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: Scarborough, Jessica

eRA COMMONS USER NAME (credential, e.g., agency login): JESSICAA

POSITION TITLE: MD/PhD Candidate, Medical Scientist Training Program (MSTP)

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)*	Start Date MM/YYYY	Completion Date MM/YYYY	FIELD OF STUDY
University of San Francisco – San Francisco, CA	B.S.	08/2012	05/2016	Biology
University of San Francisco – San Francisco, CA	M.S.	08/2015	05/2017	Health Informatics
Case Western Reserve University – Cleveland, OH	M.D.	07/2017	Expected 05/2025	Medicine
Case Western Reserve University – Cleveland, OH	PhD	07/2017	Expected 05/2023	Systems Biology and Bioinformatics

A. Personal Statement

After beginning my medical education, it became clear to me that the best clinicians think like scientists. They don't immediately accept the facts laid in front of them. Instead, they look deeper into the data to find out "why" in addition to "what." I would also argue that the best biomedical scientists think like clinicians. Translational science must answer questions that are being asked today, while improving standards that are not appropriately meeting the needs of our patients. My **long-term career goal** is to become a physician scientist, integrating my passion for discovery with critical clinical knowledge. My plan is not to simply perform best medical practice; I want to *improve* best medical practice.

My **academic training** began at the University of San Francisco, where I studied biology with a molecular concentration. During this time, I garnered my first experience in computational science, constructing phylogenetic trees to examine the evolutionary history of two human cytomegalovirus genes, US27 and US28. In this work, I was exposed to the struggles and satisfaction of data curation, organization, and analysis. I was also very interested in understanding differences between various algorithms used for sequence alignment, hierarchical clustering, and tree building. It was exciting to realize other scientists had worked to develop these methods and shared them freely to further discovery in more laboratories and fields than they could hope to engage with. Although, I thoroughly enjoyed my time as an undergraduate researcher, I remained steadfast in choosing a career focused on medicine. All of my plans changed, however, when I listened to a talk by Dr. William Bosl regarding the use of machine learning to detect autism from seemingly normal electroencephalograms (EEGs) of children as young as six months old. The idea of finding clinically relevant patterns that are invisible to the naked eye fascinated me. I was hooked, but I lacked the requisite computational skills to join Dr. Bosl's research team. Although I had previously planned to apply to medical school in just two months, I decided that I couldn't allow this interest to go unexplored. By the end of that week, I applied to the Masters of Health Informatics program, becoming the *first student at the University of San Francisco to complete a 4+1 program with a B.S. in Biology and an M.S. in Health Informatics*. Throughout my exposure to the computational sciences, I became even more steadfast in my desire to intelligently utilize the vast datasets that our healthcare system generates daily.

Moving forward, I took this passion to the Medical Scientist Training Program (MSTP) at Case Western Reserve University. Here, I work in Dr. Jacob Scott's lab, which focuses on the evolution of cancer using a variety of methods, including theoretical mathematics, data analytics, and experimental biology. Since joining this lab, I have been excited to study how we can take advantage of convergent states of drug response phenotypes to extract biomarkers of chemo-sensitivity or -resistance. Utilizing open-source software and publicly available databases, I have created a method for deriving gene expression signatures predictive of therapeutic sensitivity or resistance. Further, I analyze tightly controlled long-term evolution experiments which examine the changes in collateral drug response over time as cancer cells become resistant to first-line therapy. I am proud to utilize software that is easily transferrable between laboratories, and I will continue to make contributions to these incredible resources. In addition to publishing the results of this work, I will publish all related code and conveniently formatted data in a public GitHub repository. I believe that open science is essential to the progression of translational research, bringing diligent work from one laboratory into the hands of scientists around the world.

My educational background gives me a distinct advantage while studying the evolution of cancer. I have a strong *foundation in the biological sciences,* which was bolstered by my undergraduate research using phylogenetics to examine viral evolution. I use this knowledge to think critically about the evolutionary mechanisms employed by cancer cells to overcome the selective pressures of chemotherapy and radiation. Further, the *computational skills* I've acquired while taking health informatics courses were expanded from the research that went on to shape my Master's Thesis, where I looked for patterns in large EEG datasets to improve the diagnostic accuracy of various neurologic conditions. This bioinformatic skillset I have acquired (and continue to expand) allows me to responsibly appraise, clean, and analyze the large, messy datasets that are publicly available. And finally, my *clinical perspective* helps inform hypothesis generation and improves the translation of our work to the bedside. With this grant, I am eager to utilize my unique training to explore the evolution of cancer and devise improved treatment plans for the patients of today.

B. Positions and Honors

Positions and Employment

2017-	Graduate research assistant, Case Western Reserve University
2016-2017	Graduate research assistant, University of San Francisco
2014-2017	Copy Editor and Content Manager, Keas Inc, San Francisco, CA
2015-2016	Undergraduate research assistant, University of San Francisco
2013	Undergraduate research technician, University of San Francisco

Other Experience and Professional Memberships

2019-	American Association for Cancer Research, Associate Member
2017-	Phi Delta Epsilon, International Medical Fraternity

Honors

2019	Rising Star Award—Innovators in AYA Cancer Symposium, Case Comprehensive Cancer Center, Cleveland, OH
2016	Dean's Medal of Excellence—Collage of Arts and Sciences, University of San Francisco
2016	Graduated Summa Cum Laude with Honors—University of San Francisco
2016	Graduate Nursing Merit Scholarship ($3,000 single payment)—Health Informatics Program, Department of Nursing, University of San Francisco
2012-2016	USF President's Merit Award ($10,000 per year)—University of San Francisco
2012-2016	Dean's List (all semesters)—Collage of Arts and Sciences, University of San Francisco
2015	Carol Chihara Award—Department of Biology, University of San Francisco

C. Contributions to Science

1. **Undergraduate Research:** Early in my undergraduate education, I joined Dr. Juliet Spencer's laboratory, where our team examined the interactions between human cytomegalovirus (HCMV) and its host. As a research technician, I gained insight into the day-to-day activities of a bench laboratory and developed

an intense curiosity regarding the co-evolution of cancer and HCMV within a host. After this initial exposure, I chose to remain on this team to complete research for an honors thesis in my final undergraduate year. Here, I worked on a bioinformatics-based project that focused on elucidating the evolutionary history between two G-protein-coupled receptor (GPCR) HCMV proteins, pUS27 and pUS28. This work included pulling protein sequences from Genbank, aligning their sequences utilizing the MUSCLE multiple sequence alignment tool, and performing phylogenetic analysis with Bayesian and maximum likelihood methods. The phylogenetic analyses showed that using both Bayesian and ML methods, the US27 and US28 protein sequences clustered together with a single human GPCR, CX3CR1, as their common ancestor. From these results, I concluded that the two genes likely evolved via a gene duplication event with further neofunctionalization of US27 after duplication. Moving forward with this work, I defended my honors thesis and went on to write and publish my first, first-author manuscript.

a. Publications:
    i. **Jessica A. Scarborough**, John R. Paul, Juliet V. Spencer, Evolution of the ability to modulate host chemokine networks via gene duplication in human cytomegalovirus (HCMV), *Infection, Genetics and Evolution*, Volume 51, 2017, Pages 46-53, ISSN 1567-1348, http://dx.doi.org/10.1016/j.meegid.2017.03.013.
b. Abstracts:
    i. **Scarborough J.A**., Paul J.R., Spencer J. Virus-Host Co-evolution: Determining the origin of Human Cytomegalovirus US27 and US28 (2016). Poster presentation. Collage of Arts and Sciences, University of San Francisco Creative Activity and Research Day. San Francisco, CA.

2. **Graduate (Masters) Research:** I worked in Dr. William Bosl's laboratory at the University of San Francisco when completing a capstone research project to satisfy requirements for an M.S. in Health Informatics. The goal of our project was to develop a method for the rapid detection of benign partial epilepsy of childhood with centrotemporal spikes (BECTS). This condition can be difficult to diagnose as symptoms typically appear at night, requiring a 72-hour sleep study to confirm. Therefore, our method would require the detection of subacute disease from EEG readings that appear normal. A neurophysiology resident at Boston Children's Hospital selected 30 second EEG segments from control and BECTS patients that all appeared normal. The readings were transformed using successive averaging of the time series to create new values for each time scale. Next, variables for recurrence quantitative analysis (RQA) were calculated for each scale. It was very exciting to find that plotting the RQA values of each variable against the time scales for a given lead showed distinct differences between controls and awake patients with BECTS. Importantly, this demonstrated that despite appearing normal to medical professionals, mathematical transformation of the EEGs could differentiate between control and BECTS patients. This work became an integral part of my capstone thesis.
    a. Publications:
        i. **Scarborough, Jessica A.,** "The Acquisition and Analysis of Electroencephalogram Data for the Classification of Benign Partial Epilepsy of Childhood with Centrotemporal Spikes" (2017). *Master's Theses*. 221. https://repository.usfca.edu/thes/221
    b. Abstracts:
        i. **Scarborough, J.A.,** Loddenkemper, Tobias, Bosl, W.J. Nonlinear Analysis for Detection and Classification of Benign Childhood Epilepsy with Centrotemporal Spikes (2017). Poster presentation. American Clinical Neurophysiology Society Annual Meeting and Conference.

3. **Graduate (PhD) Research:** My ongoing research occurs in the lab of my PhD advisor, Dr. Jacob Scott of the Cleveland Clinic Foundation's Translational Hematology and Oncology Research Department. My ***doctoral dissertation project*** entails the exploitation of convergent evolution between cancer cell lines and even across cancer subtypes to extract biomarkers of therapeutic response. First, I have developed a novel method for deriving gene signatures. Beginning with differentially expressed genes between cell lines that are resistant and sensitive to a given chemotherapy, a co-expression network is built with the aim of discovering groups of genes that together promote sensitivity or resistance to a drug. This method can be used to predict response to any therapeutic regimen, including antibiotics, chemotherapy, and radiation. Additionally, it has been used for the analysis of two long term evolution experiments within our

laboratory. Both of these tightly controlled studies examine the evolution of evolutionary replicates of cell lines repeatedly challenged with various chemotherapies. The first study, a pilot, examined Ewing's sarcoma cell lines and the second will examine EGFR+ non-small cell lung cancer (NSCLC). In these long-term evolution experiments, evolutionary (biological) replicates of cancer cell lines are evolved to become resistant to standard treatment. In the case of Ewing's sarcoma, they are exposed to drug combinations of vincristine-doxorubucin-cyclophosphamide and etoposide-cyclophosphamide. With the EGFR+ NSCLC experiment, replicates are exposed to one of two targeted treatments (gefitinib or osimertinib). After each drug exposure, samples are tested for their collateral response to a panel of drugs and a portion of cells will be saved for future RNA-sequencing. This method of deriving gene signatures can be used to examine the differences of gene expression that lead to chemotherapeutic resistance, agnostic of cell line and treatment history.

a. Publications:
    i. **Jessica A Scarborough**, Erin McClure, Peter Anderson, Andrew Dhawan, Arda Durmaz, Stephen L Lessnick, Masahiro Hitomi, and Jacob G Scott. Identifying states of collateral sensitivity during the evolution of therapeutic resistance in Ewing's sarcoma. *bioRxiv*, 2020. PMCID: NA. Under review at *iScience*

b. Abstracts:
    i. **Scarborough, J.A**, Dhawan, A., Scott, J., Generating Gene Expression Signatures Predictive of Therapeutic Response in Lung Adenocarcinoma (2018). Poster presentation. Cleveland Clinic Foundation Lerner Research Day. Cleveland, OH.
    ii. **Scarborough, J.A**, Dhawan, A., Scott, J., Generating Gene Expression Signatures Predictive of Therapeutic Response in Lung Adenocarcinoma (2018). Poster presentation. Case Western Reserve University Lepow Research Day. Cleveland, OH.
    iii. **Scarborough, J.A**, Dhawan, A., Scott, J., A Novel Method For Extracting Gene Signatures Predictive of Chemotherapeutic Response (2019). Poster presentation. Case Western Reserve University Lepow Research Day. Cleveland, OH.
    iv. **Scarborough, J.A.**, McClure, E., Sedor, G., Hitomi, M., Scott, JG. Identifying States of Collateral Sensitivity During the Evolution of Therapy Resistance in Ewing's Sarcoma. (2019) Poster Presentation. Innovators in AYA Cancer Symposium. Cleveland, OH.
    v. **Scarborough, J.A**, Dhawan, A., Scott, J., Deriving Robust Gene Signatures Predictive of Chemotherapeutic Response (2020). Poster presentation. American Association for Cancer Research 2020 Annual Meeting. San Diego, CA.**

**Accepted for poster presentation, but conference was delayed due to SARS-CoV-2

D. Additional Information: Research Support and/or Scholastic Performance

MCAT Score:

USMLE Step 1 Score:

University of San Francisco B.S. Biology (Cumulative GPA)			University of San Francisco M.S. Health Informatics (Cumulative GPA)		
YEAR	COURSE TITLE	GRADE	YEAR	COURSE TITLE	GRADE
2012	Written & Oral Communication		2015	Perspectives in Health Informatics	
2012	FYS: Dance in San Francisco		2015	Medical Microbiology*	
2012	General Chemistry I + Lab		2015	Medical Microbiology Lab*	
2012	General Biology I + Lab		2016	Health Data Security, Privacy, and Confidentiality	
2013	Written & Oral Communication		2016	CS for Health Inf. Professionals	
2013	Latin American Perspectives		2016	Human Physiology*	
2013	General Chemistry II + Lab		2016	Human Physiology + Lab*	
2013	General Biology II + Lab		2016	Capstone Project in Health Informatics	
2013	Second Semester Spanish		2016	Ethics and Policy Considerations of Health and Bioinformatics	
2013	Biostatistics		2016	Semantic Organization of Health Data Information and Data Semantics	

2013	Organic Chemistry I
2013	Organic Chemistry Lab I
2013	Cell Physiology
2014	Calculus & Analytic Geometry
2014	Urban Agriculture: Spring
2014	Organic Chemistry II
2014	Organic Chemistry Lab II
2014	Genetics + Lab
2014	Great Works: Spirit of Romance
2014	Mystery of God & Human Person
2014	Introductory Physics I + Lab
2014	Ethics
2015	Introductory Physics II + Lab
2015	Gymnastics-Tumbling
2015	Undergraduate Sem in Biology
2015	Special Topic: Forensic Gen
2015	Medical Microbiology*
2015	Medical Microbiology Lab*
2015	Great Philosophical Questions
2015	Fundamentals of Biochemistry
2015	Honors Research in Biology
2015	Conservation Biology
2015	Conservation biology Lab
2016	Human Physiology*
2016	Human Physiology Lab*
2016	Evolution
2016	Honors Thesis Writing
2017	Capstone Project in Health Informatics
2017	Digital Health Entrepreneurship
2017	Statistical Computing for Biomedical Data Analytics
2017	Clinical Decision Support & Health Data Analytics

Case Western Reserve University
Medical Scientist Training Program (GPA)

YEAR	COURSE TITLE	GRADE
2017	Introduction to MSTP	
2017	Integrated Biol Sciences I**	
2017	Clinical Science I**	
2017	Research Rotation in MSTP	
2018	Integrated Biol Sciences II**	
2018	Clinical Science II**	
2018	Research Rotation in MSTP	
2018	Research Rotation in MSTP	
2018	Integrated Biol Sciences III**	
2018	Clinical Science III**	
2019	SYBB Research	
2019	Statistical Methods I	
2019	Technologies in Bioinformatics	
2019	Data Integration in Bioinformatics	
2019	Translational Bioinformatics	
2019	Fundamentals Clinical Informtn	
2020	Bioinformatics for Sys Biology	
2020	Current Issues in Genetic Epi: Design and Analysis of Seq Studies	
2020	Biomedical Informatics and Systems Biology Journal Club	

University of San Francisco grading:
B.S.: Passing is D- or better
M.S.: Capstone projects are graded P (pass) or F (fail). In all other courses, passing is C- or better.
* These courses overlapped as elective courses in both the B.S. in Biology and M.S. in Health informatics

Case Western Reserve University grading:
Research rotations and SYBB Research are graded as P (pass) or F (fail). In all other courses, passing is D- or better; IP = In progress
**These courses comprise the first two-years of pre-clinical curriculum at the CWRU School of Medicine. The medical school curriculum is organized into blocks of organ systems and clinical practices including two graded portfolios of reflections. The block system is described as follows:

Block 8: Foundations of Clinical Medicine
Block 7: Structure
Block 6: Cognition, Sensation, and Movement
Block 5: Host Defense and Host Response
Block 4: Homeostasis
Block 3: Food to Fuel
Block 2: The Human Blueprint
Block 1: Becoming a Doctor