RESOURCES

The proposal will be conducted at **Marquette University** but will also rely on some additional resources and services from the **Clinical and Translational Science Institute** (CTSI) at the Medical College of Wisconsin (MCW) of which Marquette is a partner**.** Both sites (Marquette and MCW) have all the required equipment, facilities, resources and institutional support required to successfully complete the proposal. Both Marquette and MCW are in partnership under the CTSI, and there are many active scientific collaborations between the two institutions. We will use these resources and partnership to successfully complete the proposal. Resources to conduct the experiments adequately are addressed below.

A. Clinical and Translational Science Institute at MCW (in partnership with Marquette University)

Dr Hunter and Dr Nielson both have adjunct appointments with the MCW: Dr Nielson is an Associate Professor (Department of Neurology at MCW) and Dr Hunter is an Adjunct Associate Professor within the CTSI and therefore, they both have full access to all the services offered by the CTSI core laboratory at MCW. For this current proposal we rely on biostatistical consultation and genetic analysis.

1. **Biostatistical Consultation:** This proposal has dedicated biostatistical support from faculty within the Division of Biostatistics at the Medical College of Wisconsin. A biostatistician (faculty from Division of Biostatistics at the MCW) is available on Marquette campus for one day each week. In addition, biostatistical support and consulting services are available at all working hours with faculty within Division of Biostatistics at the MCW that services the core laboratory of the CTSI (5 miles from Marquette). The Consulting Center in the Division of Biostatistics at the MCW provides comprehensive statistical consulting and data entry services for CTSI faculty and their funded studies. Faculty and staff statisticians are available, each for an allocated portion of time which will provide the equivalent of statistical consultation with 1 1/2 to 2 full-time faculty and staff statisticians, to support clinical research projects. This consulting service has been used to prepare this current proposal and will be relied upon for continued support when the project is funded and data analysis is required.
2. **Genetic Analysis:** All samples for the genotyping will be collected at Marquette and transported on regular basis (once per week) to the CTSI Core facility at MCW for processing of DNA and then shipment to University of Oregon CTSI for analysis of *APOE* genotype (see attached letter from the CTSI).

B. Marquette University

Most of the proposal research activity will occur at Marquette University in the laboratory of Dr Sandra Hunter (PI) located in within the Physical Therapy Department. All introductory and experimental sessions will be performed at this location. Management of human samples for salivary cortisol (collection, storage and analysis) and genetic analysis from buccal cells taken from mouth swabs will be overseen by Dr April Harkins who is director of the Molecular and Immunoserology Core Laboratory at Marquette University and is a certified clinical laboratory scientist.

Laboratory:

Laboratory Space for Familiarization and Experimental Sessions with Subjects and Students

The laboratory of the PI (Sandra Hunter) has the necessary space and equipment in place and in operation to perform all the required experiments at Marquette University. The PI's laboratory comprises a ~800 sq ft research space and an adjoining copper shielded room (300 sq ft) that are located in the Department of Physical Therapy. These areas will be used to conduct all familiarization sessions for both studies. Additionally, there is a shared space of 300 sq ft of office space for research assistants, associates, and graduate research students. Should new office space be required for additional students, the department has extra office space within the building and close to the laboratory that can house up to 6 extra students. There is also a separate conference room on the same floor and 20 feet from the PI's laboratory to conduct informed consents, surveys and questionnaires uninterrupted if testing is taking place in the laboratory.

Laboratory Space for Testing of Human Samples (Salivary Cortisol and Buccal Cells for APOE Genotypes)

Dr April Harkins (Co-I) is director of the Molecular and Immunoserology Core Laboratory which services molecular and serological analysis of human samples for research studies conducted within the Department of Physical Therapy, Program in Exericse Science and Department of Clinical Laboratory Sciences (College of Health Sciences) at Marquette University. The core facility comprises three key laboratory areas located on the same floor within the College of Heatlh Sciences that allow preparation and analysis of human biolgoicial

samples (see Equipment). Thus, we are able to analyze salivary cortisol samples as we have done for several studies and publications previously[53,54,56,180]. Consequently, Dr Harkins will oversee collection and analysis of saliva samples for cortisol which will be done in the core faciltiy at Marquette and will also oversee collection of buccal cells for genetic testing of *APOE*. Dr Harkins has dedicated space for collection and storage of all saliva samples and the buccal cells from mouth swabs for genotyping. Both the saliva samples and buccal cells will be collected in the laboratory of Dr Hunter but all samples will be stored in refrigerators/freezers located within the core facility of the Molecular and Immunoserology Core Laboratory. Dr April Harkins (Co-I) who will oversee and perform the analysis of the cortisol and store buccal cells prior to transportation to MCW for initial DNA analysis.

Dr Harkins own laboratory within the core facility is designed for microbiology, molecular and biochemistry testing (20 x 20 feet) with 2 computers for data analysis. It contains a centrifuge with temperature control for processing specimens, two freezers (-20°C and -70°C), a refrigerator, spectrophotometers and adequate bench top workspace. Proper personal protective equipment (lab coats, gloves, masks and eye protection) is available at all times. Any biohazardous waste is sealed in orange biohazard bags, autoclaved (located in the CLS department) and disposed of properly.

As a certified clinical laboratory scientist, Dr Harkins, is proficient in diagnostic laboratory procedures, maintaining instrumentation and interpreting quality control and data, including the assays in this project.

Clinical:

N/A

Animal:

N/A

Computer:

Five high speed PCs (3 desk tops) and (2 laptops) that are less than 2 years old are housed in the PI's research laboratory for data collection and analysis.

Office:

The PI has office space of 120 sq ft located within the Department of Physical Therapy, adjacent to the research laboratory. There is separate office space adjacent to the laboratory available for postdoctoral research associates, research assistants and students. Should new office space be required, the department has extra office space within 1 minute walk to the laboratory that houses up to 6 extra students.

Other:

This laboratory is one of many NIH-funded research laboratories within the well established Integrative Neuroscience Research Center, College of Health Sciences at Marquette University.

There is a machine shop available for our use within the Engineering (Biomedical) department located in the adjacent building should we need repairs.

1. Profile of the students of the applicant school/academic component

During the period 2007 – 2011 (the most recent timeframe for which nationally comparable data is available), Marquette University ranked among the top 10% of institutions whose undergraduates go on to complete the Ph.D. A total of 218 students from Marquette University went on to receive the doctorate degree during that period. (Source: http://webcaspar.nsf.gov utilizing the NSF Survey of Earned Doctorates/Doctorate Records File data source accessed 6/11/2013. Please note that professional degrees such as the M.D., D.D.S., O.D., D.V.M., and J.D. are not covered by the survey of earned doctorates.) Of these 218 students, **75 received a doctorate degree in a "health-related science."**

The Marquette University Department of Physical Therapy has an enrollment of ~180 students in the Doctor of Physical Therapy program and 220 students in the undergraduate programs in Exercise Science and Athletic Training. Within the last 5 years, the graduate rate for our Doctoral Program in Physical Therapy has exceeded 90% and 100% of the senior Exercise Science students earned their baccalaureate degree. Among the undergraduate students, 90% go on to earn an advanced professional academic in health related sciences.

Approximately 15% of the students in our programs come from minority or disadvantage populations. Our department has consistently received recognition for its high quality students, who have the highest admission profiles entering Marquette University and the highest academic performances in the College of Health Sciences. On average, our students rank in the 92nd percentile of their high school graduating class and carry a 3.34 university grade point average (out of 4.0 maximum).

2. Description of the special characteristics of the school/academic component that make it appropriate for an AREA award.

The Marquette University Department of Physical Therapy is committed to excellence in teaching, research, and service. The commitment is reflected in our national reputation for Physical Therapy education. We are ranked among the top 20 of all academic physical therapy programs in the United States (US News and World Report College Guide).

One of the remarkable aspects of Marquette University is its **commitment to increasing cultural diversity in health sciences and biomedical research.** A major effort of the Department of Physical Therapy and Exercise Science Program is to educate students from **underrepresented minority populations** and **disadvantaged backgrounds.** Marquette's Health Careers Opportunity Program in Physical Therapy (HCOP) is a clear result of this mission. HCOP, that has been a federally-funded program, is a comprehensive program to recruit, prepare and retain students in Physical Therapy, Dentistry, and Physician Assistant Studies. HCOP students have access to a variety of academic services, including career exploration for disadvantaged high school and college students, mentoring, career counseling, and field trips. HCOP also provides preliminary education to build science skills in disadvantaged high school students. We offer summer programs for disadvantaged physical therapy students in the professional phase of the program. The Student Educational Services Office provides retention services and academic support for an undergraduate student including tutorial support for many difficult courses, for example chemistry and physics. A writing specialist is also provided at no cost to the student or the Department. Our own HCOP staff meets regularly with students for advising, counseling and tutorials. The University's Education Opportunity Program (EOP) and the Freshman Frontier Program (FFP) have provided academic support, summer skills building program, counseling, and tuition support for HCOP students.

Other characteristics of the program that make it appropriate for an AREA award are outlined below:

(1) Strengthen the research environment of schools that are not research intensive.

A goal of the Department of Physical Therapy is to support a growing number of Physical Therapist researchers who are making substantive contributions to the rehabilitation body of knowledge. We have a PhD and Master's program that will admit students in the Fall of 2011 as a part of the newly funded CTSA and of which that Marquette University is an integral part. The PhD program has 2 full time PhD students positions funded through the CTSI and Marquette has committed to an additional 9 graduate students to be phased in over a 3 year period from 2011. The Master's program in Exercise Science Program will accommodate up to 15 students.

Marquette University also has an Office of Research and Sponsored Programs that is very supportive of research and in particular new and emerging investigators. The goal is to support researchers through the entire process of research; they provide editorial, budget, and grant writing service as well as bring researchers from around the campus together to foster interdisciplinary research.

(2) Expose students in such environments to research.

The Department of Physical Therapy is eager to involve undergraduates and professional students in research. There are numerous opportunities within the curriculum for students to take directed study courses, which are often research-based education experiences. During a directed study, students may work with a PI for a semester and be involved in planning experiments, collecting and analyzing data, or performing a literature review. Often, there is a capstone project that involves an oral or poster presentation. These experiences are designed to increase student exposure to research and encourage enrollment in the PhD and masters programs. They can also result in student abstract submissions and authorship on peer-reviewed publications. Specifically, the chair of the Physical Therapy Department supports each PI of a research laboratory year round funding for one to two graduate students to participate in a research project. Funds up are also available for undergraduates

to travel to a conference to present their capstone project. Furthermore, the College of Health Sciences funds a summer undergraduate research program. Each PI is funded one full-time undergraduate research student for a 10 week (40 hours per week) program. These sources of support at the department and College level have been invaluable in promoting student research.

(3) Provide support for meritorious research

Meritorious research is awarded at Marquette University by a variety of small and large intramural awards for research and by recognition across campus by means of newsletters, newspapers, roundtables, and seminars. Research achievements are very important in the tenure and promotion process. Teaching relief, laboratory space, and funding for equipment is also provided to individuals in the University who are striving for excellence in research. Aside from the competitive wards for summer fellowships and research grants, and in more recent years Marquette has invested in a series of research awards to young and senior investigators. One such award is the Way Klingler Faculty scholarship for Young Investigators which awards 2 early investigators a semester sabbatical and small amount of funds for research after their 3 year review and prior to the their promotion and tenure year. The PI, Dr Hunter was this recipient of this award in 2007. Competitive research awards up to $150,000 are also available for distinguished investigators in their mid- to late career.

3. Description of the likely impact of an AREA ward in the principle investigator and the school/academic component.

Impact on the PI

The impact of this new award will be substantial for the PI. Dr. Hunter is an emerging investigator, and funding would continue to support a program of research to identity the impact of muscle fatigue in old adults during tasks that are functionally relevant to daily tasks in an aging workforce. The proposed line of investigation is innovative and novel; yet it is the next logical step in building on the knowledge gained during her work from grants awarded previously. This work will also help the PI advance her long-term objective of developing more effective rehabilitative techniques in old adults and identifying those old adults most at risk of fatigue. The proposed research has the potential to help the PI become a leader in the field of the neural control of muscle fatigue and function in aging populations.

Completion of the study will enable the PI to improve her writing skills by publishing numerous articles related to the outcomes of the study. In addition, the PI's public speaking skills and visibility in the scientific community will be enhanced by presenting her work at national and international meetings. Completing this proposal will improve the PI's teaching ability by increasing her knowledge of the mechanisms that contribute to muscle fatigue and the research process. These topics are particularly relevant to her teaching the Advanced Exercise Physiology (ExSc 4192 and 5192) which focuses on research based skills and Exercise for Special Populations (ExSc 4187) which includes aging populations as a module.

Impact on the School/Academic Component

Funding for this project from the AREA program will have a positive impact on academics and research at Marquette University. The Department of Physical Therapy is launching a new PhD program and Master's program in the Fall of 2011. The goal of this program is to train Physical Therapy practitioners in biomedical research. Having a funded research program, such as the one proposed by Dr. Hunter, will enhance the PhD program. High quality students will be attracted to this important research area and will be able to complete their dissertation work in a well funded ad properly equipped research environment.

Students in Dr. Hunter's classes will be exposed to "work in progress" related to her research. This includes state of the art approaches for studying neural control of movement in young and old people. The overall academic environment is strengthened by a strong program in research and scholarship.

How will the AREA Award Expose Students to Research?

Students will have an opportunity to participate in the research proposed in this application through independent study, laboratory work, literature review, and internships for their Exercise Science clinical experiences. Up to three undergraduate and one graduate student will be devoted to this proposal each year of funding. First, for each year of the 3-year funding period, Dr Hunter will recruit 1 student to a 16 week

independent study in the laboratory. Second, for each Spring semester each year, a senior undergraduate will be recruited to complete their internship (20-40 hours per week for 16 weeks) working on this proposal. Finally, for three consecutive summers, an undergraduate student will be committed to fully supporting this award during the summer undergraduate research program. The exposure that students are able to receive on research can be very significant. For example, the PI has already involved over 24 undergraduate students with part-time and full time internships, independent study and summer research programs over the last 7 years while at Marquette. This has been made possible by funds from the NIH. During this educational experience, students will participate in experimental design, data collection, analysis, and interpretation. Students will also attend laboratory meetings, journal clubs, and research seminars where they will be encouraged to give oral presentations and contribute to discussion. It is expected that these contributions will result in student co-authorship on abstracts, poster presentations, and manuscripts as other students have experienced. Funding from this project will allow these students to attend local and national scientific meetings.

Finally, during the funding period, the PI has identified a PhD student who is a Fullbright scholar from Brazil (Hugo Maxwell Pereira, PT, MS) to work specifically on this proposal. Funding from the AREA award will ensure a strong research program in which students can obtain their scientific training.

Statement of Institutional support for the proposed research project

Marquette University and the Department of Physical Therapy strongly support research enhancement. Over the last 7 years, Marquette has committed funds that Dr Hunter has used to purchase equipment for this and other projects. The University has also assigned Dr Hunter over 800 square feet of remodeled laboratory space, and 300 square feet of office space for students and research assistants in the Department of Physical Therapy which has been tailored for her use. To allow time to accomplish her research, Dr Hunter has a modest teaching load of two classes per year and is allowed 50% of her time to pursue research and scholarship activities. The Department of Physical Therapy and the Exercise Science Program will provide secretarial support and grant account management services for purchasing, publication and other support services.