WINSTON CHURCHILL FOUNDATION OF THE UNITED STATES
Application for the Churchill Scholarship

PERSONAL INFORMATION

Name Shimko (*Last*) Tyler (*First*) C (*Middle*)

Date of Birth 01/26/1993 (*mm / dd / yyyy*) Gender Male ☒ Female ☐

Current Address [redacted] (*Address*)

[redacted] (*City*) [redacted] (*State*) [redacted] (*Postal Code*)

Telephone [redacted] Email Address [redacted]

Permanent Address [redacted] (*Address*)

[redacted] (*City*) [redacted] (*State*) [redacted] (*Postal Code*)

Telephone [redacted] Parent/Guardian Name(s) [redacted]

EDUCATION

Institution	Dates	Degree	GPA
University of Utah	05/08/2015	BS	3.891
Major/Minor, Other: Biology/Chemistry			
Major/Minor, Other:			
Major/Minor, Other:			

PROGRAM OF STUDY AT CAMBRIDGE UNIVERSITY

DAMTP	Computational Biology	MPhil
Department	Field of study	Degree

Signature _____ **Date** _____

By my signature I certify that I am a citizen of the United States and that, to the best of my knowledge, the information provided in my application is accurate and true.

LIST OTHER FELLOWSHIPS/AWARDS FOR WHICH YOU ARE APPLYING

(1) DOE CSGF

(2) Gates Cambridge

(3) Hertz

(4) Marshall

(5) NSF-GRFP

(6)

TO WHAT OTHER GRADUATE PROGRAMS ARE YOU APPLYING?

(1) Northwestern, PhD, Biology

(2) Stanford, PhD, Genetics

(3) UCLA, PhD, Human Genetics

(4) UCSD, PhD, Bioinformatics

(5) UCSF, PhD, Biology

(6) University of Washington, PhD, Genome Sciences

LETTERS OF REFERENCE

	1st Reference	2nd Reference
Name	Erik Andersen	Erik Jorgensen
Title/Position	Assistant Professor	Professor
Department	Molecular Biosciences	Biology
Address1	[redacted]	[redacted]
Address2		
Institution		
Telephone		
Email		

	3rd Reference	4th Reference
Name	Gillian Stanfield	Leonid Kruglyak
Title/Position	Assistant Professor	Professor
Department	Human Genetics	Human Genetics and Biological Chem
Address1	[redacted]	[redacted]
Address2		
Institution		
Telephone		
Email		

FUTURE CAREER PLANS

I plan to complete a PhD program in genetics with a strong focus on computation and statistics. Following the completion of my PhD, I plan to first pursue a position as an academic scientist. An academic position will afford me a close-knit yet open scientific community as well as immerse me in an environment where scientific rigor is paramount. In this academic position, I will have the opportunity to develop and hone my skills as an educator, sharing my knowledge and experience not only with graduate students in my laboratory but also with with undergraduates in a classroom setting. Depending on the direction and medical pertinence of my research, I may then seek to form a startup company to translate my research to medically relevant applications. Regardless of ability to start my own independent genomics company, I envision that my career will span the realms of academic and industrial science.

Publications

TC Shimko and EC Andersen (2014) COPASutils: an R package for reading, processing, and visualizing data from COPAS large-particle flow cytometers. PLOS ONE.

Presentations

TC Shimko (2014) Data Wrangling and Genetic Cartography: Linkage mapping with recombinant inbred lines. Northwestern U Worm Club. (Presentation)

EC Andersen and TC Shimko (2013) Using natural variation to decipher the complex genetic causes of C. elegans drug sensitivities. International C. elegans Meeting. (Presentation)

EC Andersen and TC Shimko (2013) Using high-throughput fitness assays to decipher the genetic causes of C. elegans drug sensitivities. Society for Molecular Biology and Evolution Annual Conference. (Presentation)

TC Shimko, EC Andersen, and L Kruglyak (2013) Identifying the genes that control paraquat resistance in the roundworm C. elegans. National Conference on Undergraduate Research. (Poster)

TC Shimko, EC Andersen, and L Kruglyak (2013) Identifying the genes that control paraquat resistance in the roundworm C. elegans. Utah Conference on Undergraduate Research. (Poster)

TC Shimko, C Frokjaer-Jensen, and EM Jorgensen (2012) Universal Transgene Insertion in C. elegans. University of Utah Bioscience Symposium for Undergraduate Researchers. (Poster)

TC Shimko, C Frokjaer-Jensen, and EM Jorgensen. (2012) Universal Transgene Insertion in C. elegans. Undergraduate Research Symposium. (Poster)

Non-academic interests and activities

Department of Biology Student Advisory Committee Member (Fall 2014-Present) - Reviewed faculty for retention, promotion, and/or tenure based on personal interviews and classroom feedback as well as managed dispersal of department-allocated funds from student government.

Undergraduate Research Ambassador, Undergraduate Research Opportunities Program (August 2012-Present) - Presented on research opportunities to various student groups and classes at the University of Utah as well as to high school students on outreach days.

Intramural Football Team Captain (August 2011-October 2013, 3 fall leagues and 1 spring league) - Responsible for organizing team communications and maintaining orderly and sportsmanlike conduct on the field.

PLoS Student Blog Regular Contributor (February 2013-Present) - Responsible for writing ~2 articles/semester on topics related to science (broad-sense), biology, or the role of science in society.

Data Analyst for Fossil Free U Student Group (August 2012-August 2013) - Assembled and analyzed a survey to determine student sentiment toward the notion of divestment of the school's endowment from the top 200 fossil fuel companies, organized presentation to student government leaders

Previous Foreign Travel and Study

Country:	Year:	Length of Visit:	Purpose of Visit:
Bahamas	2003	1 week	Vacation
Canada	0	Various	Vacations

Tyler Shimko, University of Utah
Fellowships/Awards

Myriad Academic Excellence Award (Merit-Based, College of Science) - Fall 2014 to Spring 2015 - One of 6 awards given to top rising seniors in the College of Science with an interest in studying genetics, cell, or molecular biology

Barry Goldwater Scholarship (Nationally Competitive, Research-Based) - Fall 2013 to Spring 2015 - Awarded as a sophomore

University of Utah College of Science Dean's Scholarship (Merit-Based, College of Science) - Fall 2013 to Spring 2014 - One of several awards given to top students in the College of Science based on academic merit

Theodore Verender Hanks Scholarship - Fall 2013 to Spring 2014 - Awarded to top applicant in the College of Science who is not a Utah resident, based on academic merit

Undergraduate Research Opportunities Program Assistantship - Spring 2012 - Provided funding for one semester to conduct independent research in a university laboratory, awarded based on written research proposal

Full Resident/Half Non-Resident Partial Tuition Waiver Scholarship (Merit-Based) - Fall 2012 to Spring 2015 - Awarded based on academic merit

Dean's List - Fall 2011 to Spring 2014

Full Resident Partial Tuition Waiver Scholarship - Fall 2011 to Spring 2012 - Awarded based on academic merit

Tyler Shimko, University of Utah
Research/Employment Experience

Undergraduate Researcher (Stanfield lab, University of Utah, volunteer 20-25 hrs/week) - Sep. 2013 to Present - Analyzed genomic sequence data and identified genetic variants implicated in abnormal sperm activation phenotypes in *C. elegans*. This work will be presented at the University of Utah's 2015 Undergraduate Research Symposium and will be published as my Honors thesis.

Undergraduate Researcher (Andersen lab, Northwestern University, paid 40-50 hrs/week) - May 2014 to Aug. 2014 - Designed and built software to process data from COPAS large-particle flow cytometers and investigated the genetics of complex traits through the analysis of genetic linkage mapping data from previous summer. This work was published in *Shimko and Andersen, 2014* and was presented to the Northwestern University Worm Club on July 30th, 2014.

Undergraduate Researcher (Stanfield lab, University of Utah, volunteer 20-25 hrs/week) - Sep 2013 to May 2014 - Genetically mapped mutations affecting sperm activation in *C. elegans*.

Undergraduate Researcher (Andersen lab, Northwestern University, paid 40-50 hrs/week) - May 2013 to Aug 2013 - Constructed high-throughput phenotyping pipeline for use in genetic linkage mapping studies with *C. elegans*. This work will be published in a paper that is currently in prep.

Undergraduate Research Advisor (Office of Undergraduate Research, University of Utah, paid 5-10 hrs/week) - Jan 2013 to May 2013 - Helped fellow undergraduates find research opportunities on campus and begin involvement in research projects.

Undergraduate Researcher (Jorgensen lab, University of Utah, volunteer 10-20 hrs/week) - Sep 2012 to May 2013 - Investigated protein involved in synaptic vesicle recycling in *C. elegans*.

Undergraduate Researcher (Kruglyak lab, Princeton University, paid 40-50 hrs/week) - May 2012 to Aug 2012 - Constructed *C. elegans* strains used to investigate the roles of genomic regions on phenotypes. This work was presented by Dr. Erik Andersen as an oral presentation at the 2013 International *C. elegans* Meeting and as a poster at the 2013 Society for Molecular Biology and Evolution Meeting. I presented this work as a poster at the 2013 Utah Conference on Undergraduate Research and the 2013 National Conference on Undergraduate Research.

Undergraduate Researcher (Jorgensen lab, University of Utah, volunteer/paid 10-20 hrs/week) - Jan 2012 to May 2012 - Constructed universal transgene landing sites in the genome of *C. elegans*. This work was presented as a poster at the University of Utah's 2012 Undergraduate Research Symposium and 2012 Bioscience Symposium for Undergraduate Researchers.

Tyler Shimko, University of Utah

Proposed Program of Study

While at Cambridge, I plan to pursue a Master of Philosophy (MPhil) in Computational Biology. The Computational Biology MPhil is an intense program that will strengthen my budding skills in the computational and statistical aspects of modern biology. Though several of my classes have introduced me to the fundamentals of common statistical methods and computational tools, I recognize that the field of biology is trending toward ever more computationally intensive techniques and protocols.

The Computational Biology MPhil will supplement my existing knowledge of computer science and statistics while challenging my skills during the internship portion of the program. The program begins with two terms of classroom instruction. During the taught modules, I will take classes such as Genome Sequence Analysis and Population Genetic Analysis of Genomic Data, which will build upon the skills that I have acquired in my study of natural variation in the roundworm *Caenorhabditis elegans* (*C. elegans).* The taught modules also include topics, such as Systems Biology and Structural Biology which will be integral to my proposed internship project. The classes associated with the program encapsulate the central dogma of biology, the progression from DNA to RNA to protein, within a computational shell. This approach will allow me to develop a skill set with which I can make fundamental contributions to the understanding of genetic and molecular interactions. Upon completion of the classroom instruction, I will have the capacity to utilize modern computational tools to rapidly analyze biological data.

For my internship, I propose to work with the research group of Dr. Eric Miska, of Cambridge's Gurdon Institute, to develop a computational model of transgenerational epigenetic inheritance (TEI). TEI has long been described in the academic literature as a method for traits to be passed from parents to progeny through a pathway external to the inherited DNA sequence. Recently, it has been shown that small RNA molecules play a role in the alteration of epigenetic signals, which have the capacity to affect gene expression and, consequently, an organism's phenotype. With Dr. Miska's group and the skills I develop during the taught portion of the program, I will model the cellular interactions that control TEI as a series of differential equations, a model which is fitting given the dynamic nature of and the feedback cycles governing the process. In order to develop a model that accurately recapitulates interactions at the molecular level, we will need to carefully consider the stability of varying sequences of small RNA molecules and their ability to interact with DNA and proteins. We will utilize our preliminary models to guide further laboratory experiments which will quantify the critical cellular feedback and control mechanisms that affect TEI. Using the data from these experiments, we will be able to refine our model so that it reflects the process that we have observed empirically and accurately predicts activity related to TEI.

The internship project will be completed using the model organism *C. elegans*, with which I have much experience. My prior research using *C. elegans* will give me an advantage in that I already understand the major biological functions associated with the animals. Therefore, I will be able to immediately immerse myself in research during the internship, which will be particularly beneficial given its short duration. By the end of the internship, I hope to have developed a working model of TEI that accurately and quantitatively depicts the process as it occurs in *C. elegans*. Additionally, I hope to produce a suite of computational tools that can be used to model TEI in higher-order organisms. I believe this project will fundamentally expand our understanding of inheritance beyond the direct transfer of DNA and provide a quantitative foundation for TEI upon which other researchers and I can build.

Tyler Shimko, University of Utah
Personal Statement

Changes in the order of the chemical bases in our entire set of DNA, our genome, shape us not only in height, weight, and hair color, but also in disease susceptibility and drug tolerance. Unfortunately, despite the massive strides made in genomics over recent decades, the genetic components of disease and treatment remain largely enigmatic. In the coming years, I hope to apply statistical and computational techniques to advance our understanding of genomics and amplify its role in human medicine. I recognize that through further instruction and practical experience, I can contribute substantially to our understanding of genomics. My pursuit of research thus far has solidified this conviction.

My first foray into biological research came during my freshman year of college. I joined the laboratory of Dr. Erik Jorgensen at the University of Utah to develop my skills in molecular biology and to assist in the construction of universal transgene insertion sites within the genome of the model roundworm *Caenorhabditis elegans* (*C. elegans*). By stitching together existing portions of sequence with known function, the lab's members could design DNA sequences that accomplished exceptional feats. I realized, however, that although Dr. Jorgensen's lab members had developed many of their techniques through empirical observations, the use of computer aided molecular design and existing sequence data could greatly augment their tool set. I also recognized that if I wanted to utilize computational tools in my own research, I needed experience working with individuals extensively trained not only in biology, but also in mathematics and computer science. Over the spring semester of my freshman year, I sought out summer internships in laboratories with both computational and molecular biological facets. I was able to obtain an offer from Dr. Leonid Kruglyak, of Princeton University at the time.

In Dr. Kruglyak's lab I worked with Dr. Erik Andersen, a post-doctoral fellow. Dr. Andersen had previously completed a mapping experiment in which he had identified a region of the *C. elegans* genome that conferred resistance to the herbicide paraquat. He enlisted my help to construct strains to identify the causal genomic variations in that region. I explored different techniques, including modern molecular biology and more classical genetic crosses to construct strains to replicate the resistance effect seen previously. Throughout the course of the summer, I supplemented my laboratory experience with instruction on the computational methods that Dr. Andersen had employed in the mapping experiments. As a geneticist with experience in computer science and mathematics, Dr. Andersen introduced me to the statistical programming environment R. I became enamored with computation as a method to streamline biological research. Since both Dr. Andersen and I found our partnership productive, we agreed to continue our collaboration in his new laboratory at Northwestern University in the following summers.

Over the next year, I continued my self-study of programming and statistics. I taught myself the basics of the R, python, and javascript programming languages. I began applying these skills whenever I saw the chance in the Jorgensen lab. Though my skills developed slowly at first, it wasn't long before I was implementing computational methods to save myself time during laboratory experiments, such as writing a simple program to calculate the masses of chemicals needed for serial dilutions. Programming helped me to think through problems as a series of discrete steps, breaking large issues down, making them seem less intimidating. I knew that biology needed computation.

Working with Dr. Andersen at Northwestern, I have had the opportunity to explore how genetic variation dictates the way in which organisms respond to their environment. I have worked to determine the ways in which the genetic variation present in the worldwide population of *C. elegans* affects responses to different chemicals including herbicides, pesticides, chemotherapeutics, and anthelmintics. In my first summer at Northwestern, I helped to construct

and optimize a high-throughput screening technique that allows us to measure the effects of the aforementioned compounds in ways indeterminable by eye. This pipeline allows for the collection of massive datasets that can then be utilized to map differences in response, such as chemical susceptibility, to specific genomic intervals.

In my second summer at Northwestern, we designed and built software to process the data from our screening experiments and run statistical procedures to correlate the phenotypic differences with variations in DNA sequence. This work resulted in the construction of a new software package for R that we made publicly available for laboratories utilizing similar screening equipment. Additionally, we successfully mapped thousands of genetic intervals implicated in resistance to dozens of compounds. Though far from complete, the results of this research could have implications for improving treatment of parasitic nematode infections, increasing the efficacy or reducing the side-effects of chemotherapy, or transforming the way we determine the ecological effects of pesticides and herbicides.

My current laboratory work, in Dr. Gillian Stanfield's lab at the University of Utah, will culminate in the publication of my Honors thesis on the genetics of sperm activation in *C. elegans*. As a part of this project, we have been able to combine classical genetic approaches, such as genetic screens and mapping crosses, with next-generation sequencing technologies and computational tools identify genetic variants which affect the sperm activation pathway. This project is affording me the opportunity to learn new computational skills and share what I have learned with lab members whose backgrounds are heavily focused on classical genetics.

In my pursuit of biological research, I have come to realize that automation, computation, and the ability to capably interact with computers can amplify research output while cleaning data from the noise of human error. Moreover, much of biology is impossible to understand or explore without the aid of computational tools to analyze sequential and physical patterns. The overwhelming majority of biology will soon be out of reach to individuals who cannot utilize computational tools to augment their research. I seek to embrace these computational tools through intense classroom instruction and diligent practice with the most advanced utilities available. I want to improve biological research, fostering the widespread use of computational tools to more rapidly solve the field's most vexing problems in a socially responsible manner.

As a researcher interested in genomics, I am acutely aware that the general public is often skeptical of the claims of researchers and corporations. Though this skepticism is certainly warranted to an extent, much of the distrust and pushback with respect to advances in the field can be explained by a lack of proper communication between researchers and the public. In the Spring of 2013, I joined the writing team at The Student Blog of the Public Library of Science (PLOS) to address this gap in communication. I found that my values as a budding researcher aligned well with those of the team at PLOS, an organization that prioritizes open access to science for both researchers and the general public. In my writing for the blog, I make use of my expertise in the field of biology to describe the fundamental workings of the scientific method and explore the nuances of genomic research. I plan to continue developing my scientific communication skills both internal and external to the academic community. I hope to have a positive impact on the rapid adoption of computational methods in biology and the improvement of scientific literacy, two goals which will assuredly lead to more agile biological research and more informed public decisions.