FA-5 Appendix: CTSA Contract

MARSHALL UNIVERSITY PARTNERSHIP

a. Personnel

i. Director:John Maher, Vice President for Research, Marshall University, member of leadership team; Co-Director, Richard M. Niles, Ph.D., Professor and Chair of Biochemistry and Microbiology, Senior Associate Dean for Research & Graduate Education, Joan C. Edwards School of Medicine, Marshall University, member of CATalyst.

ii. Key Personnel: Todd Gress, MD, MPH, Assistant Dean for Clinical Research, Joan C. Edwards School of Medicine, Marshall University, program faculty for the Participant and Clinical Interactions Resources Key Function; Jennifer Plymale, MA, Director Robert C. Byrd Center for Rural Health, Marshall University coordinator for the Appalachian Translational Research Network.

b. Goals of Component Program

Specific Aim 1. To generate a vibrant clinical research infrastructure with junior clinical research faculty and well-trained clinical research staff by utilizing KL2 program support and other educational programs offered by the UK CCTS.

1. Build awareness of KL2 opportunity in clinical departments with fellowship programs.
2. Develop the plan for basic clinical research education for one faculty member and staff coordinator in the clinical departments.
3. Begin implementation of the educational plan as course schedule allows.

Specific Aim 2*.* Foster the development of clinical and translational research by participating in pilot funding programs with the UK CCTS.

1. Solicit Marshall faculty members response to joint RFA's.
2. Conduct three meetings between Marshall and UK faculty to explore mutual research interests and establish collaborative research.
3. Provide external review assistance to faculty seeking to improve their application before re-submittal.
4. Monitor progress of awarded applications to ensure milestones are met.

Specific Aim 3. Expand the number of investigator-initiated clinical trials at Marshall through collaboration with clinical faculty and trial-network programs at UK.

1. Develop a small investigator initiated clinical trial started at Marshall into a larger clinical trial using the trial network programs at UK.
2. Explore starting one new investigator-initiated trial by a Marshall investigator in the Gynecological area using a partnership with the UK trials network.

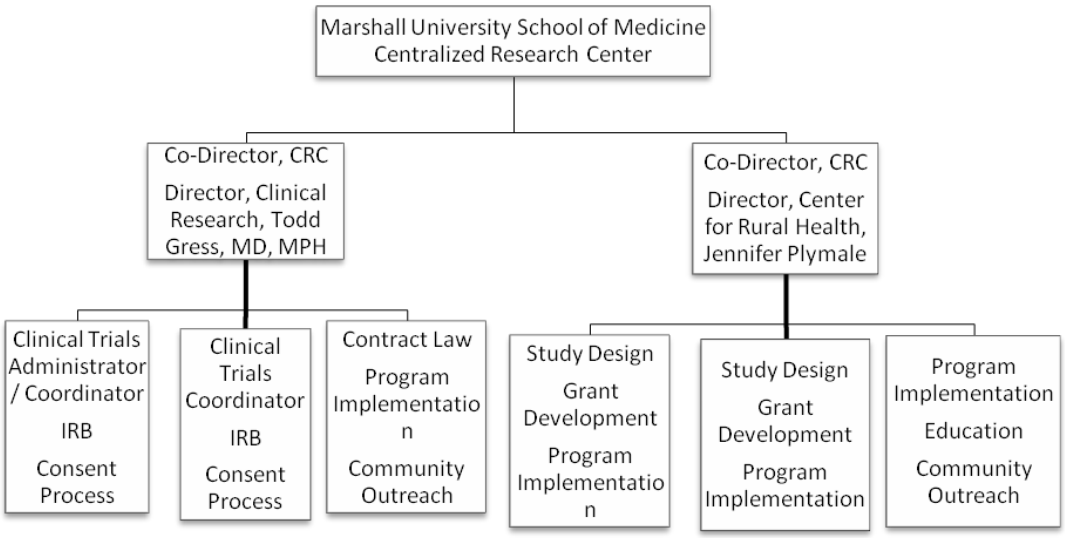
Specific Aim 4. Incorporate UK researchers into the NIH-funded Cancer Genomics Network that has been established in WV.

3. Meet with key personnel in the UK Markey Cancer Center to explain the scope and goals of the WV Cancer Genomics Network and also the capabilities of Marshall's Genomics Core Facility.
4. Accomplish RNA expression profiling and exome sequencing of at least three non-small cell lung cancers obtained through the UK tissue bank.

Specific Aim 5. Create synergies among the community participatory research programs of Marshall's Center for Rural Health and UK community participatory research programs.

c. Marshall University Partnership Characteristics

i. Marshall University Infrastructure



Marshall's centralized research center is fully operational under the co-direction of Dr. Gress and Ms. Jennifer Plymale. The CTSA is providing 50% support for a clinical research coordinator in the Clinical Research Center.

ii. **Progress**

Aim 1-Clinical Research Infrastructure Development

KL2 candidates

One of our challenges from year one of the CTSA was finding suitable candidates for the KL2 award and convincing their chairs to accept the 50-75% time commitment required for this program. With the arrival of our new Dean, Dr Shapiro and his increased emphasis on our medical school's research mission, we now have several competitive candidates and commitments from their department chairs to provide this release time. Franklin Shuler, MD, PhD a faculty member in Orthopedics will be submitting an KL2 award application.

Education

Dr. Tom Kelly (UK) and Dr. Todd Gress (MU) worked last year on providing the Introduction to Clinical Research (ICR) course offered at UK to MU for the spring semester 2012. This is a MS1 level course and planned to be offered to MU medical students by way of webinar. Dr. Gress presented this offering to the MU MS1 Curriculum Committee. There was general agreement by the committee that this was an excellent opportunity but it could not be added to the curriculum for the 2011-2012 medical school year due to lack of room in the schedule. However, this will be implemented for MU MS1 students for the 2013 spring semester.

A summer session at UK titled "Tools and Application in Biomedical Informatics" was provided via webinar to MU faculty. Six faculty members at MU reported that they participated in the course lectures via the web links provided.

Future plans are underway regarding the offering of certificates in translational science as well as degrees to MU faculty.

Appalachian Health Summit

The Marshall key component actively participated in the annual Appalachian Health Summit. Investigators submitted 10 abstracts; two were selected for oral presentation. Dr. Niles also served as a mentor for six of the poster presenters and provided feedback and constructive critique of their presentations.

Aim 2-MU/UK Pilot Grants

Two first-round awards at Marshall are in place and making excellent progress (see below). In the second round of pilot awards, Marshall investigators submitted eight letters of intent and four projects were chosen to submit full applications. After further review, the application submitted by Dr. Nalini Santanam was selected for funding. Although funds were available for two awards, the committee did not score the other three applications better than a 3.0, the benchmark required for funding.

Pier Paolo Claudio, M.D. Ph.D. ERA Commons user name CLAUDIOPP

"Phase-I Clinical Trial Investigation of Sensitivity to Chemotherapy in Appalachian Lung Cancer Patients"

May 16th, 2012 – February 28th, 2013

After an initial delay in issuance of funds due to some changes in the conditions of the award, Dr. Claudio identified milestones for his component of this project (collaborator, Dr. Rolf Craven at UK). Specific quantitative measures and their rationale for achievement of milestones were elucidated.

The first milestone is to collect lung cancer FNA from 60 patients. At present 46 lung cancer FNA biopsies have been collected. They were classified as 21 NSCC, one SCLC and six metastases from other tumor types. Although the milestone has not been achieved, there is significant progress toward achievement.

The second milestone is to successfully grow cancer stem-like cells from 50% of lung cancer-documented FNA. However, only one NSCLC and one SCLC FNA yielded suitable cancer stem-like cells for subsequent Chemo-ID assay. Therefore it was concluded that the FNA method is not ideal for implementing the Chemo-ID assay. A second IRB protocol for collection of larger samples from lung surgical resection has been submitted (#339118) and approved on 5/11/2012 with an amendment approved on 8/8/2012. Six biopsies were received, with two being diagnosed as NSCLC, and four are still waiting the pathology report. All NSCLC specimens yielded viable cancer stem-like cells.

The third milestone is to successfully perform the Chemo-ID assay on lung cancer stem-like cells. This has been accomplished on both samples.

Jingwei Xie, Ph.D. ERA-Commons user name JXIE2012

"Biomimetic Nanofiber Scaffolds Seeded with Adipose-derived Stem Cells for Rotator Cuff Injury Repair"

March 1st, 2011 – February 28th, 2012

The objective is to design, fabricate, and validate novel nanofiber scaffolds for use in the surgical repair of orthopedic tissue interface – tendon-to-bone insertion site:

- Specific Aim 1: Fabricate nanofiber scaffolds with gradation in fiber organization and mineral content and optimize the biomechanical properties of scaffolds.
- Specific Aim 2: Examine and quantify the cellular responses to the nanofiber scaffolds.
- Specific Aim 3: Study the effect of fiber organization, graded mineral content and ADSCs seeding on healing of rotator cuff injury.

Progress has been made in several key areas:

- A novel method has been developed for the fabrication of nanofiber scaffolds with gradient in fiber organization, which could be used to mimic the orientation of collagen fibers at tendon to bone insertion sites.
- A new approach to controlling the mineralization of electrospun nanofibers, which can greatly enhance their mechanical properties (i.e., stiffness, ultimate tensile strength and toughness) has been achieved. It was found that the morphology, grain size, and thickness of CaP mineral coating on poly(ε-caprolactone) fibers can be readily controlled by adjusting the composition of mineralized solution, surface property of fibers, and duration of mineralization
- Finally, a 'pulling-mineralization' approach to the fabrication of nanofibers with dual gradations in both mineral content and fiber organization has been demonstrated.

A rat rotator cuff injury repair/regeneration model has been developed, IACUC approval obtained and several trial surgeries have been performed for the implantation of nanofiber scaffolds with dual gradations to the tendon-to-bone insertion site.

An NIH R15 proposal has been submitted from this work and obtained impact/priority score of 21. The final decision for this grant will be announced in October 2012.

Future work is focusing on the proliferation, migration and differentiation of adipose-derived stem cells seeded on nanofiber scaffolds.

Publications

Xie J*, Michael PL, Ma B, Shuler FD, Fabrication of nanofiber scaffolds with gradations in fiber organization and their potential applications. *Macromolecular Biosciences*, **2012**, *12(10)*, 1336-1341. www.ncbi.nlm.nih.gov/**pubmed**/22847852

Xie J*, Zhong S, Ma B, Shuler FD, Lim CT, Controlled biomineralization of electrospun poly(ε-caprolactone) fibers for enhancing their mechanical properties *Acta Biomaterialia* **2012** Nov 3. pii: S1742-7061(12)00534-X. doi: 10.1016/j.actbio.2012.10.042. www.ncbi.nlm.nih.gov/pubmed/23131385

Nalini Santana, Ph.D. ERA-Commons user name NALINIS

"Microflora Fingerprint in Women with Endometriosis and Pain"

August 10th, 2012 – January 9th, 2014

IRB approval for this study has been obtained. The process of recruiting patients to collect tissue samples for the miRNA analysis is underway.

Aim 3, Aim 5-Clinical Trial Development

The development of a small investigator-led trial at Marshall into a larger effort using the trial network is well underway in the ADVANCE (Advancing Diabetes Care through Awareness, Compliance and Education) Study. The ADVANCE study is a randomized clinical trial examining the use of cell phone technology in a rural health clinic (Chapmanville, WV) to improve a patient's self-management of diabetes. It includes a basic science component that seeks to determine changes in known biomarkers associated with diabetic control over time as well as discovery of potentially new biomarkers.

The study officially started in March 2012 and has enrolled 19 patients to date with several having completed the three month follow-up visit. Collaboration with the University of Kentucky was sought for this project. A meeting was held at St. Claire Hospital in Morehead, Kentucky over the summer (2012) with an agreement to start up an ADVANCE study site with the St. Claire health system. A meeting with study site personnel at St. Claire is planned for October to facilitate initiation of the project at this site. Dr. Anthony Weaver is the study site investigator at St. Claire.

Further collaborative study has been developing between UK Rheumatology and MU Orthopedics. As a result of last fall's site visit by UK personnel, Dr. Leslie Crofford (UK Rheumatologist) is collaborating with Dr. Franklin Schuler (MU Orthopedics) on a study examining synovial tissue and inflammation. Samples of synovial tissue will be obtained at the time of orthopedic surgery and transferred to Dr. Crofford. The Clinical Research Center at MU is working on the process and consent with Dr. Schuler with anticipated start date within two months.

d. Project Development With Carry-Forward Funds

Due to the shortened amount of time for the first year CTSA award a carry forward request was made to the NIH. The CTSA Steering Committee decided to issue an RFA for these funds based on projects that were not proposed in the submitted CTSA application. The Marshall University Core, in collaboration with the Biomedical Informatics Core at UK, submitted a proposal to integrate the i2b2 informatics system (integrating biology & the bedside) into Marshall University's HER, Allscripts to create a federated search portal available to investigators at both institutions. This project was approved for funding and will be implemented as funds become available. This system will provide an additional rich resource for clinical research and add additional value to Marshall key function component of the CTSA.

e. Plans for Year Three of CTSA Funding

- Our WV Cancer Genomics Network will interact with the new Bio-repository being develop at UK to develop a common interface so available cancer specimens and potentially genomic data can be shared by UK researchers.
- We will monitor the progress of Marshall faculty awarded pilot grants on a quarterly basis. We will encourage a strong response in terms of numbers of viable applications for the third year RFA solicitation for pilot grant funding. We will use internal mentoring to generate two competitive proposals.
- Staff and clinical faculty training in clinical research will be pursued through courses and workshops offered by the UK CCTS. We will implement the MS1 course "Introduction to Clinical Research".
- We will have one additional Marshall investigator-initiated clinical trial linked into the UK network and provide patients that will be enrolled in the trial.
- A faculty member from Marshall's Orthopedics department will submit an application for a KL2 award
- Marshall's rural health network will develop a second mutual project of participatory community-based research in collaboration with the UK rural health network.
- Complete the i2b2 project if carry-forward funds are approved.