Forensic Measurement of Airman Fatigue State (formerly A11J.AM.2)

Research Project Description

1) Biomarkers to detect Fatigue-related impairment **(a11j.am.10)**

2) Biomarkers for cognitive performance under sleep loss, with and without countermeasure **(a11j.am.20)**

3) Fingerstick sampling for gene expression analysis **(a11j.am.10)**

4) Optimization of sample preparation and analytical methods for gene expression research **(a11j.am.10)**

5) Biorepository for aviation accident samples **(a11j.am.21)**

6) Post-mortem biomarker of THC exposure **(a11j.am.11)**

Sponsor Anticipated Outcome

- The sponsor will consider the results of this study, including biological and any other indicators of sleep loss-induced performance degradation, for further use in field-based testing. These findings will be used to guide development and/or revision of data-driven recommendations for pursuing future research, technology transfer, or regulatory efforts. (FY28Q1)
- Constituent projects, no anticipated outcomes during FY22.

Critical Milestones

- Sequencing contract award (needed for projects 1,3,6)
- Complete study protocol for project 3
- Complete study protocol for project 6
- Achieve 1/2 of subject runs for project 1
- Complete analysis and writing for study 4

Research Accomplishments in FY22

- Sequencing Contract Awarded (Baylor College of Medicine)
- Half of subjects samples received(40 of 80, project 1)
- Sampling completed, all samples processed (project 3)
- Two OAM report drafts written and in coauthor review (project 4)
- Biorepository genomics kit ready for placement in tox-boxes (project 5)
- Sampling complete and samples processed (project 6)

OC4 Forensic measurement of pilot fatigue state: program overview

1. Develop fatigue biomarker diagnostics

- BLI 4.2 Sleep loss with and without modafinil– RNA biomarkers
- BLI 4.1 Comparison across multiple types of sleep loss – RNA and SNP biomarkers
- BLI 4.13 RNA biomarkers for noise-induced sleep loss
- BLI 4.5 Postmortem biorepository of aviation victim molecular samples
- BLI 4.6 Metabolomic biomarkers
- BLI 4.7 Microbiome biomarkers
- BLI 4.8 Proteomic biomarkers
- BLI 4.9 Wearables and physiology – biomarker understanding
- BLI 4.10 DNA biomarkers

2. Validate

- BLI 4.11 Validation in fatal accident victims
- BLI 4.14 Validation in field studies (live subjects)

3. Apply

- BLI 4.12 Research Translation: roadmap for a CAMI forensic pilot fatigue impairment report to NTSB

New sample collection

Biomarker analysis and discovery

Interpretation, validation, and application of biomarkers

A11J.AM.2, Comparison Across Multiple Types of Sleep Deprivation

Status

- Continuing, 40 of expected 80 subjects run through experimental protocol.
- Samples and Data are sound.
- Spending has lagged due to 1) slower than expected recruiting and enrollment, 2) delay in award of sequencing contract.

Findings

- Initial findings only: Samples received are of desired quality, data generated to and analyzed to date displays expected patterns of performance vs sleep.

Challenges

- Recruiting: Subject enrollment has lagged from expected trend due to many factors; COVID, employment conditions. This is seen in all projects conducted by the contractor. Mitigation: Relaxed non-critical subject criteria.

Redirections

- Project rebaselined to accord with contract-related and subject recruitment delays, remains on track for final deliverables.

A11J.AM.2, Gene Expression Patterns in Response to Modafinil

Status

- Sequences received, being analyzed

Findings

- Initial findings only: Biomarker pool related to sleep deprivation found.

Challenges

- PI time restrictions have caused non-trivial delays in processing

Redirections

- None

A11J.AM.2, Utility of Capillary Blood for Gene Expression Studies

Status

- Subject runs completed, 40 subjects total, 160 samples.

Findings

- Initial findings only: Fingerstick blood RNA was of slightly higher quality, but lesser quantity, than venous blood collected in dedicated tube types.

Challenges

- Contracts: Sequencing contract delay led to missed interim deliverables; shifted schedule into FY24. Sequencing contract was awarded.

Redirections

- Rebaselined project to account for contract-related delays.

A11J.AM.2, Gene Expression and Biomarker Utility in Postmortem Samples

Status

- Sampling complete: 22 THC positive, 28 THC-negative. Samples processed and ready for sequencing lab.

Findings

- Initial findings only: Samples produced large amounts of lower-quality RNA, each sample type produced slightly different results. Sequencing not yet performed.

Challenges

- Sample Collection: Samples positive for THC accrued at a slower-than-expected rate. Contract: Sequencing Contract was award later than anticipated.

Redirections

- Project was rebaselined, final deliverable now in FY24. Project now included in expanded cannabis/drug OC (OC5).

A11J.AM.2, Assessment of RNA-seq sample preparation methodology.

Status

- Analysis and OAM drafts complete, in coauthor review.

Findings

- Sample preparation methods tested do no produce significant variance in results, optimal analytical pipelines documented.

Challenges

- Increasing publication requirements and PI time demands have delayed final publication.

Redirections

- Project rebaselined for FY23 completion.

A11J.AM.2, Postmortem Blood Genomics Biorepository

Status

- Protocols complete, supplies on hand. Filling kits to add to outgoing Tox-Boxes.

Findings

- EDTA tubes provide sufficient protection for Blood DNA.

Challenges

- Component backorders caused delay in package assembly.

Redirections

- None