Parkinson's UK Brain Bank

From Brain to Breakthrough

Dr George Gveric
Manager

19 October 2018

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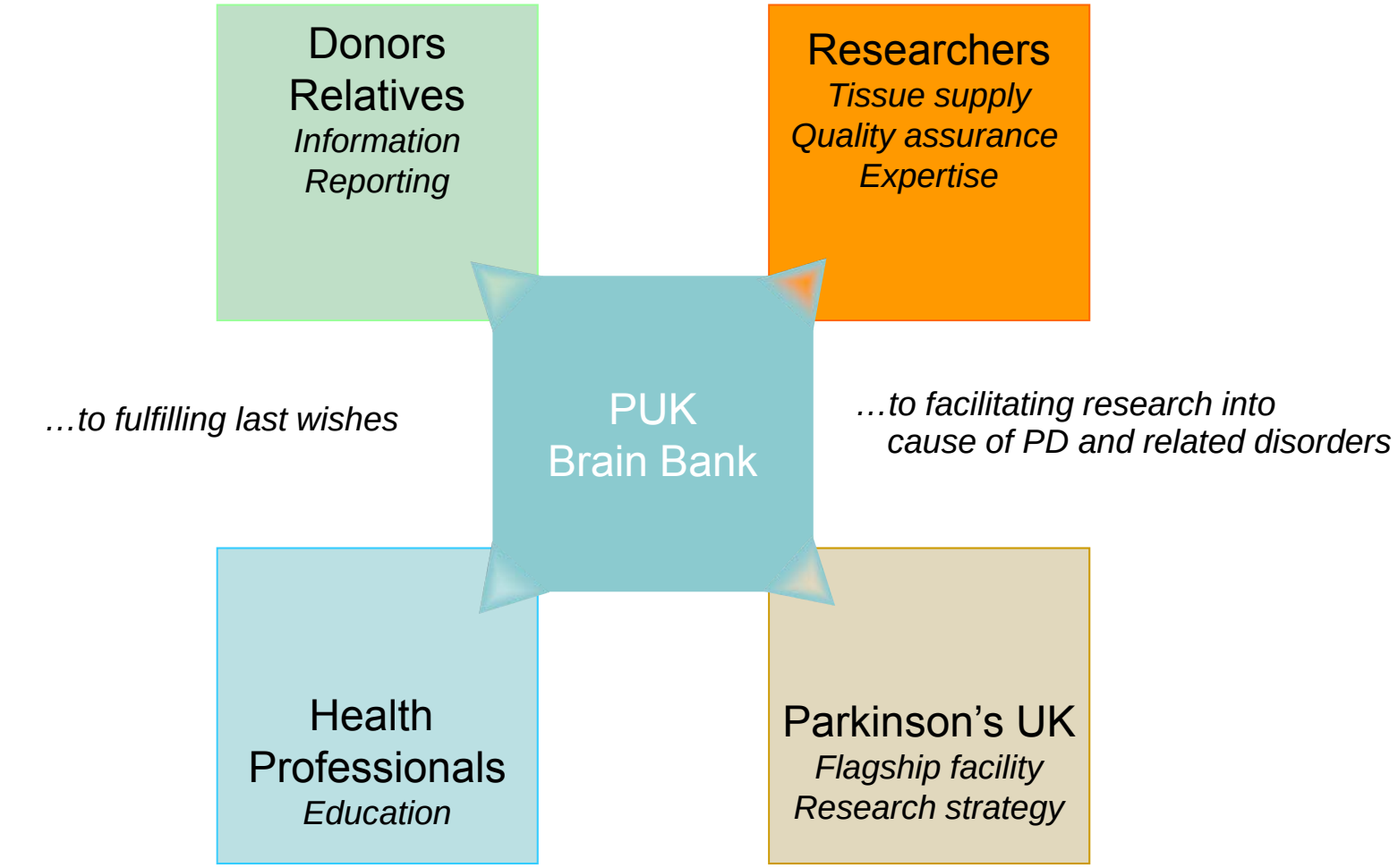
Coordinated approach…



…to fulfilling last wishes

…to facilitating research into cause of PD and related disorders

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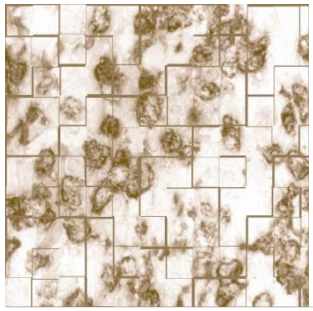

Significance of tissue banking

New scientific discipline – Biobanking

Supporting science
- In vitro studies (in a dish)
- In vivo studies (cells and animals)
- In silico studies (computers)

Translational research
Target validation
- Translating results from other systems into human system
- Finding valid targets for disease in humans

Feedback
- Providing information for relatives and health professionals

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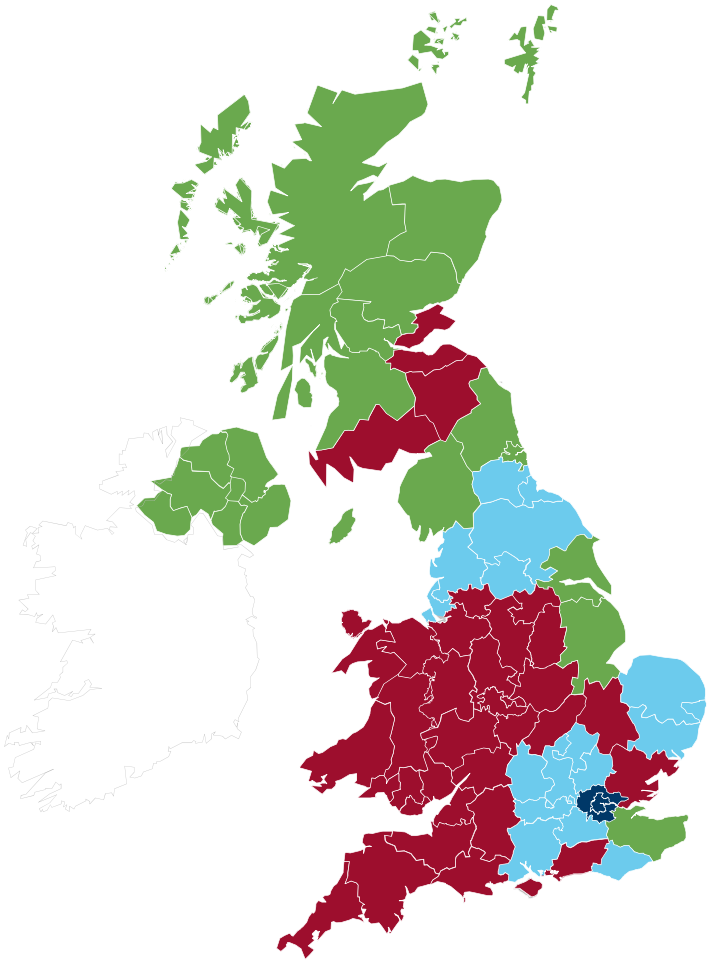
Donor scheme



UK-wide donor scheme
Community-based / no bias

Interacting with major UK PD cohorts

- Oxford Discovery
- ProBand
- PINE

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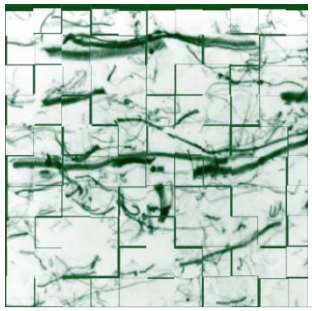

Donor information pack

Who can donate tissue?

Anyone!

- Parkinson's Disease
- Parkinson's plus movement disorders:
  - Multiple System Atrophy (MSA)
  - Progressive Supranuclear Palsy (PSP)
- Stroke, tumours, CJD, systemic infections
- Controls – very important!!!

Information pack contains:

- Information booklet
- Consent form
- Agreement of the next of kin
- Health questionnaire
- Latest newsletter
- *Freepost envelope*

"DONATION OF YOUR BRAIN IS ONE OF THE MOST IMPORTANT LEGACIES YOU CAN MAKE TO THE ADVANCEMENT OF RESEARCH INTO PARKINSON'S DISEASE!"

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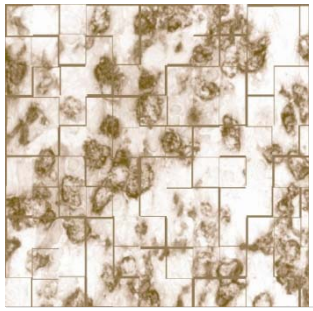

Tissue retrieval

Death of registered donor

Tissue bank informed

07 659 132 045
(24h / 365 days)

Coordinators make all further arrangements

- * Death certificate
- Administration
- * Mortuary arrangements
- Transport
- **Tissue collection**

The Tissue Bank is organised as a transplant unit and is open **24h a day** every day of the year

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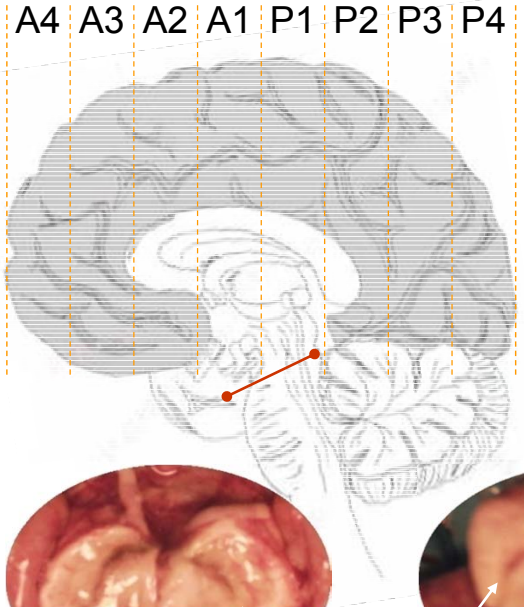
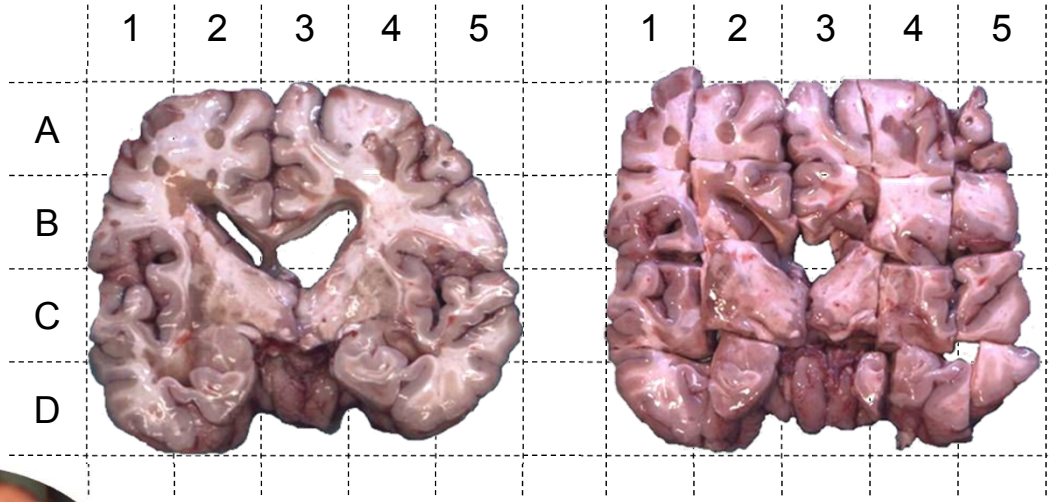
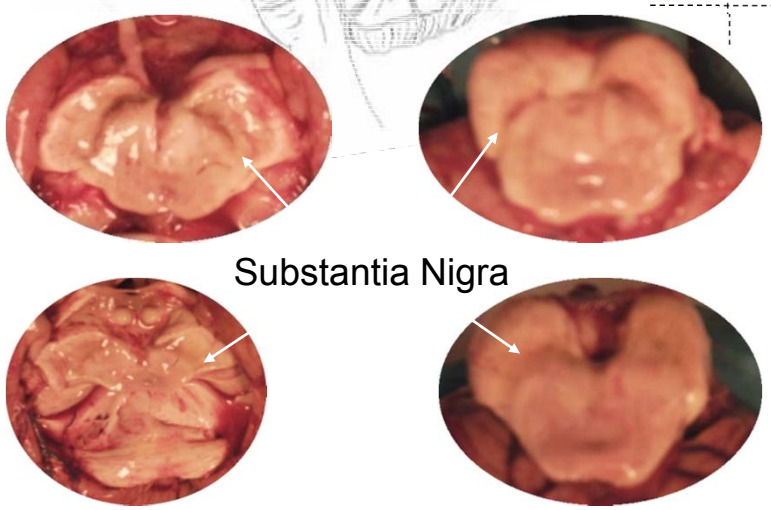
Tissue preparation and storage







Substantia Nigra

Storage

- Coding system (linked anonymisation)
- Air-tight containers
- Secure freezer banks with controlled access

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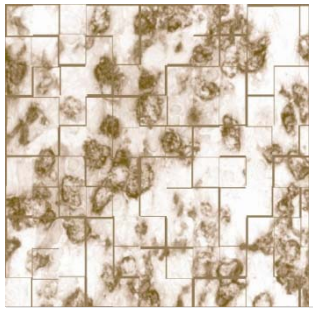


Tissue preparation and storage

Frozen tissue

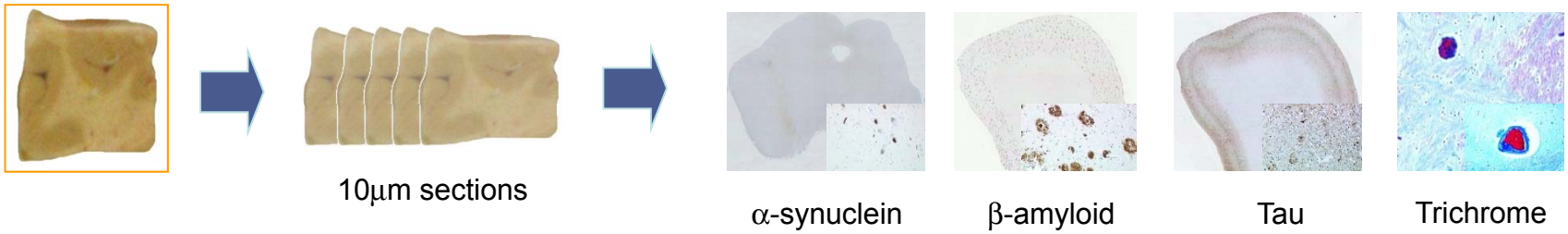
- PM time <24h
- High quality tissue
- Life-like
- Can be used in any experimental setup even for isolation of live cells
- Important for “omics” studies
    - Genomics
    - Proteomics

Fixed tissue

- PM time 24-48h
- Archival collection (easy storage)
- Preferred for pathological and imaging studies

Screening and classification

"Looking at post-mortem brain tissue is like looking at the scene of a crime.
You are trying to gather evidence to find out what has happened!"



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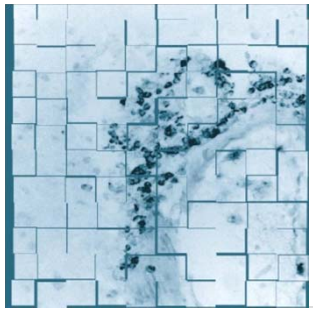

Screening and classification

Clinical diagnosis

- From medical records

- Idiopathic PD
- Vascular PD
- DLB
- MSA
- PSP
- Other ND conditions

Pre- and post-mortem variables

- Agonal state and hypoxia
- Warm ischaemic time
- Cold ischaemic time
- Tissue pH

Neuropathological diagnosis

- Confirmation of diagnosis
  - 85% of cases
- Braak staging
  - Synuclein (score 1-6)
  - Tau (score 1-6)

Braak I – II	early PD/incidental PD pre-symptomatic
Braak III – IV	established PD / motor phase
Braak V – VI	late PD / dementia

Alzheimer's and other confounding pathology

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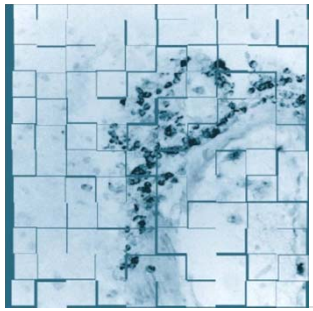
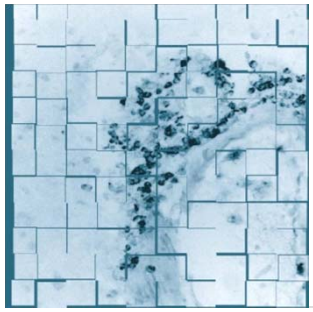


The importance of pathology!

Female, age of onset 76y, disease duration 9y, COD – chest infection, PD
Presentation: Micrographia, mild gait impairment, occasional tremor
Clinical diagnosis: Tremor-dominant Parkinson's disease,
with prominent fatigue/low energy levels
NP diagnosis: Parkinson's Disease (LBDN, B6), Alzheimer's Disease B2

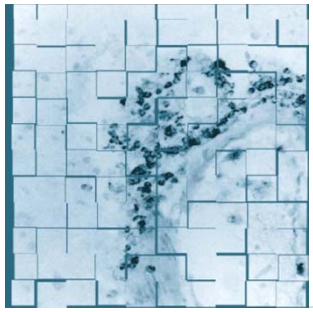
Male, age of onset 73y, disease duration 9y, COD – end stage PD
Presentation: Memory disturbance and problems with balance and walking,
postural tremor on L side
Clinical diagnosis: Idiopathic Lewy Body Disease. Motor symptoms
(Akinetic-rigid / Postural instability, Gait Difficulty-predominant) precede
dementia by several years, PDD.
NP diagnosis: Alzheimer's Disease B6, Parkinson's Disease (LBDBS, B3) – Mixed Dementia



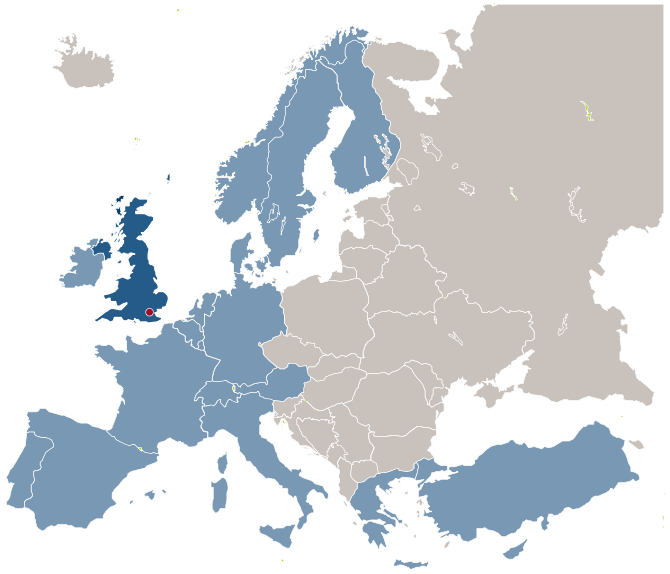
The importance of pathology!

Female, age of onset 71y, disease duration 9y, COD – unknown
Presentation: Tremor in left hand
Clinical diagnosis: Idiopathic Parkinson's Disease
NP diagnosis: Alzheimer's Disease B1 – normal control!

Male, age of onset 64y, disease duration 3y, COD – PD
Presentation: Tremor in the left hand
Clinical diagnosis: Lewy Bodies Dementia.
NP diagnosis: Creutzfeld Jacobs Disease, Alzheimer's Disease B2



Supporting Research



- Tissue Bank has a world-wide exposure
- Since 2002 we were contacted by over 500 researchers from North America to Far East asking us to supply tissue for their projects

- Understand how and why cell death occurs in PD
  - Develop better treatments for Parkinson's
- Predict and identify possible susceptibility to PD
  - Disease prevention

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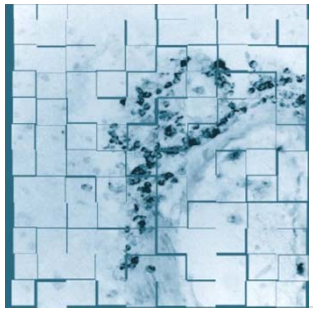
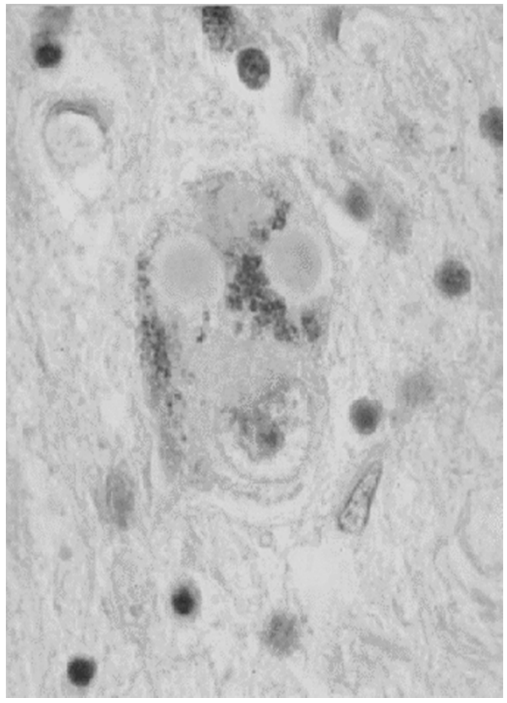


Using tissue for research

More than 400 projects supported UK and worldwide



- Understand how and why cell death occurs in PD
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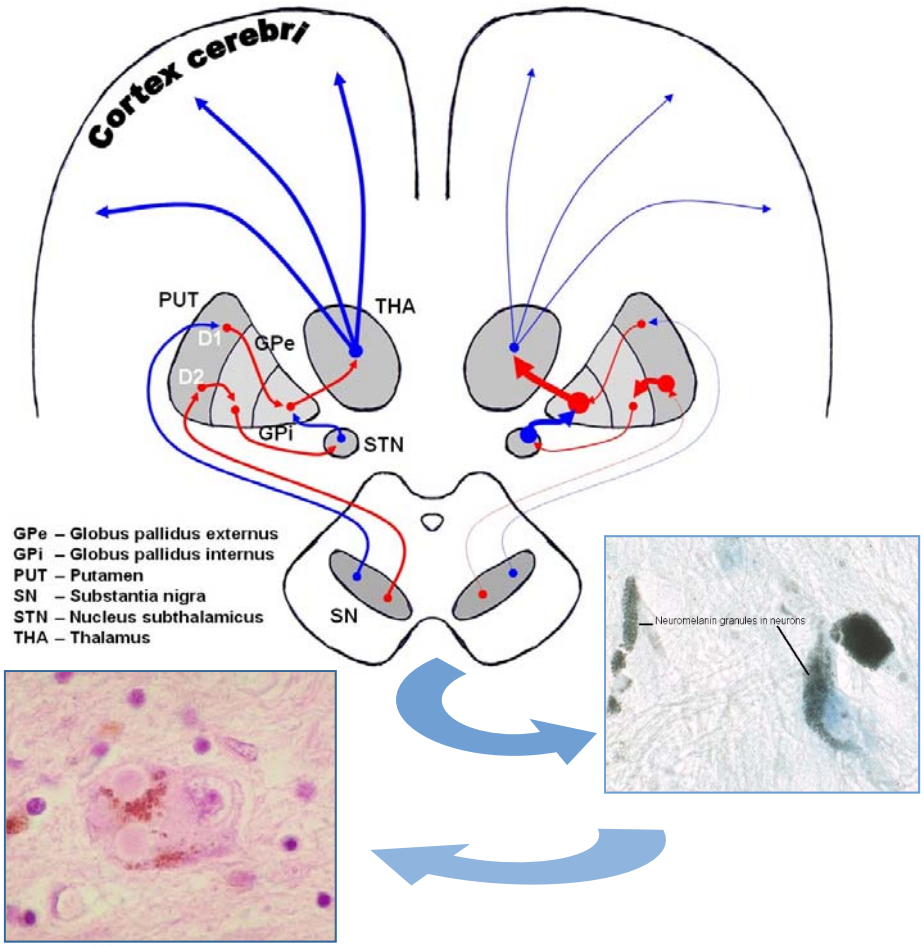
Development of a lesions



Greatly reduced activity of pigmented dopamine-secreting (dopaminergic) cells in the substantia nigra

Inhibition of the direct pathway which facilitates movement and excitation of the indirect pathway which inhibits movement

Abnormal accumulation of the protein alpha-synuclein bound to ubiquitin (Lewy bodies)

Accumulation of iron, calcium and inhibition of neuromelanin

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Mechanisms of neuronal death

- Neurotoxic components (free radicals, Fe, environmental toxins)
- A role of Lewy bodies
- Deficiency of the bodies defence systems such as antioxidants
- The role of inflammation
- Braak staging (spreading of damage)

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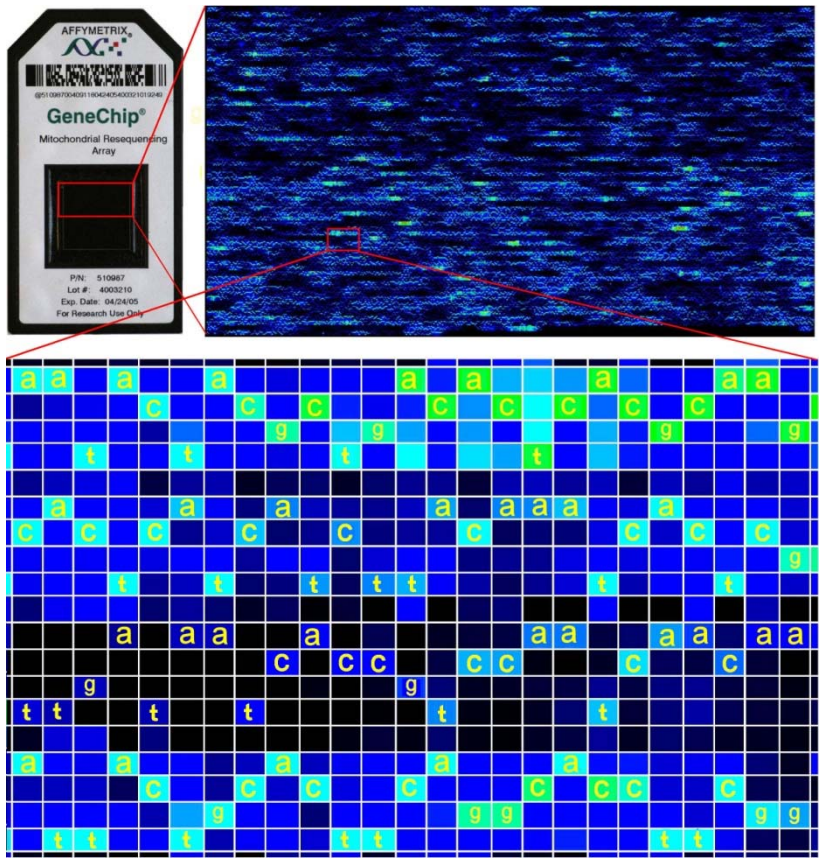
Gene expression analysis



- Thousands genes to look at!
- Gene expression profiling provides valuable insight into the role of differential gene expression in normal biological and disease processes.
- Now identified genes that are either up or down regulated looking at their expression at the cellular level i.e. does it occur in neurones, glia etc…

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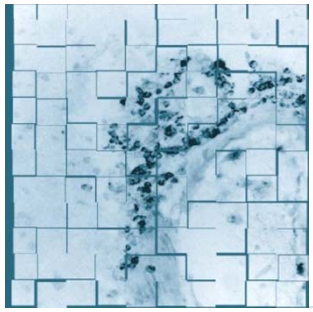
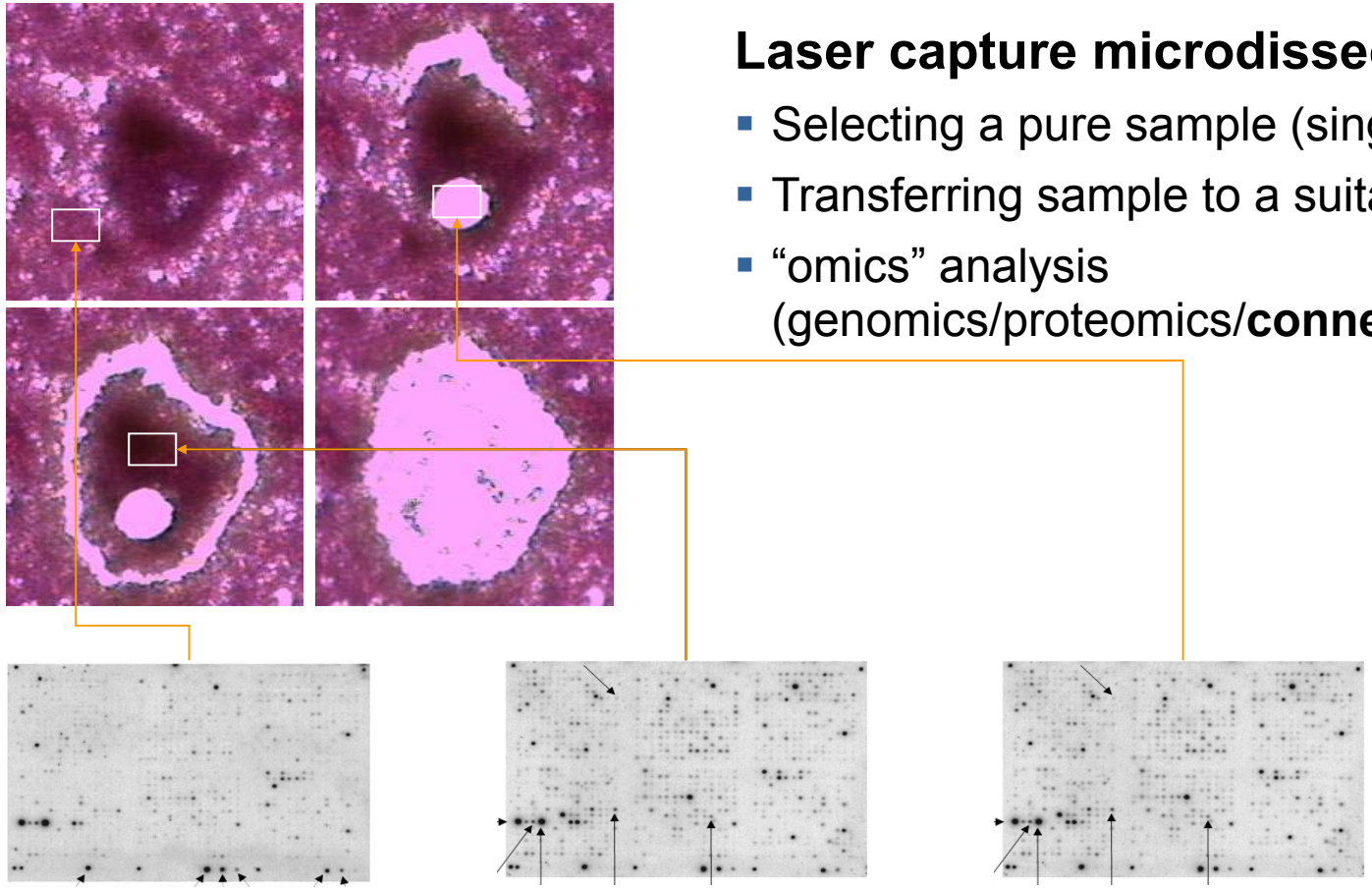


Repairing damage



Laser capture microdissection

- Selecting a pure sample (single cell)
- Transferring sample to a suitable medium
- “omics” analysis (genomics/proteomics/**connectomics**)

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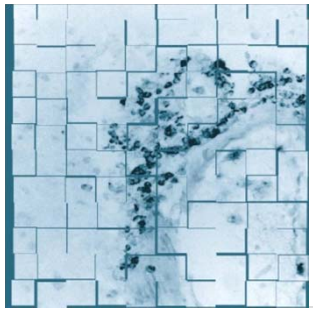

How can you help…

Tissue Bank needs more donors

- to represent at least 10% of the UK PD population (~120,000)
- to include all types of PD and related disorders (PSP, MSA)
- to identify potentially interesting genetic cases
- to increase number of donation

Demographic/epidemiological data and surveys

- tissue bank is not only about death
- working with registered donors

Parkinson's disease samples

- blood/saliva/skin samples/**DNA**/biomarkers
- **clinical data**

Resulting in publications

- through collaboration with tissue bank researchers and other scientists

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Tissue Bank Team

Directors

Professor Richard Reynolds
Director (MS research)

Professor Steve Gentleman
Director (PD research)

Management

Dr George Gveric
Manager
Tel. 020 7594 7204

Mr Ville Pitkaaho
Research Nurse
Tel. 020 7594 8902

Mrs Sue Fordham
Administrator
Tel. 020 7594 9734

Neuropathologists

Dr Federico Roncaroli

Prof. Steve Gentleman

Dr Clara Limbaeck

Technical support

Louisa McGuinness

Ines Ralha

Radhika Anand

Nadira Querido

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Visit us!

Brain Bank visits

An excellent opportunity for all those interested in inner workings of a tissue bank or Parkinson's research in general to find out more from those actually working with human tissue

- Starts 10 a.m.
- Short presentation by the Tissue Bank Manager
- Time for questions/discussion
- Tour of the Tissue Bank
- Lasting approximately 1h 30min.

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Parkinson's Disease Tissue Bank

A Vital Gift

Dr. George Gveric
Manager

10 September 2018

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