TRANSLATIONAL SCIENCE AT THE NEURAL INJURY CENTER

MUS Research and Economic Initiative

1st Quarterly Report

August-October 2015

Objective 1: Expand current clinical capabilities of the Neural Injury Center (NIC) and support translational research.

a)   *Hirings:*

- Hiring of Administrative Assistant completed—to start 11/9/15
- Currently interviewing for Clinical Research Coordinator
- HR approval and ads sent out for Neuropsychology position

b)   *Equipment:*

- N/A

c)   *Progress towards milestones:*

- Established accounting methodologies for coordination of all aspects of MUS funding
- Established administrative procedures for all aspects of all objectives.
- Established monthly meeting of MUS research team
- Established procedures for referral of clinical consulting services (ophthalmology, PT, chronic pain, speech therapy, neuropsychology).
- Initiated contacts with Ft Harrison and Colorado Regional VA Center to determine possibilities of creating a Level I Research Inst. At Ft. Harrison.
- Began process of exploring the possibility of becoming a VA Preferred Provider within state of Montana.
- Group email notifications sent to all student-veterans notifying of free NIC screening services
- Updating and re-print of brochure for new direct mailing to student veterans regarding our services
- Completed all work for November TBI continuing education meeting and arranged consultations among incoming experts and MUS researchers.
- Met with representative from Governor's TBI Council.
- Presentation of MREDI award and NIC to University Brain Initiative Committee. Arranged for two speakers who presented ideas for concussion research (Dr Valerie Moody) and Greg Johnson who would like to present a play on concussion as part of the NIC's community outreach.
- Initiated discussions with Family Residency Program to begin process for specialty rotation with the NIC for TBI. Objectives and Learning program drafted in review by Residency Director.
- Have begun to create procedures to monitor client outcomes (e.g. graduation rates).

Objective 2: Develop a comprehensive panel of objective tests to diagnose mild TBI (mTBI).

a)   Hirings:

- Hire for the RA position is currently in initial stages and we expect to have this hire concluded in the month of December. Specifically, the advertisement is currently being crafted and expectancy is to have it sent to the UM HR for approval and dissemination as soon as early November.

b)   Equipment purchased:

- Hardware is currently being purchased for the clinical prototype of the BalanceLab apparatus. This expenditure should take place along the next weeks and extend accordingly to the development of the clinical version of our experimental system.
- Software development is also being carefully considered. Dr Santos is currently finalizing the details regarding the agreement with software engineers for the development of this system that will follow accordingly to hardware development.

c)   Progress towards milestones:

The main objectives for this quarter have been achieved and some excelled.

- University of Montana IRB has approved IRB applications for all human studies conducted under these objectives.
- A data depository for all electronic recorded information has been created and implemented.
- Recruitment of control and TBI participants has been initiated (30 subjects recruited).
- Data collection and analysis from these two groups has also been started and. This will allow our group to have an extended period of time to perform further analyzes and facilitate further development of the BalanceLab apparatus.
- Advancement in the development of a new version of the balance system is under way where (1) purchasing the necessary hardware for the clinical prototype of the BalanceLab apparatus is taking place within the months of November and December and (2) development of the clinical software is in its initial stages and it is dependent on the development of the hardware.
- Plasma samples collected from recruits.

Objective 3: Develop miRNA inhibitors to reduce neuropathology after TBI.

a)   *Hirings:*

- N/A

b)   *Equipment purchased:*

- N/A

c)   *Progress towards milestones:*

- University of Montana IACUC has approved animal use protocol application for all animal studies conducted under this objective.
- First 6 microRNA (miRNA) inhibitor molecules have been synthesized and *in-vitro* testing has commenced to assess activity using luciferase reporter assay.
- Rats for *in-vivo* testing of miRNA have been purchased.

Objective 4: <u>VAST: Next Generation Learning,</u> Complete the development of a computer-based cognitive training (CCT) system for TBI subjects with cognitive impairment.

a)   Hirings:

- N/A

b)   Equipment purchases:

- *N/A*

c)   Progress towards milestones:

Despite substantial delays receiving the required subcontract and related forms to begin Objective 4, VAST: Next Generation Learning is proceeding with its CCT development on schedule. VAST projects that all of the milestones listed as part of its December 2015 deliverables will be completed on time. A detailed breakout of milestones related to the December 2015 deadline follows.

- Develop prototype HTML5 mobile app; develop initial set of 5 training levels and 40 exercises for testing in quarters 3 and 4

Technology Development (On schedule: ~80% complete)
- Backend for HTML5 app has been completed, including MySQL DB and PHP scripts to handle data transition between client and server. Websocket programming has been completed to interface quickly with mobile devices, using socket.io and JSON technology.
- Frontend development of HTML5 app for iOS and Android is still in progress, including creation of mobile screens and layout for training levels, exercises, and subject scoring, on schedule to be completed by December 2015.
- Software algorithms for scoring Divergent Thinking (DT) abilities of users have been improved to account for nuances in DT Fluency tracking and measurement.

Research Progress (On schedule: ~75% complete)
- Extensive research into valid forms of cognitive exercises for mTBI patients has been completed, which will form the basis of the 5 training levels and set of 40 DT exercises.
- Initial testing of assessment platform with ~21 UM students has been completed as part of an initial battery of mTBI tests involving consortium partners.
- CCT testing has been extended to include EEG measures of DT training impact, completed with test subjects while completing Vast DT exercises.
- Preliminary training levels and related sets of exercises that will be part of the training program have been created, and will be integrated into the HTML5 training app during November and December 2015.

External Grants and Funding
In conjunction with UM TBI Consortium partners, VAST submitted a SBIR grant proposal for cognitive training testing to the National Institutes of Health in September 2015 for $220,000.00. A decision on this grant by the NIH should be received by November 20th. Additional means to leverage consortium funding are also now being explored with the DOD and other funding agencies.

Expenditures
Through October 31st, 2015, Objective 4 total expenditures: **$37, 408.77**

Objective 5: Complete the development and testing of a novel post-traumatic epilepsy diagnostic analysis program.

Background

01030-MUSRI2015-01 Objective 5 Technical Summary Status

The purpose of this effort is to identify biomarker(s) present in EEG signals that indicate if a person who has experienced a traumatic brain injury [TBI] has a high risk for developing post traumatic epilepsy [PTE]. This knowledge is critical for future clinical and drug studies so they can focus specifically on the at risk patients.

Patient data

Previous progress in this area has been hampered by the challenge of acquiring the necessary patient data. At a minimum, EEG recordings are required for patients that: have experienced a TBI and *did* go on to develop PTE, have experienced a TBI that *did not* develop PTE, and a set of control data. Because the onset of PTE can occur many years after the injury it was necessary to acquire it from a source with a long history of prior data. The initial set of de- identified data has been received from Massachusetts General Hospital. It consists of 28 multichannel EEG recordings from 5 different patients that did develop PTE. Even this initial sample is rather large consisting of over 61GB of data in various formats.

Software, machine learning, prerequisites

Evaluating large volumes of EEG data to discover potentially subtle signal patterns simply can not be done manually. Some form of software support is required. Recent developments in machine learning such as deep belief networks have demonstrated the capability to automatically learn features present in many forms of data. However, before these techniques can be applied to the acquired EEG data we must first be able to read and transform it in to a suitable form. As of this writing, we have completed the development, testing, and deployment of a high performance stream processing application to ingest and process the EEG sample data and store the resulting feature vectors into a noSQL database. Also created is a set of web based analytical tools for reading the resulting data and transforming it further for display and use by the machine learning algorithm.

Visualization and Collaboration

Once the software has identified all the features present in the data, the research physicians will need to collaborate to evaluate them to select potential biomarkers. Because they are not in the same location, a web accessible tool is desirable for visualizing and exploring the resulting data sets. The application that has been developed for the application of the machine learning algorithm can be extended to allow the researchers to visualize and interact with the results.

Next steps

With the acquisition of some initial data and the implementation of the prerequisite software complete, the next phase of the project is to develop and apply the machine learning capability and visualize the resulting features for the researchers to evaluate.

Quarterly Budget Reports

Objective 1:

MUS MREDI Objective 1 - Operating Statement - Inception to Date

Institution: University of Montana (BMED/NIC)
PI: Dr. Sarjubhai Patel
Banner #: MPHR01

Report Date: 10/30/2015

Account	Description	Budget	Expenses to Date	Remaining
61124	Contract Professional	-	9533.67	
61199	**Personnel Services-General**	**145,000.00**	**9,533.67**	**135,466.33**
61401	FICA	-	586.88	
61403	Group Insurance	-	1867.66	
61404	Workers Compensation	-	61.98	
61409	Medicare Tax	-	137.25	
61410	State Unemployment Tax	-	23.83	
61415	TIAA-CREF Retirement	-	922.5	
61415A	TIAA-CREF 1% HB95	-	95.33	
61499	**Benefits-General**	**72,510.00**	**3,695.43**	**68,814.57**
62199	**Contracted Services-General**	**23,500.00**	**-**	**23,500.00**
62208	Laboratory Supplies	-	54.95	
62299	**Supplies-General**	**-**	**54.95**	**(54.95)**
62401	In State Personal Car Mileage	-	65.07	
62499	**Travel-General**	**-**	**65.07**	**(65.07)**
	TOTALS	**241,010.00**	**13,349.12**	**227,660.88**

Objective 2:

MUS MREDI Objective 2 - Operating Statement - Inception to Date

Institution: University of Montana (BMED/NIC)
PI: Dr. Sarjubhai Patel
Banner #: MPHR02

Report Date: 10/30/2015

Account	Description	Budget	Expenses to Date	Remaining
61123	Contract Faculty	-	24,958.99	
61199	**Personnel Services-General**	**167,239.00**	**24,958.99**	**142,280.01**
61401	FICA	-	1,489.95	
61403	Group Insurance	-	1,955.66	
61404	Workers Compensation	-	162.25	
61409	Medicare Tax	-	348.46	
61410	State Unemployment Tax	-	62.40	
61415	TIAA-CREF Retirement	-	2,362.69	
61415A	TIAA-CREF 1% HB95	-	249.58	
61499	**Benefits-General**	**64,397.00**	**6,630.99**	**57,766.01**
62199	**Contracted Services-General**	**30,000.00**	**-**	**30,000.00**
62208	Laboratory Supplies	-	52.70	
62299	**General Supplies**	**25,000.00**	**52.70**	**24,947.30**
	TOTALS	**286,636.00**	**31,642.68**	**254,993.32**

MUS MREDI Objective 3 - Operating Statement - Inception to Date

Institution: **University of Montana (BMED/NIC)**
PI: **Dr. Sarjubhai Patel**
Banner #: **MPHR03**

Report Date: 10/30/2015

Account	Description	Budget	Expenses to Date	Remaining
61123	Contract Faculty	-	8,114.81	
61125	Classified Employee	-	13,434.89	
61199	**Personnel Services-General**	**125,422.00**	**21,549.70**	**103,872.30**
61401	FICA	-	1,206.68	
61402	Retirement	-	535.05	
61402C	ORP-Staff TIAA Cref	-	589.45	
61403	Group Insurance	-	5,672.54	
61404	Workers Compensation	-	565.89	
61409	Medicare Tax	-	282.20	
61410	State Unemployment Tax	-	53.88	
61415	TIAA-CREF Retirement	-	785.19	
61415A	TIAA-CREF 1% HB95	-	81.15	
61499	**Benefits-General**	**60,165.00**	**9,772.03**	**50,392.97**
62147	Subcontract Payments	-	42,704.81	
62147A	Sub Contract Payments > 25,000	-	16,000.00	
62199	**Contracted Services-General**	**281,000.00**	**58,704.81**	**222,295.19**
62208	Laboratory Supplies	-	1,109.76	
62299	**General Supplies**	**89,945.00**	**1,109.76**	**88,835.24**
	TOTALS	**556,532.00**	**91,136.30**	**465,395.70**