BIOGRAPHICAL SKETCH

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NAME: Wesalo, Joshua

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

POSITION TITLE: MSTP Trainee

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	FIELD OF STUDY
Franklin & Marshall College, Lancaster, PA	BA	08/2009	05/2013	Chemistry, Economics (Minor: Applied Mathematics)
University of Pittsburgh School of Medicine, Pittsburgh, PA	MD, PhD	06/2014	05/2023	Medicine, Chemistry

A. Personal Statement

I am starting my second year as a graduate student in the Medical Scientist Training Program at the University of Pittsburgh. My goal is to become a translational physician-scientist in cardiology. Ultimately, I want to run a basic science laboratory, practice cardiology, and teach at an academic medical center. During my dual-degree training, I will work at the intersection of chemical biology and vascular biology. My thesis mentor, Dr. Alexander Deiters, is an expert in developing new chemical approaches to solving persistent biological problems. I will complete my thesis work in Dr. Deiters' laboratory studying spatially defined, H_2O_2-responsive inhibition of NADPH oxidase activity as a novel treatment approach for ischemia-reperfusion injury. Aside from Dr. Deiters, I have assembled a complementary team of mentors in vascular biology, taking advantage of the University of Pittsburgh Vascular Medical Institute's strong training environment. My team of mentors will enhance my skills as an experimentalist, communicator, and clinician.

My foundation of past research experiences and achievements has prepared me well to complete the proposed research. Prior to medical school, I focused on developing a new treatment approach for GM3 Synthase Deficiency, a rare neurological disease affecting the Amish population. This project taught me how to design experiments at the interface of biology and chemistry in developing a treatment approach while keeping clinical applicability in mind. Additionally, the project helped build my skills as a synthetic chemist, which I have relied upon to generate pilot data for the present proposal. Through my work, I had the opportunity to work with outstanding physician-scientists and to get to know several patients and families afflicted with this debilitating disease, which inspired me to seek dual-degree training to become a physician-scientist. This project resulted in four poster presentations and two talks, one of which took place at a national conference.

Since joining the MSTP in June 2014, I have completed the preclinical years of medical school (capped off by a clerkship in neurology and psychiatry), the United States Medical Licensing Examination (USMLE) Step 1, and three graduate school research rotations that have broadened my technical skills and my scientific understanding. My graduate school coursework and preliminary exam is complete. With the strong mentoring and rich resources available to me between the department of chemistry and the VMI as outlined in my sponsor's training plan, this fellowship will enable to execute my proposed experiments and to fulfill my goal of becoming a physician-investigator with a research program at the intersection of chemical biology and vascular biology.

B. Positions and Honors

ACTIVITY/ OCCUPATION	START DATE (mm/yy)	ENDING DATE (mm/yy)	FIELD	INSTITUTION/ COMPANY	SUPERVISOR/ EMPLOYER
Graduate Student Researcher	09/16	08/21	Chemistry	University of Pittsburgh	Alexander Deiters, PhD
Graduate Rotation 3	09/15	09/16	Chemistry	University of Pittsburgh	Alexander Deiters, PhD

ACTIVITY/ OCCUPATION	START DATE (mm/yy)	ENDING DATE (mm/yy)	FIELD	INSTITUTION/ COMPANY	SUPERVISOR/ EMPLOYER
Graduate Rotation 2	06/15	08/15	Chemistry	University of Pittsburgh	Alexander Deiters, PhD
Medical Student	08/14	05/23	Medicine	University of Pittsburgh School of Medicine	N/A
Graduate Rotation 1	06/14	08/14	Pharmacology	University of Pittsburgh	Patrick Pagano, PhD
Research Assistant	05/13	05/14	Chemistry	Franklin & Marshall College	Ken Hess, PhD
Research Fellow	05/13	05/14	Chemistry	Clinic for Special Children	Kevin Strauss, MD
Calculus Tutor	08/10	05/13	Mathematics	Franklin & Marshall College	Robert Gethner, PhD
Summer Undergraduate Researcher	06/12	08/12	Pharmacology	University of Pennsylvania	Vladimir Muzykantov, MD, PhD
Undergraduate Researcher	01/12	05/13	Chemistry	Franklin & Marshall College	Ken Hess, PhD
Undergraduate Researcher	06/11	08/11	Chemistry	Franklin & Marshall College	Ryan Mehl, PhD and Ken Hess, PhD
Undergraduate Researcher	06/10	08/10	Chemistry	Franklin & Marshall College	Ryan Mehl, PhD and Ken Hess, PhD
High School Volunteer Research	06/09	08/09	Neuroscience	Kennedy Krieger Institute	Mary E. Blue, PhD
High School Volunteer Research	06/08	08/08	Bioinformatics	Kennedy Krieger Institute	Jonathan Pevsner, PhD

Other Experience and Professional Memberships

2014 - Allegheny County Medical Society
2014 - American Medical Association
2015 - American Chemical Society
2017 - American Heart Association

Selected Honors

2013 - Phi Beta Kappa Society
2013 Magna Cum Laude
2013 Theodore Alexander Saulnier, Jr. Prize in Chemistry— to the student majoring in Chemistry who in the opinion of the faculty demonstrates an especially searching mind in probing the frontiers of the unknown.
2013 Theodore E. Woodward, MD Healing Arts Prize—to the outstanding senior who will be pursuing post-graduate study in a health professions field.
2013 Isaac E. Roberts Prize in Biology— student with the highest grades in biology.
2009-2013 Honor's List
2009-2013 National Merit Scholarship
2009-2013 John Marshall Scholarship
2010 Eric C. Rackow, MD Endowed Achievement Scholarship for the Pre-Healing Arts
2005 and 2006 Carson Scholars Fund Scholarship

C. Contributions to Science

1. **Development of methods for ganglioside GM3 production and analysis for the treatment of GM3 Synthase Deficiency** (Mentors: Ryan A. Mehl, PhD; Kenneth R. Hess, PhD; Kevin Strauss, MD).
   One in one-hundred Amish individuals carry a loss-of-function mutation in GM3 synthase (*Siat9*) that can cause GM3 Synthase Deficiency in their children. Affected children lose control of their movements, lose their vision and hearing, and suffer from profound developmental delay, typically dying before adolescence. No treatment approaches to date have been successful. I worked with a team of clinicians and scientists based at the Clinic for Special Children and Franklin & Marshall College to develop a new approach: ganglioside replacement therapy.

   Once I started work on this project, I developed an assay for quantifying serum gangliosides. Gangliosides are challenging analytes, and this required enzymatic digestion followed by conjugation to a fluorophore and detection with HPLC, so I learned molecular biology, organic synthesis, and analytical chemistry techniques as I developed the assay. Next, I worked on methods to obtain ganglioside GM3 for the therapy. At first, I developed an arduous protocol for extracting milligram quantities of GM3 from buttermilk. Next, I switched my efforts to synthesis of multigram quantities of this complex natural product. Researchers I trained have completed my work and are planning clinical trials through the Clinic for Special Children. Further work is underway at Pittsburgh Children's Hospital to determine how ganglioside replacement therapy will fit in with hematopoietic stem cell or liver transplantation and to optimize the treatment in a mouse model.

   a. **Wesalo, J. S.** Oral presentation. "Laboratory Synthesis of GM3: A Bridge to the Cure." *GM3 Synthase Deficiency Research Summit*. 11 Oct 2016. Children's Hospital of Pittsburgh, Pittsburgh, PA.

   b. **Wesalo, J. S.** Oral presentation. "GM3 Synthase Deficiency." *Genomic Medicine and the Plain Populations of North America.* 17 Jul 2013. Franklin & Marshall College, Lancaster, PA.

   c. **Wesalo, J. S.**; Mehl, R. A.; Hess, K. R. Poster presentation. "From Making Pancakes to Saving Lives: The Quest for a Cure for GM3 Synthase Deficiency in Buttermilk." *Franklin & Marshall College Autumn Research Fair*. 23 Sept 2011. Franklin & Marshall College, Lancaster, PA.

   d. **Wesalo, J. S.**; Mehl, R. A.; Hess, K. R. Poster presentation. "Hot on the Ganglioside Trail: Towards a Practical and Reproducible Assay for Serum Ganglioside Levels in GM3 Synthase Deficiency Patients." *Franklin & Marshall College Autumn Research Fair*. 24 Sept 2010. Franklin & Marshall College, Lancaster, PA.

2. **Small-molecule control of protein function** (Mentor: Alexander Deiters, PhD).
   Conditional control over protein function in living systems empowers us to dissect the molecular mechanism of biological processes. Our group recently pioneered a method for activating protein function using phosphines as a small-molecule trigger (Luo et al., *Nature. Chemistry*, 2016). The method uses site-specific incorporation of unnatural amino acids that are activated through a bioorthogonal Staudinger reduction. Currently, this process requires over an hour for protein activation, which limits its applications. I have synthesized a new amino acid that has shown significantly faster activation *in vitro* and in cells, and I am currently preparing a manuscript on its application to conditionally controlling protein SUMOylation (Luo, J.; **Wesalo, J. S.**; Morihiro, K.; Deiters, A. "Enhanced small molecule switches for protein function: conditional control of SUMOylation." *Journal of the American Chemical Society*. Manuscript in preparation).

3. **Other presentations:**

   a. **Wesalo, J. S.** Oral presentation. "Targeting nanotherapeutics to injured vascular endothelium and quantifying VCAM, a marker of endothelial injury." *CTSA Summer Internship Program Symposium*. 27 Jul 2012. University of Pennsylvania, Philadelphia, PA.

   b. **Wesalo, J. S.** Oral presentation. "Targeting nanotherapeutics to injured vascular endothelium and quantifying VCAM, a marker of endothelial injury." *Franklin & Marshall College Autumn Research Fair*. 19 Oct 2012. Franklin & Marshall College, Lancaster, PA.

   c. **Wesalo, J. S.**; Meijles, D. N.; Cifuentes-Pagano, E.; Pagano, P. J. Poster presentation. "Isoform-specific NADPH oxidase inhibitors for the investigation of the role of NADPH oxidase in tumor necrosis factor-α-induced endothelial dysfunction." *Pitt-CMU MSTP Annual Scientific Retreat*. 21 Aug 2014.

d. **Wesalo, J. S.**; Vázquez-Maldonado, L. A.; Liu, J.; Tsang, M.; Deiters, A. Poster presentation. "Light-activated circularized morpholino oligonucleotides for RNA knockdown and gene silencing in zebrafish." *Pitt-CMU MSTP Annual Scientific Retreat*. 19 Aug 2016. University of Pittsburgh, Pittsburgh, PA.

e. **Wesalo, J. S.** Oral Presentation. "Speeding up control of biomolecular function through the Staudinger reduction." *Biological Chemistry Student Seminar Series*. 25 Apr 2017. University of Pittsburgh, Pittsburgh, PA.

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

YEAR	SCIENCE COURSE TITLE	GRADE
	Franklin & Marshall College	
2009	General Chemistry 1	A
2009	Calculus 3	A
2010	Evolution, Ecology, and Heredity	A
2010	General Chemistry 2	A
2010	Linear Algebra and Differential Equations	A
2010	Principles of Physiology and Development	A
2010	Organic Chemistry 1	A
2010	Probability and Statistics 1	A-
2011	Organic Chemistry 2	A-
2011	Probability and Statistics 2	B+
2011	Cell Biology	A
2011	Fundamental Physics 1	A-
2011	Chemical Analysis	A
2011	Thermodynamics and Kinetics	B+
2012	Introduction to Biochemistry	A
2012	Directed Study–Chemistry	A
2012	Fundamental Physics 2	A
2012	Independent Study–Chemistry	A
2013	Inorganic Chemistry	B+
2013	Medicinal Chemistry	P
2013	Chemistry of Solar Energy Conversion	P
2013	Advanced Biochemistry	A
2013	Independent Study–Chemistry	A

YEAR	OTHER COURSE TITLE	GRADE
	Franklin & Marshall College	
2009	Microeconomics (AP Credit)	S
2009	Macroeconomics (AP Credit)	S
2009	English Language/Composition (AP Credit)	S
2009	English Literature/Composition (AP Credit)	S
2009	US Government and Politics (AP Credit)	S
2009	US History (AP Credit)	S
2009	World History (AP Credit)	S
2009	Calculus 2 (AP Credit)	S
2009	Mortality & Meaning	A
2009	Mathematics of Art	A
2009	Low Brass	A-
2009	Orchestra	NC
2010	Intro to Economic Perspectives	A
2010	Altered States	A
2010	Low Brass	A
2010	Orchestra	NC
2010	Value and Distribution	B
2010	Music Theory 1	A
2011	Intermediate Microeconomics	A
2011	Low Brass	A
2011	Orchestra	A
2011	Game Theory	A-
2011	Elementary Chinese 1	A
2012	Intermediate Macroeconomics	A
2012	Low Brass	A
2012	Orchestra	A
2012	Musicianship 1	A
2012	Environmental History	A
2012	Money and Banking	A
2012	History of Economic Thought	A
2013	Political Economy of Health	A

YEAR	SCIENCE COURSE TITLE	GRADE	YEAR	OTHER COURSE TITLE	GRADE
			2013	Low Brass	A
			2013	Orchestra	A

YEAR	SCIENCE COURSE TITLE	GRADE	YEAR	OTHER COURSE TITLE	GRADE
	University of Pittsburgh School of Medicine			University of Pittsburgh School of Medicine	
2014	Human Anatomy	P	2014	Ethics, Law, & Professionalism	P
2014	Biochemistry	P	2014	Medical Decisionmaking	P
2014	Genetics	P	2014	Medical Interviewing	P
2014	Cellular Pathology 1	P	2014	Introduction to Physical Examination	P
2015	Cellular Pathology 2	P	2015	Advanced Physical Examination	P
2015	Immunology	P	2015	Behavioral Health	P
2015	Medical Microbiology	P	2015	Population Health	P
2015	Neuroscience	P		MSTP Coursework	
2015	Psychiatry	P	2014-2016	Professional Development 1, 2, and 3 (Molecular Medicine, Methods & Analysis, and Grantwriting)	P
2015	Cardiology	P	2014-2016	Research Basis of Medical Knowledge 1 and 2	P
2015	Nephrology	P	2017	Ethics for Medical Scientists	P
2015	Pulmonology	P		Graduate School Coursework	
2015	Digestion & Nutrition	P	2016	Basics of Personalized Medicine	A
2015	Skin & Musculoskeletal System	P	2016	Molecular Biology	A+
2016	Hematology and Oncology	P	2017	Biological Chemistry 2	A+
2016	Endocrinology	P	2017	Imaging Cell Biology in Living Systems	A
2016	Reproduction & Developmental Biology	P	2017	Doctoral Preliminary Evaluation	P
2016	Clinical Psychiatry Core Clerkship	HS			
2016	Neurology Core Clerkship	H			

Grade Legend:

"P" – Pass

1. Franklin & Marshall College: Letter grades of "A" to "C-" are converted to Pass for courses that are taken as Pass/Fail.
2. University of Pittsburgh School of Medicine and MSTP: All preclinical courses are graded Pass/Fail.

"S" – Satisfactory

Franklin & Marshall College awards an "S" for AP credits if a student earns a 4 or 5 on the AP exam and elects to receive credit for it.

"HS" – High Satisfactory (medical school clerkships only).

"H" – Honors (medical school clerkships only).

MCAT: 37S
USMLE Step 1: 257