopkins University

During my second rotation in Dr. Powell's Lab, I attempted to establish different metabolic profiles for murine T-effector subsets, focusing on Th1, Th2 and Tregs. I used the Seahorse Extracellular Flux Analyzer, which measures oxygen consumption rate (OCR) and Extracellular acidification rate (ECAR) in a 96-well plate. To obtain murine CD4 cells with different effector phenotypes, I cultured lymphocytes in the presence of different cytokine cocktails to skew them towards a particular phenotype. To obtain the cells' glycolytic or fatty-acid-oxidation profiles, I

injected inhibitors of either fatty-acid oxidation or glycolysis into the plate after loading the cells on the analyzer and taking baseline measurements. I was then able to use the change in OCR and ECAR to determine the extent to which each effector subset relied on fatty acid oxidation or glycolysis. Results were inconsistent, and I spent much of my five-month rotation optimizing the assay, eventually opting to focus on the more promising Th9 work. The aim of this project was to determine if CD4 T cell effector subsets possess unique metabolic requirements, which would allow for inhibition of a given subset by metabolic means without affecting bystander populations.

Laboratory Assistant, Powell Lab; Johns Hopkins University

I studied a T- effector subset, Th9 cells, which have been linked to respiratory and bowel inflammation. I discovered that CD4 which lack the protein Ras Homolog Enriched in Brain (Rheb), a critical component of the evolutionarily conserved nutrient sensing complex mTORC1, had an increased rate of differentiation of Th9 cells in vitro. I also showed that pharmacological inhibition of the mTORC1 complex in WT CD4 T cells by the drug rapamycin can also enhance Th9 development. I hypothesized that an increased number of Th9 cells might lead to a heightened inflammatory response in vivo. To test this, I used an asthma model and an inflammatory bowel disease model, comparing the inflammatory responses of cells lacking the TORC-1 complex to those of wild type mice. These results are highly interesting in light of the well-documented phenomena of rapamycin-induced pneumonitis, which may be caused in part by rapamycin's ability to enhance T cell IL-9 secretion. These results led to a paper, which was submitted to the Journal of Immunology: Cutting Edge.

Consultant, The Longevity Fund

The Longevity Fund is a small venture capital fund that specializing in investments in aging and regenerative medicine. I primarily consult on technologies and therapies related to the mTOR pathway.

Publications

Inhibition of mTORC-1 enhances CD4+ T cell IL-9 production via the transcription factor TFEB (In Submission)
Adam T Waickman, Riley Drake, Robert Hagan, Kristen N Pollizzi, Jonathan D Powell

The kinase mTOR is a critical regulator of CD4+ T cell differentiation. Development of Th1 and Th17 helper lineages has been shown to be dependent on mTORC-1 activity, while mTORC-2 is required for Th2 differentiation. In the absence of all mTOR signaling, it has been thought that CD4+ T cells preferentially develop into FoxP3+ regulatory T cells. Herein, we demonstrate that, in contrast to all other previously described CD4+ T cell effector subsets, the development of IL-9 producing Th9 cells is significantly enhanced in the absence of mTOR activity. Specifically, the inhibition of mTORC-1, either by genetic deletion of members of the signaling complex or treatment with macrolide rapamycin, results in robust IL-9 production in both murine and human CD4+ T cells. This phenomenon is not accompanied by any increase in expression of the canonical Th9 associated transcription factors PU.1 or IRF4, but instead appears to be facilitated by the master regulator of lysosomal biogenesis TFEB.

Awards

Recipient: Boston College Legacy Grant for Service (2016), Fellow: Thiel Fellowship (2013), AP Scholar with Distinction (2012), AP Scholar with Honor (2011) , National Merit Commended Scholar (2011), Mock Trial Maryland Final Four (2011), Cum Laude National Latin Exam (2010)

Invited Talks

"Role of the mTOR Kinase in T-Cell Differentiation" Boston Biophysics Hangout of MIT and Harvard Cambridge (May 2014)

"Trend Versus Truth: Statistics in the Biosciences" South by Southwest Interactive Austin, Texas (Mar. 2014)

"Scientific Communication" Innovations in Medical Education Forum Antigua, Guatemala (Oct. 2013)

"Innovations in the Field of Medicine" Universidad Franscisco Marroquin Guatemala City, Guatemala (Oct. 2013)

"How Great [Scientific] Ideas Spread" Uncharted: A Festival of Ideas Berkley, California (Oct. 2013)

Education

Boston College, BS in Biology (in progress, expected graduation in 2017)

Relevant Coursework: Molecular Biology, Physics, Chemistry, Statistical Analysis of Scientific Data, Interacting Biomolecules, Psychopharmacology

Extracurriculars

Patient Advocate Candidate, Boston Area Rape Crisis Center (2017- present)
Member, Infrequencies Acappella Group (2017-present)
Director, Splash for MIT, MIT Educational Studies Program (2017)
Trip Leader, MIT Caving Club (2016-present)
Winter School Trip Leader, MIT Outing Club (2015-2016)
3-Season Hiking Leader, MIT Outing Club (2015- present)
Instructor, Industrial Rope Access Seminar (2015)
Seminar Teacher, Junction Summer Program, MIT Educational Studies Program (2015)
Risk Manager, Tau Epsilon Phi Xi Chapter (2014-2015)
Director, Delve Advanced Placement Preparatory Program (2013-2014)
Director, Spark Walk-In Classes, MIT Educational Studies Program (2013)
Director, Spring HSSP Lunchtime Programming, MIT Educational Studies Program (2013)
Member, Boston College Society of Physics Students (2012-present)
Member, Boston College Cycling Team (2012-2013)
Teacher, MIT Educational Studies Program (2012-present)