

HARVARD BRAIN TISSUE RESOURCE CENTER

FRANCINE M. BENES, M.D. PH.D., DIRECTOR

McLean Hospital ♦ 115 Mill Street ♦ Belmont, MA 02478

Phone: 1-800-BRAIN BANK or (617) 855-2400 ♦ Fax: (617) 855-3199 ♦ E-mail: BTRC@mclean.harvard.edu
[1-800-272-4622] <http://www.brainbank.mclean.org>

Dear Investigator:

Thank you for your inquiry about receiving postmortem human brain tissue from the Harvard Brain Tissue Resource Center. In order to evaluate your request, the Brain Bank requires that you provide the following information:

1. Complete the INVESTIGATOR REQUEST FOR BRAIN TISSUE FORM.
2. Provide a list of approved GRANT SUPPORT for your research program (i.e., Federal grant number, foundation or other private support, or identify current collaboration or mentor-trainee affiliations).
3. Provide an ABSTRACT or SPECIFIC AIMS that clearly describes the project for which you will use human postmortem brain tissue.
4. Provide a copy of your CURRICULUM VITAE or NIH BIOSKETCH.
5. Read and sign the HUMAN TISSUE HANDLING RISKS & SAFETY PRECAUTIONS STATEMENT. This will acknowledge your responsibility in understanding of and adherence to appropriate safety standards for the protection of yourself and other laboratory personnel under your supervision while handling human postmortem brain tissue.
6. Read and sign the HUMAN TISSUE SINGLE USER AGREEMENT. This will acknowledge your responsibility in not distributing any portion of the tissue disbursement to colleagues or other investigators, and that all such inquires will be directed to the HBTRC Director.
7. Read and sign the HBTRC ACKNOWLEDGMENT AGREEMENT. This will indicate that you have agreed to provide specific acknowledgment of the Harvard Brain Tissue Resource Center and its Federal grant number in any publications related to the use of these tissues.

All requests undergo a review process in the order which they are received. Upon approval, the tissue order will be shipped to your laboratory as such samples become available to the Brain Bank. The Brain Bank charges no fee for providing this service. The cost for shipping, however, will be assumed by the recipient. We ship by Federal Express, and we do require that you provide us with your FedEx account number.

Please feel free to contact me regarding the status of your request for tissue or with any other questions you may have. The Brain Bank is pleased to be able to provide this specialized service to help facilitate your research program.

Sincerely,

Francine M. Benes, M.D., Ph.D.

Director

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INVESTIGATOR REQUEST FOR BRAIN TISSUE

Investigator Name: _____ Phone #: _____

Institution Name: _____ Fax #: _____

Laboratory Shipping Address: _____ Email: _____

FedEx Account #: _____

Name of Laboratory Director if different from above: _____

PLEASE ATTACH LIST OF SPECIFIC AIMS AND PROPOSED METHODS FOR THIS RESEARCH PROJECT.

TISSUE REQUEST:

- Refer to list of diagnoses for available tissue resource. Please note that for some diagnoses tissue samples can only be distributed, as they become available.
- Please provide a detailed outline of your specific tissue needs.

I.	DIAGNOSIS CATEGORY	# OF CASES	BRAIN REGIONS	AGE, SEX, PMI RESTRICTIONS
1.	_____	_____	_____	_____
2.	_____	_____	_____	_____
3.	_____	_____	_____	_____
4.	_____	_____	_____	_____
5.	_____	_____	_____	_____
6.	_____	_____	_____	_____

II. TISSUE PREPARATION

- Passive Frozen at -20° C
- Quick Frozen in Liquid Nitrogen Vapor (-160° C) or at dry ice temperature (-70° C)
- Fixed in 10% buffered formalin

- Coronal Slices
- Individual Tissue Blocks
- Dissected & Chopped
(frozen sample in 1.0 ml cryotube)
- Frozen CSF

Dissected Brain Regions
Frozen In Liquid Nitrogen Vapor (-160°C)

Please indicate by placing a check mark in the BLOCKS REQUESTED column, which brain regions you are requesting for your studies.

LNV Block #	Dissected Brain Region	BLOCKS Requested
1.	Superior frontal cortex (Brodmann area 9)	
2.	Posterior frontal cortex (Brodmann area 4)	
3.	Parietal cortex (Brodmann area 7)	
4.	Calcarine cortex (Brodmann area 17 and Brodmann area 18)	
5.	Hippocampal formation with parahippocampal gyrus	
6.	Caudate, putamen and accumbens (CAP)	
7.	Globus pallidus (GP) and putamen with claustrum	
8.	Amygdala	
9.	Thalamus at level of centrum medianum	
10.	Midbrain including substantia nigra	
11.	Upper pons at level of locus coeruleus	
12.	Lower pons at inferior border of cranial nerve V	
13.	Medulla oblongata at level of inferior olivary nucleus	
14.	Cerebellum with dentate nucleus	
15.	Temporal pole	
16.	Cingulate gyrus	
17.	Anterior thalamus with subthalamic nucleus	
18.	Anterior hippocampus with entorhinal cortex	
	Hypothalamus	
	Olfactory bulbs	
	Pituitary gland	
	Dura matter (1 cm ² pieces)	

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HUMAN TISSUE HANDLING RISKS & SAFETY PRECAUTIONS STATEMENT

Working with postmortem human brain tissue carries the potential risk of exposure to infectious diseases that may be communicable to other humans. All human brain tissue should be treated as a potential contamination risk for certain diseases and should be handled with extreme care. Infectious agents that have been identified as possible risks include, but may not be limited to, Human Immunodeficiency Virus (HIV-1, HIV-2), Hepatitis-B, and Creutzfeldt-Jakob disease. Although a relatively rare disease entity, Creutzfeldt-Jakob disease has been reported to be able to remain infectious for long periods of time in fixed tissue and it may withstand standard autoclave sterilization procedures.

It is recommended that **UNIVERSAL PRECAUTIONS** be followed when working with postmortem human brain tissues irrespective of the method of tissue preparation. Investigators are encouraged to incorporate double gloving, appropriate protective garments, and face or eye protection when working with brain tissue. Disposable instruments and/or an effective regimen of appropriate decontamination should be used routinely. All waste material should be considered as a biohazard. Waste should be disposed of according to your institution's policy for handling such material, which may include incineration, autoclaving and burial, or other approved methods. All laboratory staff that will be working with human brain tissues should be trained in the proper and approved methods of handling of such specimens.

The HBTRC collects tissue specimens representative of a wide variety of diagnoses from throughout the United States. The HBTRC does not knowingly distribute tissue known to be infectious. The HBTRC, however, does not guarantee that any of the donors of brain specimens were not exposed to or infected by potentially transmissible infectious agents. Ultimately, it is the responsibility of the recipient investigator to insure that proper, safe handling techniques are employed by all laboratory staff in handling postmortem human brain tissue.

HUMAN TISSUE HANDLING RISKS & SAFETY PRECAUTIONS STATEMENT CONTINUED:

PLEASE READ AND SIGN THE FOLLOWING STATEMENT:

I have read the Human Tissue Handling Risks & Safety Precautions Statement, and I understand the potential safety risk in handling human brain tissue and acknowledge these safety precautions and recommendations as essential to my safe handling of brain specimens.

As the Investigator of Record, I accept full responsibility to insure that proper, safe handling techniques are employed in my laboratory when working with postmortem human brain tissue, and I further accept responsibility to train staff in approved and customary safe handling techniques before they work with these tissues.

I understand the HBTRC does not distribute specimens known to have been exposed to or infected with agents such as, but not limited to, HIV (HIV-1, HIV-2), Hepatitis-B, or Creutzfeldt - Jakob disease, and I understand that the HBTRC is unable to guarantee that any of its tissue donors were not exposed or infected with such agents.

Investigator of Record Name: _____
Print Name

Investigator of Record Name: _____
Sign Name

Date: _____

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HUMAN TISSUE SINGLE USER AGREEMENT

PLEASE READ AND SIGN THE FOLLOWING STATEMENT:

As the Investigator of Record, I understand that the HBTRC has disbursed postmortem human brain tissue to me for research purposes only. I acknowledge that this tissue has been disbursed for my expressed use only, that I will exercise a good faith effort to keep control over such tissue, and that I will not distribute any samples or fractions of samples to other investigators without the expressed permission of the HBTRC. I acknowledge that providing any amount of tissue sample to colleagues, other investigators, or other laboratory facilities is specifically prohibited without expressed permission from the HBTRC. I will direct all such requests for tissue inquires to the HBTRC central office.

Investigator of Record Name: _____

Print Name

Investigator of Record Name: _____

Sign Name

Date: _____

HARVARD BRAIN TISSUE RESOURCE CENTER ACKNOWLEDGMENT AGREEMENT

PLEASE READ AND SIGN THE FOLLOWING STATEMENT:

As the Investigator of Record, I agree to provide specific acknowledgment of the Harvard Brain Tissue Resource Center and its Federal grant number in any publication related to the use of this tissue sample. Specific citation of the contribution of the HBTRC will be included in both the Materials and Methods section and the Acknowledgment section of the manuscript. Prior to publication, I will contact the HBTRC central office in order to obtain the current Federal grant number. *I understand that no member of the HBTRC staff may be listed as a co-author on any publication unless there is a substantive scientific contribution above and beyond the provision of tissue specimens. To include a HBTRC staff member as a co-author, formal permission of the HBTRC Director must be petitioned in writing.*

Investigator of Record Name: _____

Print Name

Investigator of Record Name: _____

Sign Name

Date: _____

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POSTMORTEM TISSUE APPLICATION

Funding Source Information Is Required

Please list below the **GRANT SUPPORT** that is funding this research project. Please include federal grant numbers, names of sponsoring foundations or other private support, or identify current collaborations or mentor-trainee affiliations with the collaborations or mentor's grant support listed.

Alternatively, you can provide a copy of the **Other Support** page from the standard NIH grant application.

Grant Number: _____

P.I. Name: _____

Project Title: _____

Budget Period: _____

Grant Number: _____

P.I. Name: _____

Project Title: _____

Budget Period: _____

Grant Number: _____

P.I. Name: _____

Project Title: _____

Budget Period: _____

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Cortical Areas:

- ___ Frontal pole (Brodmann area 10)
- ___ Superior frontal (Brodmann areas 6, 8, 9)
- ___ Inferior frontal (Brodmann areas 11, 12, 44-47)
- ___ Medial frontal (Brodmann areas 10, 46, 9)
- ___ Precentral frontal (Brodmann area 4)
- ___ Cingulate (Brodmann areas 24, 25)

- ___ Temporal pole (Brodmann area 38)
- ___ Superior temporal (Brodmann areas 22, 41/42)
- ___ Middle temporal (Brodmann area 21)
- ___ Inferior temporal (Brodmann areas 20, 36)
- ___ Parahippocampal
- ___ Entorinal

- ___ Parieto-temporal (Brodmann area 39)
- ___ Postcentral parietal (Brodmann areas 3, 1, 2, 5)
- ___ Superior parietal (Brodmann area 7)
- ___ Inferior parietal (Brodmann area 40)

- ___ Occipital (Brodmann area 17)

- ___ Cerebellar cortex
- ___ Dentate nucleus

Subcortical Areas:

- ___ Caudate ___ Nucleus Accumbens ___ Putamen
- ___ Amygdala ___ Globus pallidus, undifferentiated
- ___ Subthalamic nucleus ___ Globus pallidus, lateral
- ___ Hypothalamus ___ Globus pallidus, medial
- ___ Thalamus, undifferentiated ___ Thalamus, lateral nuclei
- ___ Thalamus, medial nuclei ___ Thalamus, pulvinar

- ___ Hippocampus with parahippocampul gyrus ___ Anterior hippocampus with entorinal cortex

Brain Stem:

- ___ Red nucleus ___ Medulla ___ Pons
- ___ Substantia nigra ___ Medulla, inferior olivary nucleus

White Matter:

- ___ Corona radiata ___ Corpus callosum ___ Periventricular

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Alzheimer's disease

Alzheimer's changes

Alzheimer's changes-mild

Alzheimer's changes-moderate

Alzheimer's changes-severe

Amyotrophic lateral sclerosis

Alzheimer's disease, lewy body variant

*Autism

Bipolar depression (manic-depression)

Bipolar disorder-first degree relative

Control

Dementia

Diffuse lewy body disease

Depression, unipolar (endogenous)

Huntington's disease, ungraded

*Huntington's disease, juvenile

*Huntington's disease, at risk

*Huntington's disease, grade 1

*Huntington's disease, grade 2

Huntington's disease, grade 3

Huntington's disease, grade 4

*Rett syndrome

Schizophrenia

Probable schizophrenia

Schizo-affective

Probable schizoaffective

Schizophrenia-first degree relative

Parkinson's disease

Pick's disease

Progressive supranuclear palsy

*Tourette syndrome

- *Restricted Distribution*

CONTRACTUAL AGREEMENT

THE PROPER USE OF POSTMORTEM BRAIN TISSUE DISTRIBUTED BY THE HARVARD BRAIN TISSUE RESOURCE CENTER (HBTRC)

The Harvard Brain Tissue Resource Center (HBTRC) is a federally-funded resource whose mission is to acquire and distribute postmortem brain tissue to the neuroscience community for research applications. It is intended that the tissues we provide to investigators be used to expand our understanding of the human brain and its diseases and to develop new and more effective forms of treatment.

Historically, the HBTRC has primarily provided postmortem brain tissue to investigators receiving research support from the National Institutes of Health, the National Science Foundation and other private organizations. Until recently, these investigators have been exclusively affiliated with non-profits organizations, such as universities, colleges, hospitals and other non-profit research centers. More recently, however, the HBTRC has been receiving requests for tissue from organizations in the commercial sector, i.e. corporations and companies formed for the purpose of marketing new products that can be sold for a profit. The justification for this change in policy is the growing appreciation that "for-profit" companies do make fundamental contributions to our basic understanding of the brain. There has also been an increasing tendency for NIH-funded investigators to also seek patents for their discoveries so that a marketable product might eventually be developed. There is a significant concern within the neuroscience community in general, and the NIH in particular, that scientists using postmortem brain tissue from federally-funded national resources, like the HBTRC, may potentially withhold or otherwise delay, the publication of scientific data for proprietary reasons. Such "data hoarding" could potentially result in significant delays in the progress with which the field of neuroscience is able to devise novel treatment strategies, ones that could potentially increase longevity and improve quality of life. Accordingly, the HBTRC, with the support of the NIH, is requiring that Principle Investigators seeking tissue from the HBTRC sign this contract. In so doing, you will agree to make public scientific results emanating from these tissues in a prompt and timely manner that does not exceed one year from the time of discovery. If the HBTRC has reason to believe that you or other members of your research group have not complied with this agreement, an ad hoc subcommittee of the External Scientific Advisory Board will consider whether it is more likely than not that such a violation of the agreement has transpired. If so, then a range of options will be considered including the immediate suspension of any further tissue distribution to you into the indefinite future, and/or lesser alternative sanctions.

Name

Signature

Date

Title

Organization