



# Brain Bank Bulletin

Issue 4  
Spring  
2005

The PDS Tissue Bank at Imperial aims to help understand what causes Parkinson's and assist in the development of better drug treatments by providing high quality brain tissue to researchers working in the field of Parkinson's and related neurological disorders. The Tissue Bank also aims to enhance the public's awareness of Parkinson's, promote the work of the Tissue Bank and increase the numbers of volunteers who are willing to sign up to the donor scheme. The Tissue Bank also aims to collect the tissue so that it is suitable for all research needs and that it is collected in the most ethical manner.

## European Tissue Banks Working Together

The European Union (EU) has funded a network of excellence projects (Brain Net Europe II) where 19 Tissue Banks across Europe can start to work closer together. This involves the two disease dedicated Tissue Banks at Imperial College, namely the UK Parkinson's Disease Society (PDS) Tissue Bank and the Multiple Sclerosis (MS) Tissue Bank, and 17 other tissue banks that collect tissue from a variety of neurological/neurodegenerative diseases. At the present time it is difficult for Tissue Banks to work together and share tissue etc since all of the Tissue Banks have different tissue collection, processing and storage procedures. The funding is for 5 years and will allow the Tissue Bank to identify "best practice" and harmonise procedures for processes like tissue collection and storage, and will also allow us to update and standardise neuropathological criteria/histological techniques for the identification of different neurological/neurodegenerative diseases. The range of techniques available for researchers is ever changing and it is important that Tissue Banks meet the demands of researchers. There are exciting techniques to examine our genetic makeup (our DNA), the genetic messages (mRNA) that instruct our cells to synthesise protein that are essential for their survival and the proteins themselves. However, at the present time, it is unclear whether such tests can be carried out on all

of our existing tissue stocks across Europe. We need to find the optimum techniques for collection and storage of tissue so that we can preserve the sensitive cellular products that may reveal so much about Parkinson's and other neurodegenerative disorders. The funding by the EU will allow a number of mini projects to be run across Europe to examine these issues. At Imperial College the PDS and MS Tissue Banks will work together to look at the mRNA stability in existing stocks of tissues and examine what are the best techniques for extracting and measuring the quality of mRNA obtained from these tissues. This will identify the most appropriate way of collecting and storing future tissue so that the mRNA can be best preserved for future research. It is hoped that in the future, this project will allow the sharing of tissue between Tissue Banks, particularly tissue from healthy donors that is in very short supply, so that more research can be carried out and on a greater number of subjects. If you want to read more about the Brain Network Europe II you can visit the web site at

<http://www.brainnet-europe.org/>

**Dr David Dexter**  
Scientific Director



## Tissue Bank Manager to Run Marathon

Dr Kirstin Goldring, the Tissue Bank Manager, is joining a team of runners doing the 25th London Marathon in aid of the PDS. If you would like to find how the sponsorship is going or would like to sponsor her please visit the website:

[www.justgiving.com/pdskgol](http://www.justgiving.com/pdskgol)

"Being the manager of the Parkinson's Disease Society Tissue Bank, I know how important it is for the Society to raise money to help find a cure for Parkinson's Disease. Many people agree to donate their brains to

the Tissue Bank, so the least I can do is run a marathon (in pink).

I am going to put a lot of effort in to my training with the aim of doing it in under 5 hours this time. No promises, but I am really going to try and be faster and will put in the work to make it happen." Watch out for the PDS runners on 17th April 2005.

**Dr Kirstin Goldring**



### Inside this issue:

<b>European Tissue Banks Working Together</b>	<b>1</b>
<b>London Marathon</b>	<b>1</b>
<b>Neuropathological Assessment</b>	<b>2</b>
<b>Research News</b>	<b>3</b>
<b>Statistics</b>	<b>3</b>
<b>Contact Information</b>	<b>4</b>
<b>Future Branch Talks</b>	<b>4</b>
<b>Our Team</b>	<b>4</b>

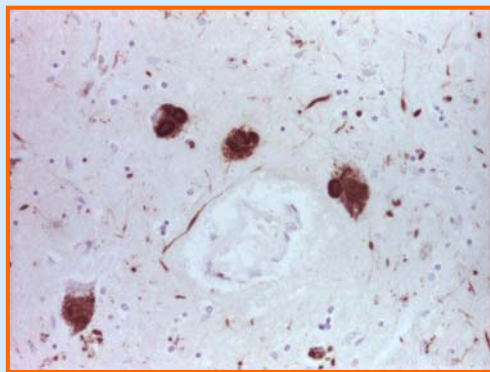
**This year's Tissue Bank Open Day will take place on 17th April 2005 1pm-5pm at Imperial College Charing Cross Campus**



**Parkinson's Disease Society**

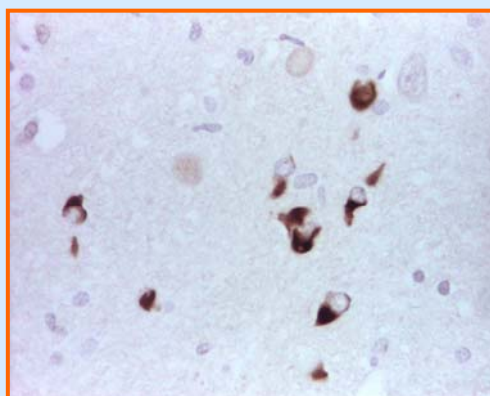
## Neuropathological Assessment of Brains Donated to the Parkinson's Disease Society Tissue Bank

The diagnosis of movement disorders such as idiopathic Parkinson's disease, multiple system atrophy and progressive supranuclear palsy can be suspected on clinical grounds but it is only with neuropathological examination of brains that a definite diagnosis can be established. Overall, pathological assessment is intended to determine the exact nature of the disease and its severity, evaluate preservation of the tissue, identify co-existent pathologies, and support research studies. To do so, brains donated to the Parkinson's Disease Society Tissue Bank (PDSTB) are examined by the three members of the Department of Neuropathology of the Imperial College London who examine gross appearance, take samples and do microscopic studies.



**Substantia nigra from a patient with idiopathic Parkinson's disease contains alpha-synuclein positive Lewy bodies.**

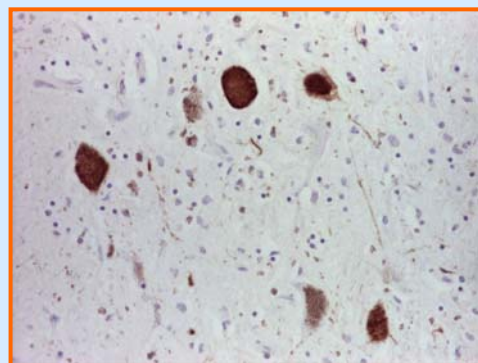
Macroscopic examination of the whole brain is always mandatory in neuropathology. At the PDSTB this is performed when the organ arrives and includes measure of brain weight, evaluation of meningeal coverings, and evaluation of conformation of gyri, midline structures, cerebellum and vascular structures. When possible, the right half of the brain is frozen and stored and the left half is put in a solution called formalin that preserves the tissue by blocking all processes of degradation. Fixation takes at least 4 weeks and, when it is complete brains are examined again, cut and sampled. Extensive sampling is performed according to a standardised protocol that includes eighteen different regions. Thorough sampling is of paramount importance in the diagnostic procedure because although the characteristic feature of PD is considerable loss of pigmented nerve cells of substantia nigra, equally important is the observation of other structures affected in movement disorders and in other neurodegenerative diseases.



**In patients with multiple system atrophy, alpha-synuclein inclusions are mainly found in oligodendrocytes.**

Microscopic studies come after macroscopic examination.

Over the last year, neuropathologists and technical staff of the PDSTB have developed a protocol for diagnosing cases. Histological sections are cut from each of the regions sampled and then stained with a routine method for histopathology named haematoxylin-eosin. Haematoxylin-eosin stained sections are reviewed and discussed by neuropathologists and technical staff during weekly meetings in order to look at preservation of the tissue and quality of samples and sections. This step represents a sort of screening because haematoxylin-eosin does not allow recognition of all pathological changes present in neurodegenerative diseases and has to be followed by immunohistochemical reactions. For this, seven selected brain regions are investigated for the presence proteins that may accumulate in movement disorders and other neurodegenerative disorders. These are alpha-synuclein, which is abnormally accumulated in Parkinson's disease, dementia with Lewy bodies and multiple system atrophy, phosphorylated tau characteristically seen in Alzheimer's disease and progressive supranuclear palsy and beta-amyloid which is pathologically accumulated in Alzheimer's disease. In general, microscopic assessment is meant to determine which of the brain structures is involved, the type and amount of protein accumulated and the cell type affected.



**Typical tau-positive globoid tangles in dopaminergic neurons in a patient with progressive supranuclear palsy.**

At the PDSTB, neuropathological diagnosis is always the result of a close cooperation between neuropathologists and neurologists. The final report is issued only after the cases are reviewed by all the three of the neuropathology team and neuropathological findings subsequently discussed with the referring neurologist. In some instances, additional histochemical and immunohistochemical stains have to be requested, particularly if there are signs or symptoms in the clinical history that require further pathological investigation.

This diagnostic approach to brain donated to the PDSTB takes time but we believe that it guarantees a careful assessment and is therefore of help to support research studies.

**Dr Federico Roncaroli**  
Clinical Neuropathologist





## Research News from Ellen Sidransky

Researchers from the National Institute of Mental Health and the National Human Genome Research Institute in a team led by Ellen Sidransky M.D., have discovered an association between the degenerative neurological disorder, Parkinson disease, and Gaucher disease, a recessively inherited metabolic disorder. Gaucher disease is caused by mutations in the gene for the enzyme glucocerebrosidase and results in the accumulation of harmful quantities of a substance, glucocerebroside, in patients' cells.

While mutations in the glucocerebrosidase gene (GBA) are rare in the general population, their study, published in the January 2004 issue of *Molecular Genetics and Metabolism*, showed that GBA mutations were found in brain samples of subjects with Parkinson disease more frequently than expected. Five American repositories supplied autopsy brain samples from 57 individuals with pathologically confirmed parkinsonism and from 44 controls, the GBA gene was investigated in these samples. Alterations were identified in 14% of the samples, more frequently than mutations in other known Parkinson disease genes. These findings suggested that carrying a GBA mutation may be a risk factor for the development of parkinsonism.

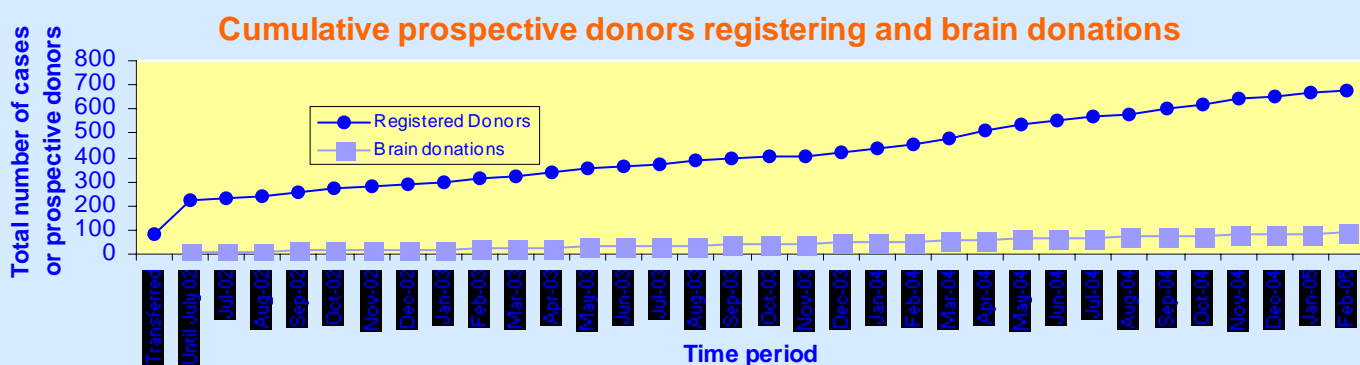
To expand this study, the UK PDS Tissue Bank contributed brain samples from 26 British subjects diagnosed with Parkinson disease between age 42-78 years. Two subjects (8%) carried GBA mutations. Additional samples from this tissue bank are being screened as they become available.

The results obtained from brain samples have recently been substantiated in blood samples from three different patient groups. A group in Israel screened 100 Ashkenazi Jewish pa-

tients from a Parkinson disease clinic in Northern Israel and identified GBA mutations in 31%. Two other groups, from New York and Toronto, found GBA mutations in their patients with Parkinson disease at a rate of 11% and 5.6%, respectively. A fourth study documented that in several families of patients with Gaucher disease, there were more close relatives suffering from parkinsonism than expected. It is important to note, however, that most Gaucher patients and carriers do not develop Parkinson disease, and mutations in glucocerebrosidase may be one of many risk factors leading to parkinsonism.

The identification of GBA mutations in patients with Parkinson disease from different countries supports the theory of a role for glucocerebrosidase in the development of parkinsonism. Having access to brain bank samples is incredibly important, because detailed pathology studies of autopsy samples can confirm and clarify clinical diagnoses, and allow more accurate comparisons between different patient populations. The contributions of donors to brain banks in Britain and other countries will help develop a better understanding of the connection between Gaucher disease and parkinsonism.

**Dr Ellen Sidransky**  
**Chief, Section on Molecular**  
**Neurogenetics,**  
**National Institutes of Health USA.**



The graph above shows the progression of the Tissue Bank with respect to donor registration and brain donations.

### Change of Address/ Comments Form

Date:  Name of Donor:  Donor No:

Old Address:

New Address:

Post Code:

Date of address change:

Contact No:



### Contact Information

**UK Parkinson's Disease Society  
Tissue Bank at Imperial College**  
 Division of Neuroscience and  
 Psychological Medicine  
 Imperial College London  
 Faculty of Medicine, Charing Cross  
 Campus, Fulham Palace Road,  
 London W6 8RF  
**Phone: +44 (0)20 8383 4917**  
**Fax: +44 (0)20 8383 4918**  
**Emergency Bleep :07659104537**  
**Email: [pdbank@imperial.ac.uk](mailto:pdbank@imperial.ac.uk)**  
**Website:**  
[www.parkinsonstissuebank.imperial.ac.uk](http://www.parkinsonstissuebank.imperial.ac.uk)

**The Parkinson's Disease Society**  
**215 Vauxhall Bridge Road**  
**London**  
**SW1V 1EJ**  
**United Kingdom**  
**Phone: +44 (0)20 7931 8080**  
**Fax: +44 (0)20 7233 9908**  
 Registered Charity No. 258197. A Company  
 Limited By Guarantee. Registered No.  
 948776 (London)

Clockwise from top left: Dr David Dexter, Scientific Director; Dr Kirstin Goldring, Tissue Bank Manager; Helen Cairns, Research Assistant; Louisa Djerbib, Research Technician; Laura McKay, Tissue Bank Secretary; Professor Richard Reynolds, Technical Advisor; Dr Ronald Pearce, Consultant Neurologist; Neuropathology Team; Dr Stephen Gentleman, Dr Federico Roncaroli and Professor Manuel Graeber

## Future Branch Talks

- 7th April 2005, Sutton, Kingston & Epsom 7:30pm
- 9th April 2005, YAPP&Rs AGM Rugby
- 11th April 2005, Open Day
- 14th April 2005, Bexley & Dartford
- 26th April 2005, Hillingdon 2-4pm
- 5th May 2005, Lincoln 2:30pm
- 14th May 2005, Spring AGM
- 15th May 2005, Hull 2-4pm
- 18th May 2005, York 8-9pm
- 1st June 2005, Derbyshire
- 21st June 2005, Farnborough 7:30pm
- 9th July 2005, North West Somerset 10.30am
- 12th July 2005, Minehead 2:30pm
- 20th July 2005, Southport 2pm
- 25th August 2005, Birmingham Support Group
- 20th September 2005, Barnsley 2pm
- 3rd October 2005, West Midlands YAPP&Rs 7:30pm
- 19th October 2005, Stockport 2pm
- 11th November 2005, Canterbury
- 15th November 2005, Eastbourne 2-4pm
- 21st November 2005, Cirencester

Please contact us if you require further details.

### Our Team



Please tear this section off and return to us free of charge with your comments or change of address.

Comments/ Suggestions/ Questions:

Please detach slip and return to us in an envelope free of charge using the enclosed label.