Phenome Hub

1.0 Overview

The Phenome Hub comprises two parts, a clinical part and the biobank, which complement each other.

Both parts complement each other in that the neuropathological examination of the brains of deceased patients with neurodegenerative diseases is an essential feedback for the treating physicians. This knowledge is not only important for relatives of the individual patient, but ultimately also flows into clinical studies. On the other hand, clinically and neuropathologically characterized brains represent an important module in translational research.
1.1 Organisation

PHENOME Hub (Clinical Part: cohorts with deep phenotyping)

Location and Coordinators:

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PHENOME Hub (Part: Biobank/human brain tissue)

Location and Coordinators of the Neurobiobank Munich:

Zentrum für Neuropathologie und Prionforschung (LMU), Feodor-Lynen-Str. 23, 81377 München:

https://www.neuropathologie.med.uni-muenchen.de/neurobiobank_muenchen/index.html

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1.2 Clinical Part: cohorts with deep phenotyping & imaging

Objective

The principal function of the Phenome Hub is to foster translational research within the SyNergy cluster.

Key services represent:

- facilitation of the conduction of on-going cohort studies (see below)
- counsel and support
  - For clinicians: in setting up novel translational research studies (read out, power calculation/group size, feasibility/recruitment estimations, application process)
  - For basic science: in setting up translational projects (GCP, access to biomaterial, access to data, data protection, application processes for ethics and authorities approvals)
1.2.1 Ongoing cohort studies

*Alzheimer’s disease:*

**Alzheimer-21:** Down Syndrome - local, longitudinal.

Due to their genetic condition with includes a triplication of the APP gene (coded on chromosome 21), adults with Down Syndrome (DS) are destined to develop AD. Therefore we set up and run a national longitudinal observational study with individuals with DS that is part of a joint European initiative. Longitudinal assessments include clinical and cognitive testing, brain imaging, and biological fluid collection (blood, cerebrospinal fluid).

**ActiGliA**

ActiGliA: AD and CBS - local, longitudinal

This longitudinal Munich single site study investigates the complex interactions between neuroinflammation, connectivity and amyloid-β across the entire clinical spectrum of Alzheimer disease (AD) in a prospective cohort of study participants with AD and participants with corticobasal syndrome (CBS). The participants receive two assessments within 18 months including positron emission tomography (PET), magnetic resonance imaging (MRI), electroencephalography (EEG), cerebrospinal fluid/blood biomarkers and genetics.
DELCODE - early stages of AD - national, longitudinal

Over a period of several years, the DELCODE study focuses on participants in early stages of Alzheimer disease, along with various risk groups. The research is aimed at the development of procedures for characterizing early stages of the disease, at improving prediction of the course of the disease and at identifying new markers for early diagnosis of Alzheimer’s-related dementia. The examinations include detailed clinical and neuropsychological examination, blood and MRI as well as optional CSF.

DIAN - genetic AD - global, longitudinal

The Dominantly Inherited Alzheimer Network (DIAN) Observational Study is a global longitudinal study to monitor changes in individuals who carry one of the gene mutations (Presenilin1, Presenilin2 or APP) known to cause dominantly inherited Alzheimer’s disease. Longitudinal assessments include clinical and cognitive testing, brain imaging and biological fluid collection (blood, cerebrospinal fluid).
**Frontotemporal Dementia (FTD):**

**DESCRIBE-FTD – all forms of FTD - national, longitudinal**

The aim of the DESCRIBE-FTD longitudinal German (DZNE) study is to describe in detail the course of FTD in its various clinical manifestations, to gain a better understanding of the underlying pathology and to identify parameters that allow diagnosis and prediction of the course of the disease. This includes medical history, medication taken, clinical-neurological and neuropsychological assessments as well as genetic testing. Blood, urine and CSF sampling can be done upon clinical indication as well as MRI and PET imaging.

**GENFI – genetic FTD – European, longitudinal**

The aim of the longitudinal European study is to understand more about genetic FTD, particularly in those who have mutations in the progranulin (GRN), microtubule-associated protein tau (MAPT) and chromosome 9 open reading frame 72 (C9ORF72) genes. GENFI investigates both people who have developed symptoms and also people who have a risk of developing symptoms in the future because they carry an abnormal genetic mutation. Assessments and sapling including clinical, neuropsychological and MRI data as well as blood and CSF sampling. The key objectives of GENFI are therefore to develop markers which help to identify the disease at its earliest stage as well as markers that allow the progression of the disease to be tracked.
**Parkinson/Progressive Supranuclear Palsy (PSP):**

**DESCRIBE-PSP** – all forms of PSP - national, longitudinal

This study is a longitudinal, multicenter German (DZNE) observational study. Included are patients with suspected PSP. Patients are examined at various points in time (in 12-monthly intervals) during personal visits with a focus on the development of disease symptoms. In addition, biomaterials and MRIs are being investigated in order to monitor the course of the disease.

**DESCRIBE-PD** – Parkinson's disease - national, longitudinal

This study aims to study patients with Parkinsonian syndromes (PD) with a focus on genetic Parkinson’s Disease (PD) variants and another focus on multiple system atrophy (MSA). Assessments are largely similar to DESCRIBE-PSP.

**1.3 Biobank/human brain tissue**

**Objective**

The phenome hub (biobank) supports SyNergy projects that require human brain tissue from clinical and neuropathological deeply phenotyped patients with various neurodegenerative diseases (mainly proteinopathies) and controls. This brain tissue has been collected for more than 20 years in the Neurobiobank Munich (NBM; www.neurobiobank.org) and can draw on a large pool of tissue samples. Tissue samples are allocated to the scientists in accordance with the guidelines laid down in the rules of procedure together with the Scientific Advisory Board of the brainbank (tissue request procedure see below).
The support of the SyNergy Phenomen Hub to Tandems by NBM researchers takes place in a number of ways:

- comprehensive neuropathological advice to scientists in project planning, in order to achieve the intended scientific goals with the available tissue
- help to write the tissue request for the NBM
- obtaining the approval by the ethics committee
- preparing the paraffin sections or frozen samples as required
- neuropathological characterization of tissue relevant for a certain scientific questions
- establishing technics for special purposes (e.g. staining methods)
- histological evaluations and data analysis in close collaborations

1.3.1 Technical portfolio

Help in establishing techniques on fresh or fixed human brain tissue for special purposes for example:

- paraffin embedding and embedding for special purposes (EM, tissue clearing)
- thick formalin-fixed floating sections, paraffin sections, frozen tissue sections
- preparations for laser capture microdissection
- extraction of neuronal nuclei for FACS and single cell transcriptomics
- isolation of certain cells (such as microglia, astrocytes and endothelial cells)
- isolation of cell compartments (nuclei, mitochondria, synaptosomes)
- isolation of aggregated proteins (e.g. tau, alpha-synuclein) from frozen brain tissue
- immunohistochemistry on human brain tissue sections
- quantification of specific structures on tissue sections (stereology, Imaris)
1.3.2 Tissue request procedure

submit a written tissue request &
a valid ethics vote for your project
(tissue request form see below “download”)

to the NBM-coordinator feedback (takes 3-4 weeks)

The tissue request will first be reviewed in-house

We will send the final version of the tissue request
to the control committee of the NBM (feedback takes 2 weeks)

after approval by the control committee the tissue will be handed over

The NBM charges an expense allowance for the provision of tissue. The amount depends on the amount of tissue requested as well as the anatomical region and is used exclusively to cover the costs incurred with the tissue collection.

1.4 Downloads

Tissue request Form
Please contact the phenome hub staff for project requests or further questions:

Clinical part: Johannes Levin (johannes.levin@med.uni-muenchen.de)

Biobank part: Otto Windl (otto.windl@med.uni-muenchen.de)
1.5 Publications


Mori K et al.…. Edbauer D, Haass C Reduced hnRNPA3 increases C9orf72 repeat RNA levels and dipeptide-repeat protein deposition. EMBO Rep 17(9):1314-25, 2016


Mori K et al.…. Edbauer D Bidirectional transcripts of the expanded C9orf72 hexanucleotide repeat are translated into aggregating dipeptide repeat proteins. Acta Neuropathol 126(6):881-93, 2013