BIOGRAPHICAL SKETCH

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NAME:JOSHUA MUIA

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POSITION TITLE: INSTRUCTOR IN MEDICINE

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
University of Nairobi, Nairobi, Kenya	B.Sc.	05/2004	Chemistry/Biochemistry
Western Michigan University, Kalamazoo, MI	Ph.D.	05/2010	Bioinorganic Chemistry
Washington University in St. Louis, MO	PostDoctoral	07/2015	Biochemistry and Hematology

A. Personal Statement

I am a basic scientist with broad training and expertise in chemistry, biochemistry and molecular biology. My thesis was on the characterization of Wilson disease protein and during that period of study I developed skills in the use of DNA recombinant technology to express and purify recombinant proteins on a large scale, and biophysical characterization of proteins using circular dichroism, light scattering and gel chromatography techniques. As a postdoctoral fellow in J. Evan Sadler's lab, I gained new skills in tissue culture, bioinformatics, peptide-dye conjugation, and preparation of protocols for patient oriented research. My postdoctoral training not only opened up other areas of research and personal career growth, but also opportunities to have an impact on other people's lives. Throughout postdoctoral fellowship, and now as an Instructor, I have collaborated with scientists within the University and at institutions throughout the world to conduct my research. In terms of my contributions, I helped to develop a patented fluorogenic ADAMTS13 assay with increased sensitivity for ADAMTS13 activity and inhibitors. ADAMTS13 is the enzyme deficient in patients with thrombotic thrombocytopenic purpura (TTP). While characterizing plasmas from TTP patients, I identified an activating antibody in one unique patient that led to the discovery of allosteric activation of ADAMTS13 by its substrate von Willebrand factor (VWF). My current work seeks to understand the regulation of the antithrombotic metalloprotease ADAMTS13. My long term goal is to decipher how regulatory mechanism of ADAMTS13 contributes to hemostasis, and how defects in it can cause bleeding or thrombosis. My research has also involved mentorship of high school students through the Young Scientist Program (YSP) at Washington University in St. Louis. One of my recent students was highlighted in the local newspaper, the St. Louis Dispatch (http://www.stltoday.com/news/local/education/washu-grows-young-scientists/article_c83195d9-36a9-5f54-b4e9-59dc1f3628b2.html). I expect to continue this focus on teaching and mentorship while I establish myself as an independent scientist through this K01 award, working at the interface between basic and clinical research.

1. Sadler, J. E., Muia, J., and Gao, W. Fluorogenic Substrate for ADAMTS13, U.S. Patent Number 8,663,912, March 4, 2014.
2. Muia, J., Gao, W., Haberichter, S. L., Dolatshahi, L., Zhu, J., Westfield, L. A., Covill, S. C., Friedman, K. D., and Sadler, J. E. An Optimized Fluorogenic ADAMTS13 Assay with Increased Sensitivity for the Investigation of Patients with Thrombotic Thrombocytopenic Purpura, J Thromb Haemost, 2013; 11: 1511-8. PMCID: PMC3807872.

3. Muia, J., Zhu, J., Gupta, G., Haberichter, S.L., Friedman, K.D., Feys, H., Vanhoorelbeke, K., Westfield, L.A., Roth, R., Tolia, N.H., Heuser, J.E., and J. Evan Sadler. Allosteric Activation of ADAMTS13 by Von Willebrand Factor. *Proc Natl Acad Sci U S A*. 2014; 111(52):18584-18589. PMCID: PMC4284596.
4. Hubbard, R.A., Heath, A.B., and Hovinga, J.A.K. Establishment of the WHO 1st International Standard ADAMTS13, plasma (12/252): communication from the SSC of the ISTH, J Thromb Haemost 2015; 13: 1151–53 (International Collaborative Study). PMID: 25714758.
5. Deforche, L., Roose, E., Vandenbulcke, A., Feys, H., Springer, T.A., Mi, L-Z., Walz, T., Muia, J., Sadler, J.E., Soejima, K., Rottensteiner, H., De Meyer, S.F., Deckmyn, H., and Vanhoorelbeke, K. The Flexible Tail of Hemostatic Enzyme ADAMTS13 is Able to Shield the Active Site. J Thromb Haemost 2015; 13: 2063–75. PMID: 26391536
6. Reflections on scientific collaboration between basic researchers and clinicians. J Thromb Haemost 2016 (accepted manuscript online): DOI: 10.1111/jth.13447.

B. Positions and Honors

Positions and Employment

2001-2004	Research Assistant, Departments of Chemistry and Biochemistry, University of Nairobi, Nairobi, Kenya
2005-2010	Research and Teaching Assistant, Department of Chemistry, Western Michigan University, Kalamazoo, MI
2010-2015	Postdoctoral Research Associate, Division of Hematology, Washington University, St. Louis, MO
2015-	Instructor in Medicine, Division of Hematology, Washington University, St. Louis, MO

Other Experience and Professional Memberships

2006-	Member, National Organization for the Professional Advancement of Black Chemists and Chemical Engineers (NOBCChE)
2010-	Member, American Society for Biochemistry and Molecular Biology
2013-	Member, International Society on Thrombosis and Haemostasis
2013-	Member, Young Professionals Task Force of the International Society on Thrombosis and Haemostasis
2015-	Member, American Heart Association
2015-	Member, Kenya Society of Thrombosis and Haemostasis

Honors

2007	Graduate College Research Grant, Western Michigan University
2007	Graduate College Travel Award, Western Michigan University
2007	Graduate Student Advisory Board International Travel Award, Western Michigan University
2007	CERM Visiting Fellowship, Center for Magnetic Resonance, University of Florence, Florence, Italy
2009	Western Union Cash for Education African Diaspora Awardee
2010	Service Award, National Organization for the Professional Advancement of Black Chemists and Chemical Engineers
2013	Young Investigator Award, International Society on Thrombosis and Haemostasis
2014	Faculty Reach Out Program (F.R.O.P), Washington University, St. Louis, MO
2014	Young Investigator Award, International Society on Thrombosis and Haemostasis
2016	Judges' Travel Award, Annual Biomedical Research Conference for Minority Students
2016	Outstanding Student Mentor, Young Scientist Program, Washington University
2016	African Born Academic Fellow, the Carnegie African Diaspora Fellowship Program

C. Contribution to Science

1. My very first scientific contribution was the development of biodegradable polymer blends for medical applications. Polylactic acid (PLA) is widely used biodegradable polymer in many pharmaceutical, biomedical and environmental applications. For example, PLA is used to make sutures and implantable orthopedic medical devices. The goal of my work was prepare polymer blends from polylactic acid (PLA)

and gum arabic (GA) with good mechanical strength but faster degradation rates *in vivo*. Such properties would favor applications in tissue injury repair and wound healing. I contributed this work by characterizing two gum arabic sources; prepared polymer blends film with varying composition of PLA and GA. I also performed stability studies and analyzed rates of biodegradation by thermophilic bacteria. We published these studies in the Journal of Polymer and Environment (Onyari et al. J Polym Environ (2008) 16:205–212).

a. Onyari, J., Mulaa, F., Muia, J., Shiundu, P. Biodegradability of Poly (lactic acid), Preparation and Characterization of PLA/Gum Arabic Blends, J Polym Environ 2008; 16: 205-212

2. I worked on Wilson disease, a rare autosomal disease of copper overload, for my dissertation. The defective protein in this disorder is a copper ATPase pump, ATP7B. My major focus was to characterize how the cytosolic domains of ATP7B acquire copper and translocate it through the membrane. I also wanted to know how disease-causing mutations in these domains could cause Wilson disease *in vivo*. Using biophysical and biochemical characterization tools, I found that disease-causing mutations disrupted the pump's protein structure and thereby undergoing rapid degradation. My work was recognized by several Graduate College (Western Michigan University) awards, and my adviser, Professor David L. Huffman, was recognized by the Wilson Disease Association by the award of a research grant (https://www.wmich.edu/wmu/news/2007/01/059.html).

3. My recent contributions have been in the study of the metalloprotease ADAMTS13, von Willebrand factor (VWF) and thrombotic thrombocytopenic purpura (TTP). I led the development of an optimized fluorogenic substrate, FRETS-rVWF71, for the characterization of patients with thrombotic microangiopathy and for patient-oriented research on TTP. My work on ADAMTS13 assays led to the discovery of activating antibodies, which provided the first clue that ADAMTS13 might be autoregulated. We then described the allosteric activation of ADAMTS13 by its substrate VWF. My contributions in this work were recognized by the International Society on Thrombosis and Hemostasis with Young Investigator Award.
   a. Muia, J., Gao, W., Haberichter, S. L., Dolatshahi, L., Zhu, J., Westfield, L. A., Covill, S. C., Friedman, K. D., and Sadler, J. E. An Optimized Fluorogenic ADAMTS13 Assay with Increased Sensitivity for the Investigation of Patients with Thrombotic Thrombocytopenic Purpura, J Thromb Haemost, 2013; 11: 1511-8. PMCID: PMC3807872
   b. Muia, J., Zhu, J., Gupta, G., Haberichter, S.L., Friedman, K.D., Feys, H., Vanhoorelbeke, K., Westfield, L.A., Roth, R., Tolia, N.H., Heuser, J.E., and J. Evan Sadler. Allosteric Activation of ADAMTS13 by Von Willebrand Factor. Proc Natl Acad Sci U S A. 2014; 111(52):18584-18589. PMCID: PMC4284596
   c. Deforche, L., Roose, E., Vandenbulcke, A., Feys, H., Springer, T.A., Mi, L-Z., Walz, T., Muia, J., Sadler, J.E., Soejima, K., Rottensteiner, H., De Meyer, S.F., Deckmyn, H., and Vanhoorelbeke, K. The Flexible Tail of Hemostatic Enzyme ADAMTS13 is Able to Shield the Active Site. J Thromb Haemost 2015; 13: 2063–75. PMID: 26391536

Complete List of Published Work in My Bibliography:
http://www.ncbi.nlm.nih.gov/sites/myncbi/1jGUibHWOWsAg/bibliograpahy/49329153/public/?sort=date&direction=ascending

D. Research Support

Ongoing Research Support

1. Scientist Development Grant Award, 7/2016-6/2019
   American Heart Association Midwest Affiliate
   Title: Regulation of VWF Cleavage by the Antithrombotic Protease ADAMTS13.
   This proposal seeks to understand why the largest known protein in our body, von Willebrand factor (VWF), which prevents us from excessive bleeding, can turn lethal by forming blood clots. These blood clots are clinical manifestation of thrombotic thrombocytopenic purpura (TTP) and major targeted organs are heart and brain where they cause tissue damage and death.
   Role: PI/Scholar
2. Carnegie African Diaspora Fellowship Program: 2016-2017 funding cycle.
   Title: Research Collaboration on Assays of Hemostatic Proteins ADAMTS13 and VWF, and Strengthening of Medical Curriculum in Coagulation Biochemistry.
   Role: Visiting African Born Scholar at Kenyatta University School of Medicine, Kenya.