May 24, 2019

Committee members,

I write with great interest to request consideration for the TL1 Health Sciences Innovation and Entrepreneurship (HSIE) training program. I am a second-year postdoctoral fellow under the mentorship of [Name] at UAMS. My mentoring team also consists of [Name] and [Name]. My field of expertise lives at the intersection of cutting-edge proteomics applications, high-throughput data processing and analysis, and software application development. I am interested in the HSIE training program for the following reasons:

- Expand my professional network in the biotechnology industry
- Build my entrepreneurial skill set
- Learn the current status of the rapidly-evolving biotechnology industry
- Accelerate commercialization of proteomic software and technologies I am currently developing

My exposure to entrepreneurial endeavors stems directly from my area of research. Proteomics is an equal mixture of academic research and commercial development. For example, I have attended the national conference for the American Society for Mass Spectrometry (ASMS) for the past three years. Each year, companies make their impact by announcing a new mass spectrometer, proprietary software upgrades for instrument control, or optimized commercial kits for sample preparation. These technological advancements enable scientists to conduct more sophisticated experiments and solve greater biomedical challenges. It is apparent that proprietary information drives science in proteomics, and I plan to utilize the HSIE training to hone in on the commercial aspects of the field.

The opportunity to expand my entrepreneurial skills draws my interest to the HSIE training program. My professional discipline is heavily intertwined with technological innovation and advancement. Over the next decade it is apparent that proteomics will present a wealth of business opportunities. Therefore, obtaining a strong skill set of marketing principles and entrepreneurship through the HSIE training program will synergize greatly with my career development. I feel that the opportunities offered through the HSIE training will complement my current technological training and help me develop a unique skillset for my future endeavors.

I am currently working on two projects with the potential for commercialization: a proteomics technique for rapid bacterial identification from clinical samples, and a software pipeline for interactive visualization of proteomics data. Through the mentorship, collaborations, and knowledge gained through this program, I will be able to translate these projects into patentable intellectual property, and in turn, provide these applications to scientists and clinicians at large. In the following sections, I’ll describe two ideas which I would like to pursue during the training period.

Rapid bacterial identification from synovial fluid samples using mass spectrometry

In 2018, I was awarded an Arkansas Children’s Research Institute Postdoctoral Fellowship titled “Rapid bacterial identification from synovial fluid of pediatric septic arthritis cases using mass spectrometry”. I am currently leading this
study in collaboration with [redacted] and [redacted] at Arkansas Children’s Hospital to improve bacterial identification rates of pediatric septic arthritis cases using cutting-edge mass spectrometry. I have personally established all interactions with clinicians for the outlined, translational studies.

Pediatric septic arthritis is a rapid-onset bacterial infection of joint fluid in infants which can lead to irreversible joint destruction, organ failure, or death. Diagnosis and treatment of these cases must occur quickly and accurately to avoid long-term consequences from the infection. Because of the increasing prevalence of antibiotic-resistant bacteria, a reliable bacterial identification is needed to guide antibiotic selection. However, traditional culturing methods fail to identify the pathogenic species of pediatric septic arthritis in one-third to one-half of cases. This lack of growth delays treatment and increases the risk of long-term complications. These poor diagnostic markers, coupled with the narrow window of effective therapeutic intervention for septic arthritis, highlight the urgent need for the development of rapid, sensitive, and accurate techniques for bacterial identification of clinical samples.

Mass spectrometry is an increasingly sensitive and precise technique for the detection and quantification of biomolecules in complex mixtures. Proteomics has developed tremendously over the past decade, due to advances in instrumentation, sample preparation, and data analysis techniques. These advancements enable proteomic workflows to be applied to a greater range of clinical and translational settings. In this project, I am using the latest generation of mass spectrometry instruments and data processing workflows to identify bacterial species directly from synovial fluid samples, without the need to culture bacteria.

This technology could be used by diagnostic laboratories in hospitals worldwide for rapid pathogen detection. Additionally, the targeted mass spectrometry workflow is applicable for the sensitive detection of biomarkers across many different disease states and sample types. My interest in pediatric septic arthritis comes from my son, Jackson Storey, who was diagnosed and treated at Arkansas Children’s Hospital. Personally experiencing the limitations for rapid and accurate treatment drove me to establish interactions with the physicians to develop new diagnostics for commercialization that could be used to help treat children in the future.

Analytical dashboards for interactive proteomic data analysis

Proteomics, like all other high-throughput “omics” biotechnology, generates increasingly large and complex data sets. These data sets require innovative software and algorithms to extract information, find insight, and transform the data into discoveries. To facilitate this process at our institution, I have designed several novel computer programs in my graduate and postdoctoral career. These range from simple scripts which automate time-consuming computational or spreadsheet-related tasks, to specialized data processing workflows which enable complex analyses of high-throughput proteomics data sets (PMID: [redacted]). Most recently, I have developed a pipeline to deliver proteomics data to end users in customized, interactive dashboards (see Figure 1). My motivation to write this software was driven by a desire to improve the efficiency of proteomic workflows, and to improve my knowledge of various programming languages through applied problem solving. However, over the course of the HSIE training program, I hope to obtain an entrepreneurial perspective on the intellectual property value and marketability of this software. In addition, I would like to work with a team of scientists and entrepreneurs to make this application more commercially available to proteomics scientists.

The interactive dashboards are designed to bring data analysis to life. Typically, the results of high-throughput omics experiments are delivered as a static list of differentially expressed features (genes, proteins, etc.) and associated p-values. Although this output is well suited for simple experiments, it does not scale well for more sophisticated experimental designs and increasingly large biological data sets. The results can be overwhelming and difficult to interpret for the end-user. Since most high-throughput biology experiments involve a significant investment of time and resources, a failure to transform the experimental results into knowledge means a loss of time and resources. To alleviate this problem, I have developed a software workflow to deliver the results of proteomics experiments in interactive analytical dashboards. The dashboards render the experimental results through a combination of interactive visualizations, publication-quality figures, and responsive tables. This interactive format facilitates exploration of the data, and insight into the biological system being studied. The dashboards are hosted on a cloud-based server and are
displayed in a web browser, and have no software requirements outside of a modern web browser (Google Chrome) and an internet connection.

In the past 6 months of developing this workflow, I have deployed 8 dashboards to collaborators, and am receiving a growing number of requests for this service. As I continue to develop this software, I would like to explore the potential to transform this workflow into intellectual property. In terms of target customers, the dashboards could be provided to individual clients in a fee-for-service format, or the underlying software could be licensed and sold to other proteomics cores, who would then be able to construct and deliver the dashboards to their clients.

In summary, I believe that my expertise in proteomics technologies and experience with software development and deployment make me an ideal candidate for the HSIE training program. The entrepreneurial skill set obtained through this training program will allow me to translate the projects described above into better diagnostics for pediatric septic arthritis, more efficient analysis of large proteomic data sets, and will foster my continued education and professional development.

Sincerely,

Postdoctoral Fellow
University of Arkansas for Medical Sciences

Figure 1: Snapshot of a dashboard for phosphoproteomic analysis. In the top-left panel, the statistical results of a phosphoproteomic study are displayed as an interactive heat map. Hovering over a point displays relevant metadata for the observation. Selecting points from the volcano plot generates a heatmap in the top-right panel, which reveals two clusters of data: transiently downregulated and stably downregulated phosphosites (right three columns). In the bottom-left panel, a sequence logo of the selected phosphosites is rendered. Parameters for motif enrichment analysis are shown in the bottom-right panel. Program completely developed by the applicant.
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: [Redacted]

eRA COMMONS USER NAME: [Redacted]

POSITION TITLE: Postdoctoral Fellow

EDUCATION/TRAINING:

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A. Personal Statement

My long term research interests involve the development and application of cutting-edge molecular biology and data-analysis techniques to improve the practice of medicine. My academic career has provided me with a wide range of knowledge of many multidisciplinary fields, including neuroscience, genetics, proteomics, statistics, and data science. During my undergraduate training, I helped coordinate mouse research studies investigating the role of serotonin modulators in spatial learning. My graduate studies focused on elucidating the precise molecular mechanisms of establishing meiotic recombination hotspots, using fission yeast as a model organism. This work exposed me to the latest developments in molecular biology like CRISPR-based genome editing, and allowed me to utilize the most advanced mass spectrometry instruments in the world to increase our understanding of recombination during meiosis. In addition, this project presented a unique set of challenges, most notably the interpretation of increasingly large biological data sets. Through these obstacles, I developed the necessary skills to transform big data into big insights, which was instrumental in my success as a graduate student. My postdoctoral position has allowed me to lead independent research, develop my expertise in both proteomics and data analysis, and engage in collaborative team science. I plan on incorporating the entrepreneurial training and experiences from the HSIE program to develop a well-rounded skill set for my future career.

B. Positions and Honors

Positions and Employment

2011-2017 Graduate Student, University of Arkansas for Medical Sciences
2018-present Postdoctoral Researcher, University of Arkansas for Medical Sciences

Professional memberships

2016- Member, American Society for Mass Spectrometry

Honors

2013 Paul Day Award, Department of Biochemistry, UAMS
2013 Travel Award, Southeastern Regional Yeast Meeting
C. Contributions to Science

1. Graduate career: My graduate career focused on combining proteomic techniques and genetic assays to elucidate the mechanism of meiotic recombination hotspot activation. This work led to a genetic finding which challenged previous models regarding the function of two suppressor alleles in *S. pombe*, the development of a genetic screening tool to combine high-throughput genome editing with phenotype selection, and an implementation of the CRISPR-Cas9 system to purify specific genomic loci for characterization by mass spectrometry.


2. Post-doctoral career: My unique combination of mass spectrometry expertise and programming skills has led to several scientific contributions in a short period of time. Through a collaboration formed by attending the annual ASMS conference in 2017, I developed analysis pipeline for a project which studied the role of ethanol consumption on the acetylation of histones in the liver (Kriss et al). In the second collaboration, I helped process and analyze a single-cell RNA sequencing data set to elucidate the role of melanoma E-cadherin expression in responsiveness to immunotherapy (Shields et al). In the third project, I employed a targeted mass spectrometry approach to quantify proteins for which no antibody was available (Byrum et al). In all of these projects, my contributions facilitated the processing and interpretation of data sets that were impractical to analyze manually.


3. **Teaching data analysis and visualization:** During my graduate studies, I learned to use the programming languages R and Python, and I am proud to teach these skills to other scientists. I have taught data science techniques to mass spectrometry core directors, faculty members, and students at the last three IDEAS national workshops, given lectures at departmental interest group meetings, and personally mentored a student at the University of Arkansas at Little Rock to learn to use R for data analysis and visualization. In June, I will teach a portion of a data visualization workshop at the national conference for the American Society for Mass Spectrometry (ASMS).

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

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Classes were taken on a graded ABCDF scale, with passing requiring a C or better. The dissertation course was graded as credit (CRE) or no credit (NC).
Members of the HSIE Committee,

To put this letter into context, I will first briefly inform you about my qualifications. I am an Associate Professor of Medicine at the University of Arkansas for Medical Sciences where I also co-direct the proteomics core laboratory. My areas of expertise include mass spectrometry, proteomics, bioinformatics, biomarker discovery and multiple myeloma cancer biology. I have published over 45 peer-reviewed manuscripts, and have spent the last 12 years of my career in academic research at UAMS. Prior to that I worked for the FDA’s National Center for Toxicological Research and in the private sector performing proteomics related research. With my background performing research from the private sector to academia, I am excited to see the Health Sciences Innovation and Entrepreneurship (HSIE) Training Program take shape.

I am honored to write this letter to provide my full support for [redacted] application for the 2019 TL1 HSIE Training Program on behalf of his postdoctoral mentoring team. The team consists of me, [redacted], Associate Professor of Biochemistry & Molecular Biology, and [redacted], Professor of Biochemistry & Molecular Biology, and Pediatrics. Each of us on the mentoring team are in full support of [redacted] pursuit of the graduate certificate in Health Science Innovation and Entrepreneurship. The business foundation courses, snapshot sessions, and partnering project will provide excellent complementary training to [redacted] career development, and we fully support his commitment to participate in the training program.

[redacted] is the ideal candidate for this training program, with a gift for finding more efficient solutions in proteomics and data analysis workflows. For example, during his graduate studies, [redacted] was faced with a challenging task of quantifying the abundance of histone peptides containing post-translationally modified residues. Previously, this process required dozens of hours of manually extracting intensity data from the high resolution mass spectra raw files. This bottleneck consumed many hours of personnel time which could be spent on other tasks, and imposed severe restrictions on experimental designs. On his own volition, [redacted] discovered that this intensity extraction process could be performed programmatically, using parsing libraries for mzml-format mass spectrometry files. Without any prior computer science training, [redacted] taught himself how to code using R, and started writing scripts to automate the intensity extraction. Since he developed this script, validation data sets that would have previously taken months to process manually can now be processed in minutes. His code is now being used by other students and by the bioinformatics department.
used this unique opportunity to foster collaborations and engage in team science. While attending the national conference for the American Society for Mass Spectrometry in 2017, he met with a speaker at a platform session who sought help in extracting intensity data. Their lab faced a unique set of challenges in the extraction process, due to the isotopically labelled ethanol used in their experiments. He made a few adjustments to the code, helped with the data analysis, and earned co-authorship on the resulting manuscript. Thanks to his efforts and this collaboration, we now know that the ethanol molecules in alcoholic beverages are metabolized and post-translationally added to specific histone residues in the liver.

continues to develop his expertise in both data processing and proteomic workflows as a postdoctoral fellow. And his eye for efficiency has impacted nearly every aspect of our proteomics workflow. When we first acquired the Orbitrap Fusion mass spectrometer, he helped design a sample processing workflow that could be combined with an isotopic labelling method for multiplexed relative quantitation. His experiments with isoelectric focusing and high pH HPLC as offline fractionation techniques have led us to adopt these methods in the proteomics core. In short, has made, and continues to make a tremendous impact on the efficiency of the proteomics core at UAMS.

Very recently, has created a software application with potential commercial appeal. Using his R coding skills, he is creating interactive dashboards for visualization of proteomics data. In just a few months, he has prepared and deployed several dashboards for our collaborators, which has generated extremely positive feedback, and made for some very exciting lab meetings. In multiple circumstances, presenting the data in this unique format has revealed biological discoveries that would not have been otherwise detected.

With the entrepreneurial training and opportunities provided by the HSIE program, I have no doubt that will create outstanding and innovative technologies. For this reason, my co-mentors and I provide the highest level of support in his participation of the HSIE training program, and his professional development.

Sincerely,


(Ricky D. Edmonds)
BIOPGRAPHICAL SKETCH

NAME: [Redacted]

eRA COMMONS USER NAME: [Redacted]

POSITION TITLE: Associate Professor

EDUCATION/TRAINING

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<td>Texas A&amp;M University, College Station, TX</td>
<td>PhD</td>
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A. Personal Statement

My role in this project will be to mentor [Redacted] in the development of innovative bioinformatic and proteomic technology. I have more than 20 years of experience in quantitative mass spectrometry. My own research group is currently studying proteomic biomarkers isolated using laser capture isolation of glomeruli from FFPE tissues. I am the director of the UAMS proteomics core laboratory and I have been involved in collaborative proteomics projects since my scientific career began in 1992, these include projects with researchers at the Myeloma Institute and with those working in other fields at the University of Arkansas for Medical Sciences (UAMS). I constantly develop workflows to use protein mass spectrometry to answer the biological question at hand. I have spent 20 years working with precious clinical samples and have optimized workflows to maximize the analyses that can be accomplished with minute sample amounts. I have 20 years of experience identifying proteins as biomarkers and using global proteome analyses to elucidate biological pathways. I also have substantial experience with hands-on maintenance and operation of liquid chromatography nanospray ionization mass spectrometry instrument systems. I have the background, skills, and expertise to fulfill the duties associated with my role in this proposal.

B. Positions and Employment

**Positions and Employment**

1997 – 1998 Research Scientist, Rhone Poulenc Rorer/Aventis Pharmaceuticals, Collegeville, PA
1998 – 1999 Senior Research Scientist, Rhone Poulenc Rorer/Aventis Pharmaceuticals, Collegeville, PA
1999 – 2000 Group Leader, Protein Mass Spectrometry, Aventis Pharmaceuticals, Collegeville, PA
2000 – 2001 Manager, Protein Mass Spectrometry Genomic Solutions, Ann Arbor, MI
2001 – 2002 Director and Co-Founder, Proteomic Research Services, Ann Arbor, MI
2002 – 2007 Director, Center for Proteomics, National Center for Toxicological Research, Jefferson, AR
2003 – Adjunct Assistant Professor, Department of Biochemistry and Molecular Biology, UAMS, Little Rock, AR
2007 – Associate Professor of Medicine, UAMS, Little Rock, AR
2007 – Director of Proteomics, Myeloma Institute for Research and Therapy, UAMS, Little Rock, AR

**Other Experience and Professional Memberships**

1993 – Member of the American Society for Mass Spectrometry
C. Contributions to Science

My early research leveraged the cutting edge of analytical instrumentation in mass spectrometry and applied it to the early stages of peptide and protein identification. These techniques were known as peptide and protein mass spectrometry, but before long the term proteomics was coined halfway around the globe and it soon became the catch all term for peptide and protein identification using mass spectrometry. Accurate mass measurements were once only used in the analysis of small organic compounds on magnetic sector instruments, but I showed that low PPM mass measurement accuracy could be made on peptides using time of flight instruments. From those early days of pushing the limits of the high voltage power supplies and electronics to achieve accurate mass measurements on time of flight mass spectrometers, I continue to push the limits of modern mass spectrometry equipment to handle biological samples. In the early days when the sensitivity of mass spectrometers was an issue, efficient low abundant sample handling was often the difference between success and failure in the identification of a protein. As the sensitivity of modern instruments has increased, now those same sample handling skills allow for the identification of low abundant proteins as well as modified peptides with sub stoichiometric concentrations such as phosphorylation. As the speed of the duty cycle of mass spectrometers has increased through the years, it has been critical to continually optimize the separation techniques to limit the complexity of the samples to the range in which the instrument can efficiently operate. As the complexity of the data has increased through the years, from a single protein in a spot on a 2D gel to now 10,000 plus proteins from a cell lysate, the need for statistical analysis of the data and data visualization has increased as well. These large protein datasets can now be integrated with RNA and DNA data to allow a systems approach.

1. My early research pioneered the use of accurate mass measurements for identifying peptides and proteins. My research focused on the fundamental factors of the ionization process and how these impacted the ability to accurately measure a peptide’s mass. After it became possible to routinely obtain accurate mass measurements with commercial mass spectrometry equipment, we used these measurements to improve identifications of peptides and proteins.


2. My research has focused on improving the sensitivity and efficiency of peptide identification with mass spectrometry-based proteomics. As the electronics that drive mass spectrometry equipment advance and instruments are able to generate accurate mass measurements with increasing speed, the manner in which the samples are introduced into the mass spectrometer must be adapted accordingly. My research has focused on optimizing handling of low-abundance samples and chromatographic techniques that allow the peptides to be sampled by the mass spectrometer at an optimal rate for sensitivity and throughput.


3. I continue to focus my laboratory studies on improving the methods used to investigate post-translational modifications, especially those that occur in low abundance. For years, mass spectrometry techniques have shown promise for characterizing and analyzing post-translational modifications. Often the modification occurs on a low-abundance protein or is present at a low stoichiometry, and, in these cases, optimal sample handling and advanced instrument techniques must be used.

4. Application of large-scale proteomics is often limited to preclinical samples; my research has allowed us to bridge the gap between what is possible with abundant preclinical samples and low-abundance samples from clinical isolates, as well as tying together the data from proteomic and gene expression experiments.

Complete List of Published Work in MyBibliography:

D. Research Support

Ongoing Research Support
P20GM121293 (Tackett) 07/11/2017-06/30/2022

Center for Translational Pediatric Research
This COBRE award provides funds to develop the Center for Translational Pediatric Research. Funding supports research programs of four junior investigators, an extensive mentoring program, and infrastructure through core facility support. The scientific theme of the CTPR is the study of how pediatric diseases develop from systems biology and mechanistic standpoints with the ultimate goal of identifying intersections of disease
and development, which, in turn, will produce targets for therapeutic intervention and the development of new treatments for children.
Role: Proteomic Core Director

P20GM103429-15S1 (Cornett) 8/15/2016-8/14/2018
NIH/NIGMS Partnerships for Biomedical Research in Arkansas
Supplement: Formation of the IDeA National Resource for Proteomics
Role: co-investigator

NIH/NIDDK Biomarkers of early renal functional decline in type 2 diabetes
Role: Investigator

Completed Research Support
P01 CA055819 (NCI) (Barlogie) 09/01/2009 - 08/31/2015
Growth Control of Multiple Myeloma
The major goals of this project were to understand myeloma growth in the context of its interaction with the bone marrow microenvironment. In light of our theme of growth control in MM, toward achieving cure in an increasingly higher proportion of patients, investigators of four projects and five cores continued to collaborate in a highly integrated and synergistic fashion. Project 1 planned to achieve better growth control via risk-based treatment strategies. Project 2 postulated achieving better growth control in the relapsed setting by optimizing the clinical activity of haplo-identical NK cells. Projects 3 and 4 dealt with the role of bone disease in MM pathogenesis. This work was accomplished with access to five shared resource cores.
Role: Co-Investigator, Core C
May 22, 2019

Members of the HSIE Committee,

It is my pleasure to provide my strongest possible recommendation for [redacted] for the HSIE training program. [redacted] is an excellent scientist with an exceptional talent for problem-solving. His expertise in molecular biology and proteomics, combined with his skill set in computer programming, make him the ideal candidate for this program. He has all the tools to become a successful entrepreneur in the biomedical field: work ethic, intelligence, teamwork, and a passion for learning. I am excited to see the innovative products and technologies he develops over the course of his career.

[redacted] joined the department of Biochemistry and Molecular Biology as a graduate student in August 2011. He excelled academically, and earned the Paul L. Day award in 2013 for outstanding academic achievement. He has a passion for cutting-edge science across a variety of disciplines. Despite working in a different laboratory, he would frequently meet with me and discuss exciting new papers in my field. His presentation skills are excellent; he won awards for best poster and best platform session at national and local conferences, and always gave outstanding presentations at our departmental seminar series.

[redacted] thesis work was truly groundbreaking. He applied state-of-the-art proteomics techniques to study the process of meiotic recombination in unprecedented detail. His work yielded a new understanding of how recombination is initiated within the context of chromatin, and laid out new areas of research which are actively being studied by current members of his graduate lab.

In his last year as a graduate student, he taught himself how to process large biological datasets using the programming languages R and Python, and enjoyed teaching this skill to his peers and colleagues. He graduated in 2017 and began his postdoctoral work under the mentorship of [redacted], where he continues to use his expertise in molecular biology and knowledge of programming to create innovative technological and computational solutions for proteomics.

In summary, [redacted] the perfect candidate for the HSIE program. It was a privilege seeing him develop into an outstanding and innovative scientist. I give him my highest recommendation for the program.

Sincerely,

[redacted]

Ph.D., Professor and Chair, Department of Biochemistry and Molecular Biology