Proposal All Reviews: 1827903

In the context of the five review elements, please evaluate the strengths and weaknesses of the proposal with respect to intellectual merit.

STRENGTHS
- Selection of the high-resolution mass spectrometer is justified based on logistical and research needs. Notably, per the proposal, the university only has a 10-year old quadrupole instrument that no longer can serve the research aspirations of faculty. Drs. Kim, Albu, and Carver have used high-resolution mass spectrometry to aid their project, leading to publications.
- Several of the planned research projects align well with the capabilities of the requested instrument. For example, Drs. Kim and Albu can address quinone-induced protein modifications, as also supported by their preliminary data using a high-resolution mass spectrometer. The proposed activities to map oxidation, adduct formation, and covalent modifications is feasible using the requested instrument. Other plans on assessing DNA modifications are also likely to succeed theoretically, although these experiments will require method development. Future plans on amyloid modifications via lysosomes show long-term thinking by the PIs, suggesting that the research team will be able to benefit from this instrument beyond the scope of this MRI program.
- Dr. Carver's plan to monitor metabolism changes in cell cultures is interesting and has the potential to provide new insights to better regulate related medical devices. These projects will also be interesting to students, thus enhancing retention of youth in science.
- These strengths are enhanced by Dr. Qin's plans on using the mass spectrometer to quantify protein expression as a function of yeast replicative lifespan. Dr. Symes' studies on lipid profiling are exciting, because they could provide new insights into how bacteria use lipids to thrive.
- The depth of descriptions on how bottom-up proteomic (e.g., SILAC) and metabolomic experiments (e.g., LIPID MAPS) will be performed is encouraging and representative of the investigators' abilities to leverage mass spectrometry to advance their respective research fields. The need for a separation system was well articulated on grounds of eliminating ion suppression during these measurements (Dr. Symes).
- The investigators have been very successful at publishing original work from a PUI institution.

WEAKNESSES
- The scientific endpoints (outcomes) of some of the proposed projects are less clear in the proposal. Dr. Carver's metabolomic experiments seek to detect metabolic changes, but how the investigator plans to advance our understanding of toxicity is not articulated in sufficient detail for the reader to understand where the project will lead.
- Some of the projects may not be feasible or may be too difficult using the type of liquid chromatography mass spectrometer selected. Specifically, Dr.
In the context of the five review elements, please evaluate the strengths and weaknesses of the proposal with respect to broader impacts.

STRENGTHS
- University of Tennessee at Chattanooga serves a sizeable population of students (~10k in FY2017). About 50-60% of student population is female and ~20-30% is underrepresented in STEM fields. The Chemistry program ranks well among PUI institutions, positioning the Department to leverage the high-resolution mass spectrometry system to aid education and training of students, including many underrepresented students in science, 30-50% of who enter the job market and 20% of whom pursue graduate education.
- 12 researchers with broad backgrounds will benefit from the instruments, ranging from nearly all subdisciplines of chemistry and biochemistry to biology. These investigators have mentored 10-20 students each over the last year; thus, students will also benefit from this instrument.
- Besides investigators at U. Tennessee at Chattanooga, the requested instrument will also aid research, training, and education in the greater Chattanooga metropolitan area and will be the only instrument in a 60 mi radius. Several schools, companies, industries, and hospitals in the area will potentially be able to benefit from the instrument. Therefore, positioning of this instrument will serve well this geographic area.
- Multiple courses will be enhanced by the instrument. Basics of separation and mass spectrometry (e.g., ion suppression) will be taught.

WEAKNESSES
- A large number of courses are listed to benefit from this instrument, but specifics are lacking as to how (see D1.2. second paragraph).

Please evaluate the strengths and weaknesses of the proposal with respect to any additional solicitation-specific review criteria, if applicable

Instrument Management Plan
STRENGTHS
- The investigators have been successful at receiving multiple external support (e.g., CAREER, S-STEM) for their respective research programs and to enhance institutional resources (e.g., MRI). These successes lend credence that the research team will be able to make the most of the requested high-end mass spectrometer to advance basic and translational research areas.
- The investigators have hands-on expertise in mass spectrometry, which was also evidenced by the way the proposal was written (mass spectrometry-specific language used). For example, Dr. Kim has in-depth experience in mass spectrometry, even using TOF and Orbitrap type systems, as also demonstrated by prior publications. Dr. Symes has used an LC triple-quad mass spectrometer.
- Per Institutional support letter from the College of Arts and Sciences, the Provost's Office, and the Office of Research and Graduate School, the Institution appears to be committed to support the installation and maintenance of the mass spectrometer by providing key infrastructural and logistical components: power, plumbing, exhaust lines, and water-purification system for the room housing the instrument as well as funding for instrumental fixes. Furthermore, Dr. Kim will receive a 2-semester teaching release to help set up the mass spectrometer and related analysis program.
- The management plan is realistic and well developed (Table 4).

WEAKNESSES
- Plans toward the long-term maintenance of the instrument will become risky if/when the institution stops covering maintenance contracts, fixes, etc. In fact, the Institutional letter states: "4) annual service contract fees as needed during and after the funding period." This language is confusing, because i) the service contract fees are already included in the requested budget for the first 3 years and ii) service contracts must be paid upfront for mass spectrometer vendors; these expenses are not an "if needed" basis they must be paid ahead of time by the institution in out years. This language gives this Reader the impression that the Institution may not be fully aware of how much the service contracts may cost.
- Therefore, although free access to the instrument is attractive, to a great deal, a fee-for-use model (perhaps with discounts) would serve the investigators better to accrue funds that will be needed for instrumental maintenance at some point or another. However, the proposal offers no cost analysis and model to this end to evaluate. This Reviewer views this model risky for the long-term maintenance of the instrument.

Data Management Plan
STRENGTHS
- The data management and sharing plan is generally well developed.

WEAKNESSES
- The plan to store data on user PCs is not realistic for mass spectrometry data that can range from tens and hundreds of megabytes to gigabytes. There are no details offered on how data would be stored on servers, and what the associated costs would be.

Summary Statement
University of Tennessee at Chattanooga requests the acquisition of a liquid chromatography high-resolution quadrupole mass spectrometer with electrospray and atmospheric pressure chemical ionization sources. This is an exciting proposal by a group of highly productive and successful investigators. The requesting PUI that will leverage this high-end instrument to address interesting questions in various subdisciplines of chemistry and biochemistry.
biology, specifically protein modifications, DNA modifications, protein-protein interactions, organic synthesis, medical device safety for regulatory science (e-cigarette). The need for the LC high-resolution mass spectrometer is well articulated by the investigators in terms of need (currently only low-resolution mass spectrometry instrumentation is available at the host institution), requirement for high mass resolution for various projects, logistical challenges associated with outside collaborations with access to high-end instruments, and a developing education program. The requested instrument will advance research and training in the host institution and the greater Chattanooga area. The host institution will use the instrument to aid training of students via multiple courses. Although the institution appears to provide initial support, concerns about the long-term plans to maintain the instrument beyond the scope of the proposal slightly damp enthusiasm over this otherwise exciting proposal.

Review 2

Rating:

Good

Review:

Summary

In the context of the five review elements, please evaluate the strengths and weaknesses of the proposal with respect to intellectual merit.

Strengths

Kim and Albu propose to use the requested HPLC-MS/MS (QTOF) to investigate quinone-induce protein modifications by looking at p-benzoquinone RNAase fragments. Their work is hindered by not having regular high-resolution MS access. Albu and Kim seek to use the requested instrument to look at the effect of Rh and Ir complexes on DNA damage. Carver would use the requested HPLC-MS/MS (QTOF) to investigate differences in lung cell culture expression for cells grown in e-cigarette refill solutions vs. normal culture media. Knight would use the requested instrument to investigate steroid-derived dendrimer nanostructure. Lee would use the HPLC-MS/MS(QTOF) to characterize synthesized cobalt(III) organometallic complexes. Qin would use the HPLC-MS/MS(QTOF) to investigate the impact of dietary/caloric restriction on the proteome of yeast cells. Symes will use the HPLC-MS/MS(QTOF) to profile lipids produced by bacteria which have incorporated fatty acids as carbon sources.

There appears to be need by most projects for the requested instrumentation and a clear theme of use of the requested instrumentation to investigate critical areas of biochemistry.

Weaknesses

Kim and Albu project difficult to follow (figure 2 low resolution). The Albu and Kim Rh/Ir work was unclear on exactly what the requested instrumentation would be used to do (and why their work was limited currently). The specific application of the HPLC-MS/MS(QTOF) to Carver's e-cigarette work was also unclear. Knight's work does not seem to require a high resolution TOF instrument. The need for the specific HPLC-MS/MS(QTOF) requested here (as compared with a low resolution HPLC-MS/MS) was not clear for Lee's work. Qin's application was also unclear, since it used instrumental jargon to describe proposed analyses.

In the context of the five review elements, please evaluate the strengths and weaknesses of the proposal with respect to broader impacts.

Strengths

There appears to be clear plans to for local/regional users to use the requested HPLC-MS/MS(QTOF) for their work, indicating that the instrument will be a regional resource. The instrument would be used in research in training for the institution's relatively high numbers of women and underrepresented groups in STEM.

Weaknesses

There appears to be high numbers of female students and some other traditionally underrepresented groups in the requesting department's student populations, however, only Fall 2017 data. Other common categories (first in family to attend college) are not listed. A long list of courses that will use the instrument is given, little information on their specific analyses or projects is not given.

Please evaluate the strengths and weaknesses of the proposal with respect to any additional solicitation-specific review criteria, if applicable

Instrument Management Plan
Strengths
The letter from the institution's deans and chancellor indicates strong institutional support for the requested instrumentation, including laboratory renovations and support for post-grant service contracts and installation of water-purification systems. The PIs seem to have ample experience with MS and QTOF-MS instrumentation.

Weaknesses
The scheduling and reservation system seemed vague, especially given what seems to be likely high demand given the number of projects and courses. The PI/co-PI's research will have priority, but how will this interfere with use by courses? When will training take place? What will training consist of?

Data Management Plan
The data management plan seems adequate and well-considered.

Strengths
NA

Weaknesses
NA

Summary Statement
The PIs have a diverse group of research interest that look to have sufficient intellectual merit and the potential to produce impactful data/findings. The specific application of the requested instrumentation was difficult to see in many of the project descriptions and in some cases the need for HPLC-MS/MS (QTOF) was not clear.

Quantitative data on the dissemination products from previous MRI instruments to the institution (of which there were three listed) were inconsistent. A large number of instruments have been awarded to the institution recently but it is not clear how productive these instruments have been.

The team is well qualified and has sufficient space to perform their proposed work, relatively few have funded research projects. The management plan seemed vague in areas. The description of use in courses was also vague.

Review 3

Rating:

Multiple Rating: (Very Good/Good)

Review:

Summary
In the context of the five review elements, please evaluate the strengths and weaknesses of the proposal with respect to intellectual merit.

Strengths
PIs at University of Tennessee Chattanooga request funds to purchase an Agilent Q-TOF LC/MS system. The instrument would be used to enhance a range of research areas at the University.

Proposed work in PI Kim and Co-PI Albu laboratories involves study of protein modification that are induced by quinones. Specifically the researchers hope to study quinone-induced protein aggregation. In addition the two researcher seek to use the requested instrumentation to study the photo induced cleavage mechanism of DNA by Ir(III) and Rh(III) complexes. Acquisition of the high-resolution accurate-mass LC/MS system could enhance the proposed work.

Additional research that may be impacted thought acquisition of the requested instrument includes study of the biological effects of e-cigarette filling solutions on cells in the lab of researcher Carver, investigation of steroid-derived dendrimer nanostructures by Co-PI Knight, and study of transition metal complexes for breaking chemical bond in the lab of Co-PI Lee.

Proposed work in the lab of researcher Qin would involve the study of proteomic profiles in yeast. Research in the lab of Co-PI Symes involves lipid profiling of bacterial membranes. Access to the Q-TOF system may aid that proposed work.

Results from Prior NSF support:
NSF Award #0951711 Acquisition of a Benchtop Single Crystal X-ray Diffractometer for the University of Tennessee at Chattanooga. Co-PIs: Kim and

https://www.research.gov/research-portal/appmanager/base/desktop?_nfpb=true&_window... 6/28/2018
Knight. 2010-2013. The Co-PIs indicate that use of the instrument has resulted in many presentations as well as publications. Additional details would have aided in assessment of the award.

NSF Award #0922941 Acquisition of a Microscopy Core System. Co-PI: Kim. 2009-2012. Related research has resulted in several regional and national presentations and two student coauthored papers. The award appears to have enabled research productive at the institution.

NSF Award #0821057 Acquisition of a Microarray Scanner and Real Time PCR system for Interdisciplinary Research and Teaching in an Undergraduate College Setting. Co-PI: Kim. 2008-2011. The Co-PI indicates the system has been used in classes and in research. Additional details would have aided in assessment of the award.

Weaknesses
Several of the research projects have limited detail on the need for a high-resolution accurate-mass system. A more detail research description including how the requested system could significantly enhance the proposed work what have strengthened the proposal. Additional detail on research funding for several of the research areas would have aided assessment of the intellectual merit of the proposal.

In the context of the five review elements, please evaluate the strengths and weaknesses of the proposal with respect to broader impacts.

Strengths
The requested instrument could enhance the research and student training infrastructure at the institution. A wide range of research areas could be impacted through use of the instrument.

The University consists of over 20 percent underrepresented groups. The requested instrument may improve research and educational opportunities for these groups.

In addition to research use the instrument would be used in a range of courses. Specifically the Q-TOF would be used in wide range of courses throughout the department curriculum. This course based use could significantly enhance the broader impacts of the requested instrument.

Weaknesses
Additional detail on how the instrument would be meaningfully incorporated in the curriculum would have strengthened the proposal. Specifics on how the instrument could be used effectively in lower-level classes would have aided in assessment of this potential broader impact.

It is not clear what impact the requested instrument would have on attracting researchers. Additional information on research user recruitment at the University would have enhanced that area of the proposal.

Please evaluate the strengths and weaknesses of the proposal with respect to any additional solicitation-specific review criteria, if applicable

Strengths
The grant budget, including nitrogen generator and diode array detector, is appropriate and reasonable given the range of research projects described in the text of the project description and budget justification.

The PI and Co-PIs will be in charge of routine maintenance and care of the instrument. The PIs appear qualified to maintain the requested instrument.

The University provided a letter of support for the research. Included in that letter was a commitment to infrastructure needed for the instrument, funding for short- and long-term care of the instrument, and purchase of ancillary equipment needed for successful use of the instrument.

The data management plan is appropriate for the scope of the work proposed.

Weaknesses
The need for an extended service contract during the grant period does not seem to be well justified in the proposal text and budget justification. The letter of support from the University commits to the annual service contract during and after the grant period.

While the University did supply a letter committing to the short- and long-term maintenance and care of the instrument it is not clear as to the source of those funds. Additional information on how the funds to support the instrument would be above and beyond funds currently used to support the department would have strengthened the proposal.

Greater detail on instrument scheduling would have strengthened the proposal. The plan for six investigators to be in charge of overseeing maintenance and management of the instrument is concerning.
Summary Statement

Researchers at University of Tennessee Chattanooga seek funds to purchase an Agilent Q-TOF LC/MS system for research. Several of the proposed research projects could benefit from the requested LC/MS system. As a broader impact, the requested instrument could enhance the research and student training infrastructure at the institution. Additionally, the use of the requested instrument in coursework may significantly impact on students at the institution. The PIs are well qualified to care for the requested instrument.