GWIC

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Boston Biorepository, Recruitment and Integrated Network for GWI

# Military Veteran Biorepositories

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# What is a Biorepository and what do they do?

- A biorepository is a center that collects, processes, stores, and transports biospecimens or biological samples to aid research or scientific investigations.
- All biorepositories have four main operations:
  - Collection – This is where the arrival of the samples is recorded. These biospecimens are assigned a unique identification. This information along with the data associated with the specimen is then recorded in the laboratory information management system.
  - Processing – The samples at this stage are tested to ensure that there is minimal variation in the handling and preparation stage.
  - Storage – The samples are held in their proper storage environments such as room temperature or freezers depending on the requirement.
  - Distribution – The required samples can be retrieved and transported to their designated locations when requested by research teams.

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# Your biobank is only as good as its samples, its associated data, and the rules to play

- Excellent samples are not useful without excellent associated clinical data sets.
- What kind of samples?
  - Typically blood and its fractions (sera, plasma PBMCs, RBC, RNA, DNA) but compartment specific collections can increase utility (eg spinal fluid, sputum, saliva, tears, urine, stool ) as can tissue collection (fat, skin, muscle). Autopsy samples can provide brain specimens and organ tissue.
- What kind of linked data?
  - Clinical: validated assessment platforms, both subjective and objective.
    - See common data elements platforms for many conditions through NIH CDE project. Gulf war illness CDE also available.
  - Lab and procedures data : imaging, procedures (echo, tilt table, exercise testing, actigraphy, sleep lab data etc)
  - Shared data (can be a condition of sample usage): SNP, gene activation, regulation, proteome, lipidome, metabalome)

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"A well managed biorepository should eventually be an empty biorepository"

# Biobanks are overarching organization/management structures who oversee, manage, and coordinate collection and distribution of samples

- Types of collections
  - Clinical - pathology archive, surplus surgical
  - Diagnostic – surplus blood, urine, biopsy
  - Research – drug trial, health surveys
  - Therapeutic – stem cells
  - Virtual - hold no physical specimens but offer location and retrieval services for samples held globally or nationally
- Patient or population based
  - Population - large scale prospective studies – range of conditions
  - Patient/clinical – focus on specific disease categories e.g. toxic exposures
- Annotation/Data
  e.g. Sample history, patient information, clinical data, pathology, pedigree
- For future use - not project specific - Research Tissue Banks
- Appropriate governance mechanisms

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# Issues

- Respect donor privacy and the conditions of the donation (Informed Consent)
- Responsible custodianship - a well-maintained collection annotated with data
    - Processing
    - Quality control
    - Fair and rapid process to request samples
    - Maintaining a LIMS system
    - Maintaining a linked de-identified clinical data system

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# Gulf War Illness Consortium (GWIC)

- 16 collaborators from 9 study sites including US and Australia
- Designed to bring preclinical (cell and animal) and clinical (human) researchers together to speed development of understanding pathobiology of Gulf War Illness (GWI) and to develop treatments. *Created in-demand biorepository*.
- Our focus - study brain-immune pathways and chronic release of chemical messengers from immune cells of the brain that lead to chronic inflammation.

*CDMRP #GW120037*

# Gulf War Illness

- Clearly the opportunity to have access to well characterized patient materials has increased the number of bench scientists responding to funding opportunities.
- GWIC experience
- BBRAIN design to continue this work with longitudinally collected samples from a very well characterized cohort
- Bringing a critical mass of interdisciplinary scientists together, and sharing the data collected through a collaborative agreement will continue to advance the field

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*CDMRP #GW170055*

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## Boston GWI Consortium affiliated studies Timeline

2013
**GW120037**
GWI Consortium

GWIC

2014
***GW130100***
PET imaging of neuroinflammation in GWI

***GW130045***
Lipid markers of neuroinflammation

2015
**GW140140**
CNS autoantibody in GWI

**GW140086**
GW hiPSC Stem cell study

2016
**GW150116**
GW women's health study

PON1
**GW150037**
biomarker study

2017
***GW160053***
BChE biomarkers of GWI

***GW160096***
Epigenetic studies Of GWI

***GW160151***
Tau markers in GWI

***GW160032***
Machine learning in GWI

2018
***GW170068***
Gut microbiome study

***GW170055***
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***GW170044***
GWICTIC

***GW170103***
CNS autoantibody screening

***1808884709R001***
HMGB1 in GWI

2019
***GW180150***
Mitochondrial Functioning in GWI

***GW180099***
GW White matter brain imaging study

***GW180103***
PET imaging of microglia and astrocytes

***GW180121***
CNS autoantibodies and brain imaging outcomes

# KEY RESEARCH ACCOMPLISHMENTS

- Began 10 GWIC studies planned for consortium
- Submitted 7 additional pilot studies
- Collaborating on 6 current treatment trials and now a treatment consortium -GWICTIC
- Collaborating on 19 additional biomarker studies
- 21 publications, 35 abstracts, 3 symposia
- Built a successful biorepository and actively sharing with many GWIC and other GWI investigators
- Now funded for a recruitment and biorepository network (BBRAIN) with the GWI research community.

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CDMRP #GW170055

# GWIC Biorepository: bringing new investigators to the field

- Nearly 30 years after the Gulf War, we had not had sufficient momentum to move mechanistic studies forward to targeted therapeutics.
- Through the GWIC biorepository, and CDMRP funding mechanisms that encouraged new investigators and linked them to the resources
- The Boston GWIC provided samples and data for studies to 17 investigators which resulted in 19 applications and 17 investigators that would otherwise have not had access to materials to support this important work.

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*CDMRP #GW170055*

- Due to the highly successful research collaboration of the GWIC, It was the natural next step to increase this highly valuable resource by replenishing GWIC samples and by increasing the diagnostic and treatment capability by including investigators from 8 additional study sites in addition to the current GWIC sites

- BBRAIN includes investigators from 10 study sites around the country so far…

- Additional researchers will be applying for funds to share more samples with BBRAIN in the coming years

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## BBRAIN Inventory

### Biological Samples

- Whole blood
- Stem cells
- CSF
- Saliva
- DNA
- Plasma
- Serum
- Fecal samples
- Urine
- PBMC
- Buffy coat

### Clinical Data

- Fitbit measures (heart rate, sleep, exercise)
- Cognitive tests (executive functioning; attention, vigilance, and tracking; motor function; visuospatial function; memory; motivation; mood; general intellectual abilities)
- Brain imaging (PET, MRI, DTI, fMRI)

## Data Sharing

Requests to access data in our repository can be made through our website:
sites.bu.edu/bbrain

## Contact Us

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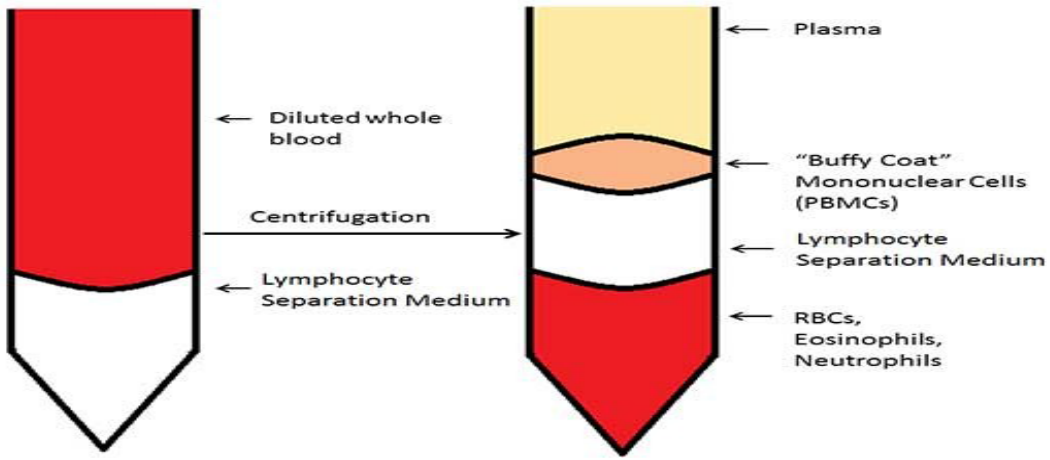
# Prospective Data Collection

- The BBRAIN Network structure will provide support and coordination for prospective data collection of total blood for RNA or DNA analysis, plasma, serum, saliva, stool and urine samples for 500 GW veterans in addition to demographic surveys and cognitive test data

- Prospective specimen collection at 4 sites including BUSPH, Miami VA, Bronx VA and San Francisco VA



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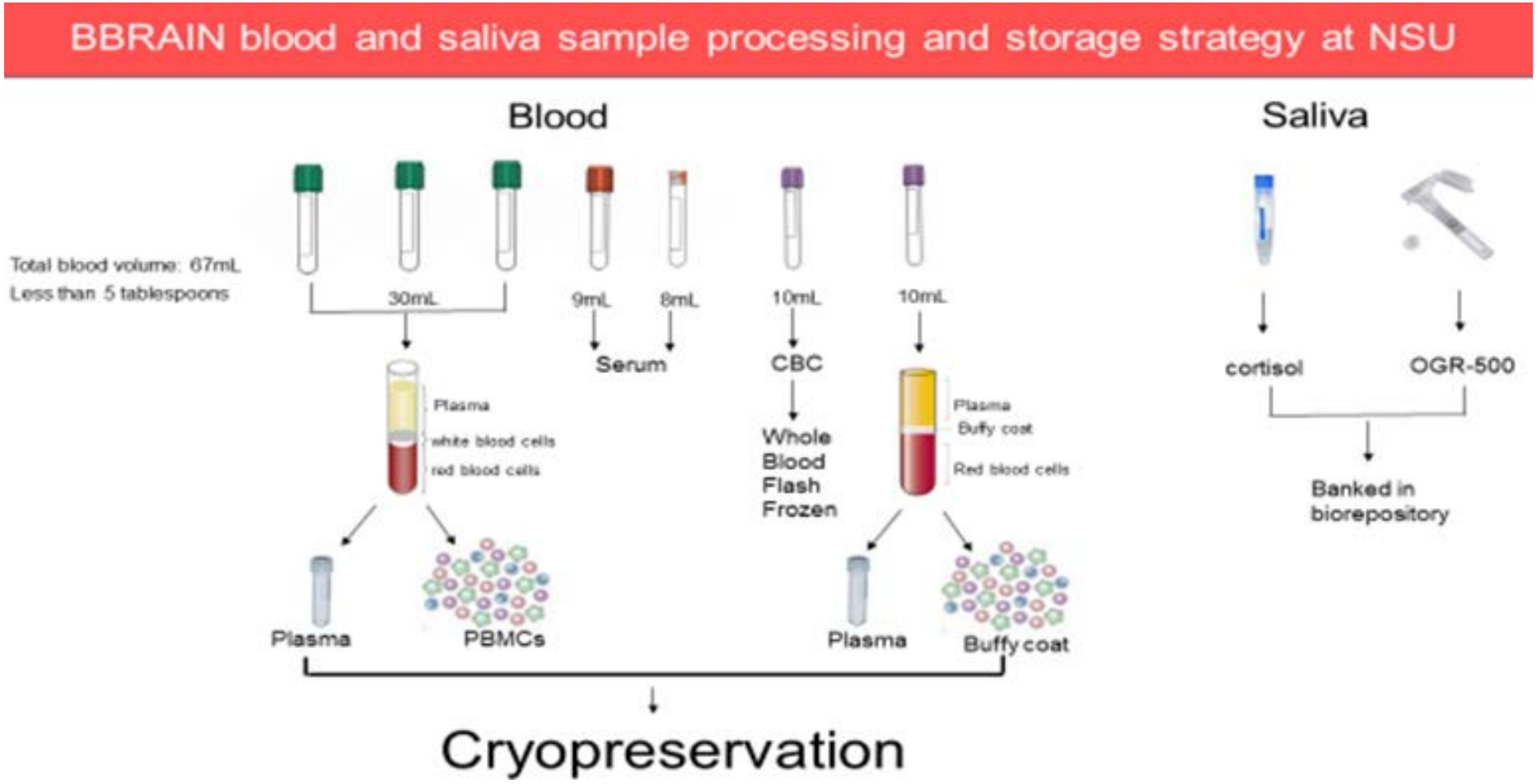
# Biorepository Specimen Storage Plan

- Five hundred prospectively collected blood and saliva samples will sent to the EM Papper biorepository at NSU



# Current Military Veteran biorepositories

- CDMRP GWIC and BBRAIN (viable PBMCs, plasma, sera, saliva, stool, urine)
- CDMRP also lists investigator held samples with contact information – BBRAIN Virtual repository
- VA Biorepository Brain Bank - Created in response to ALS linked to GW deployment, samples in Tucson VA, diagnostic neuropathological analyses at VABHS, 1 or 2 GWV samples available but serum and survey data is available.
- VA Million Veteran Program (MVP) - with survey information, limited exposure data (includes a question on burn pit exposure), 800K enrolled to date, merit review funded and special RFAs
- CSP585 - Gulf War Era and Biorepository - 1200 vets (of 10k) enrolled approx. 60% with GWI 10ml blood, DNA, survey data. Established method to request sample access but on-hold for sharing plasma.
- DOD serum repository – over 60 million serum samples available but must have DOD PI for use.
- NHLBI – Gold Standard but no military specimens

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# What are the Challenges of Using Military Repositories?

- Small amount of samples per participant available limiting number of studies that samples can be shared with
- Extensive and lengthy approval processes often with many delays due to multiple levels of approval for sharing
- Often require PI at DOD or VA for access to samples
- Can require very high information security levels often not available outside VA/DOD even for de-identified data/samples
- BBRAIN designed to address many of these issues to provide samples to many GW investigators and speed up biomarker discovery and translation of results from animal/cell to clinical samples.

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# Possible Burn Pit and Air Hazard Exposures

- Particulate matter and respirable sand
- Heavy metals and dioxins
- Diesel fuels
- Chemicals and paint products
- medical and human waste
- munitions and other unexploded ordnance
- Solvents - petroleum and lubricant products
- Plastics and rubber

# Better Understanding of Chronic Health Risk Pathogenesis

- Data of exposures should be connected to biomarker specimens
  - Determine frequency of exposures as part of a Health Risk Assessment
  - Create CDEs for exposure assessment like GW veterans on CDMRP website
  - Could utilize SNAC and other occupational exposure and hobby questionnaires
  - Can use GIS modeling of air plumes and wind patterns to correlate with specimens
- Consider detoxification systems and compartments at risk
- Design a biorepository for health consequences seen years after the exposure determines what is collected

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# What could be added to a repository for use in Burn Pit and Air Hazards Research?

- Blood and cells
- Sputum and Saliva
- Lung biopsy tissue
- Kidney biopsy tissue
- Urine
- Stool

# Thank You