

Biomedical Examples

Title: *The Medical Civil War: Utilizing Mass Spectrometry to Assess the Validity of Divisions in Medical Care During the 18th and 19th Centuries*

Project Description:

Medical practices during the pre-and post-civil war eras were not a product of scientific research, rather a result of deep political tensions. In the northern US, burgeoning scientific discovery, Louis Pasteur's Germ Theory, aided in altering public mindset towards more scientifically-based allopathic medical practices. Therefore, once-popular alternative treatments (i.e. homeopathy) became heavily scrutinized. This transition towards scientifically-based medical initiatives was met with hostility in the south due to politicization. Southern medical practitioners continued the use of alternative treatments from the previous century, often in discord with allopathic discoveries. This rebellious mindset resulted in epidemics plaguing southern states and coined the term: "The Sickly South."

We have applied previous URCA funding to utilize mass spectrometry, both liquid chromatography-tandem (LC-MS/MS) and inductively-coupled plasma (ICP-MS), to offer the chemical framework for two northern-based homeopathic remedies. LC-MS/MS was used to identify and account for ~70% of pill components; both sucrose and plant-sourced additives. This resulted in a scientific publication: LaFave, et al., IJHA: 2021. To address the unknown 30% contents of the pills, we incorporated ICP-MS to detect metal contaminants to specifically look for additional ingredients and potential contaminants that could be present in much lower amounts. We were able to confirm the presence of individually-labeled elemental additives (As, Zn, P), as well as identify Pb-based contaminants at low level parts-per-billion in physician-administered remedies. We recognize that sample age and storage conditions prior to museum acquisition can result in possible degradation of components (i.e. volatile compounds). Our focus here is to provide comparisons in composition of similarly-advertised treatments for use only in the context of historical debate.

Here we propose multiple aims: (1) Identification of the remaining ingredients. Using historically-based research, we hypothesize that calcium (Ca) carbonate may compose the major unaccounted portion of these remedies. MS techniques are not amenable for Ca; therefore, a colorimetric study (Ca assay kit) will be used to determine the presence and amount of Ca in each pill to quantify its amount. (2) Use our previously developed methods to analyze the components in a newly acquired New Bern based apothecary kit. We will also be able to use the Ca colorimetric method for these analyses. By applying all three analysis techniques, we hope to unveil the most common ingredients used in a small southern community during the time of the Civil War. In doing so we will be able to use a chemically-based approach to assess the contribution of southern medical practices to the "Sickly South" without historical politicization, allowing for the opportunity to dissect and compare regional eastern North Carolina history to larger northeastern US-practices.

Budget Requested: Assistantship \$750 for each of two investigators and Other Expenses \$1000;
Total of \$2500

Other Expenses Description:

Total costs of plant-based standard (\$75 ea. x 8). In order to effectively analyze the host of old medicines, we will be using a variety of standards to compare active ingredients once identified in the largely-unlabeled apothecary chest. Such standards can include active ingredients, as well as 'sources', commonly found in herbs, plants, vitamins (e.g. rosmarinic acid and rosemary), in this example we would initially use the rosmarinic acid as an active ingredient to identify rosemary as the source. Based on our previous research, all items contain at minimum one distinct ingredient.

We will be using a Ca Assay Kit for a colorimetric study (\$445). This assay will allow us to determine Ca ion presence and concentration in the old remedies. Once validated, we will be able to employ all three analytical techniques to more effectively compare and contrast common ingredients in both regions of the US.

The students will be co-presenters in "Rethinking the Museum":Fifteenth International Conference on the Inclusive Museum (April 2021).

Title: *Timing effects of ephrinA1 on the onset of an ischemic event*

Project Description:

Cardiovascular Diseases (CVD) are the most common cause of death in the modern world, with myocardial infarction and myocardial infarction related issues constituting the major of CVD deaths. Reperfusion is the reestablishment of blood flow to cardiomyocytes that is done by reopening the affected blood vessel, reperfusion is the most common treatment option currently for ischemic attacks. However, reperfusion comes with the risk of oxidative stress that can cause further damage to myocardial cells. An effective treatment regimen to improve outcomes in patients suffering acute myocardial infarction (MI) on the scene for emergency response personnel or in the hospital during reperfusion is a critical unmet need. We have discovered that ephrinA1, a protein present in the plasma membrane of healthy mouse and human cardiomyocytes, expression is reduced or lost following an ischemic event. An injection of recombinant ephrinA1-Fc into heart tissue has been shown to reduce myocardial cell damage and dysfunction but the timing of administration relative to injury onset in the presence or absence of reperfusion is unknown. This research seeks to determine the optimal timing effects of ephrinA1-Fc administration relative to the onset of an ischemic event by simulation in human inducible pluripotent stem cell-derived cardiomyocytes (hiPSC-CMs). These cells have demonstrated high fidelity in terms of translatability of the effects observed in vitro to anticipated outcomes in vivo. This will help to determine the most effective time frame for ephrinA1 administration to minimize infarct size and dysfunction. We plan to investigate the timing of this protection by studying cell viability as it changes over varying lengths of ischemic

duration as well as the oxidative stress burden in the cardiomyocytes at the time of initiation and conclusion of reperfusion. To do this, iPSC-cardiomyocytes will be made anoxic with oxyrase and ephrinA1 will be administered at varying time intervals. After specified time intervals, the iPSC-cardiomyocytes will be examined for damage/death compared to controls. These time intervals will be determined based on current EMS response times of 1-6hrs that are known to be effective in reducing injury (such as arriving to the scene and time to the hospital) and additional times 8, 12, and 24 hours after onset of ischemic event to determine if ephrinA1 could be a useful adjunct to reperfusion therapy and even extend this narrow window of therapeutic value. This research is looking for a \$1,385.20 grant to fund reagents to produce iPSC-CMs to test timing intervals for ephrinA1-Fc effectiveness after an ischemic attack.

Budget Requested: Assistantship \$500 and Other Expenses \$885.20; Total of \$1385.20

Other Expenses Description:

- mTeSRplus (StemCell 100-0276, 500ml, \$596.00)- Needed for iPSC-CM development
- DPBS (no calcium magnesium) (gibco (Thermofisher) 14200075, 500ml, \$94.98)- Needed for iPSC-CM development
- B-27 supplement (gibco (Thermofisher) 17504044, 10ml, \$116.00)- Needed for iPSC-CM development
- DMEM/F12 (L-glutamine and sodium bicarbonate) (gibco (Thermofisher) 11320033, 500ml, \$78.22)- Needed for iPSC-CM development