OPEN JOURNAL OF BIORESOURCES

Witt, S et al 2016 Biobank of Psychiatric Diseases Mannheim – BioPsy. *Open Journal of Bioresources,* 3: e2, DOI: http://dx.doi.org/10.5334/ojb.18

BIORESOURCE PAPER

Biobank of Psychiatric Diseases Mannheim – BioPsy

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High quality biomaterial from patients and controls is a core prerequisite for research into the biological causes of mental disorder. BioPsy is the biobank of the Department of Genetic Epidemiology in Psychiatry at the Central Institute of Mental Health in Mannheim, Germany, and one of the largest psychiatric disorder biobanks worldwide. Here, ongoing collection is in progress for blood, DNA, mRNA, plasma, serum, saliva, urine, hair, and other biomaterials. Reuse of samples is permitted in a collaboration-based context. BioPsy operates according to German and European quality and data privacy standards.

Keywords: Biobank; psychiatric disorder; genetics
Funding statement: The biobank currently receives third party-funding from the German Federal Ministry of Education and Research, the German Research Association, and the German State of Baden-Wuerttemberg. The biobank is also supported by the institutional funding of the Department of Genetic Epidemiology.

(1) Bioresource Overview

Project description

The Department of Genetic Epidemiology in Psychiatry explores the genetic basis of mental disorders occurring across the entire lifespan. The aims of this research are to: (i) make decisive contributions to understanding the underlying molecular-pathogenic mechanisms; (ii) facilitate the development of a biologically-guided classification system; and (iii) enhance precision medicine within the field of mental health. The Department studies a broad range of mental disorders, such as bipolar disorder, major depression, schizophrenia, the autism spectrum disorders, attention deficit hyperactivity disorder, personality disorders, and addiction disorders, as well as co-morbid somatic conditions. Other research foci include investigation of the genetic basis of response to therapy (pharmacogenetics), and analysis of the role of gene-environment and gene-gene interactions in the development of mental disorder. This work involves the decoding of the genetic basis of complex endophenotypes, such as personality dimensions and correlates of neuronal plasticity. In terms of its contribution to public health, the Department is engaged in an ongoing process of attempting to develop prevention strategies for mental disorders on the basis of biological parameters.

A core prerequisite for research into the biological causes of mental disorders is the availability of appropriate biomaterials. The Department has a state-of-the-art Molecular Genetic Laboratory, and this is responsible for the biobanking of blood, DNA, mRNA, plasma, serum, and other biomaterials. The facility operates a laboratory information management system (LIMS); a controlled automated liquid-handling system; and an automated DNA/RNA extraction system. All samples are processed according to state-of-the art biobanking guidelines and standard procedures, and are stored in the Department's Biobank of Psychiatric Diseases (BioPsy, https://www.zi-mannheim.de/biobank). **Figure 1** provides an overview of the biobank workflow. Since its establishment, the BioPsy bioresource has been used by the Dept. of Genetic Epidemiology in Psychiatry, by diverse collaboration partner and in large consortia, and has contributed to more than 280 peer reviewed publications.

This biobank contains biomaterials from all patients, relatives, and controls recruited by the Department and its collaboration partners, and expansion of the collection is ongoing.

Classification (1)

Human psychiatric diseases.

Species

Human.

Classification (2)

Biological samples and associated data.

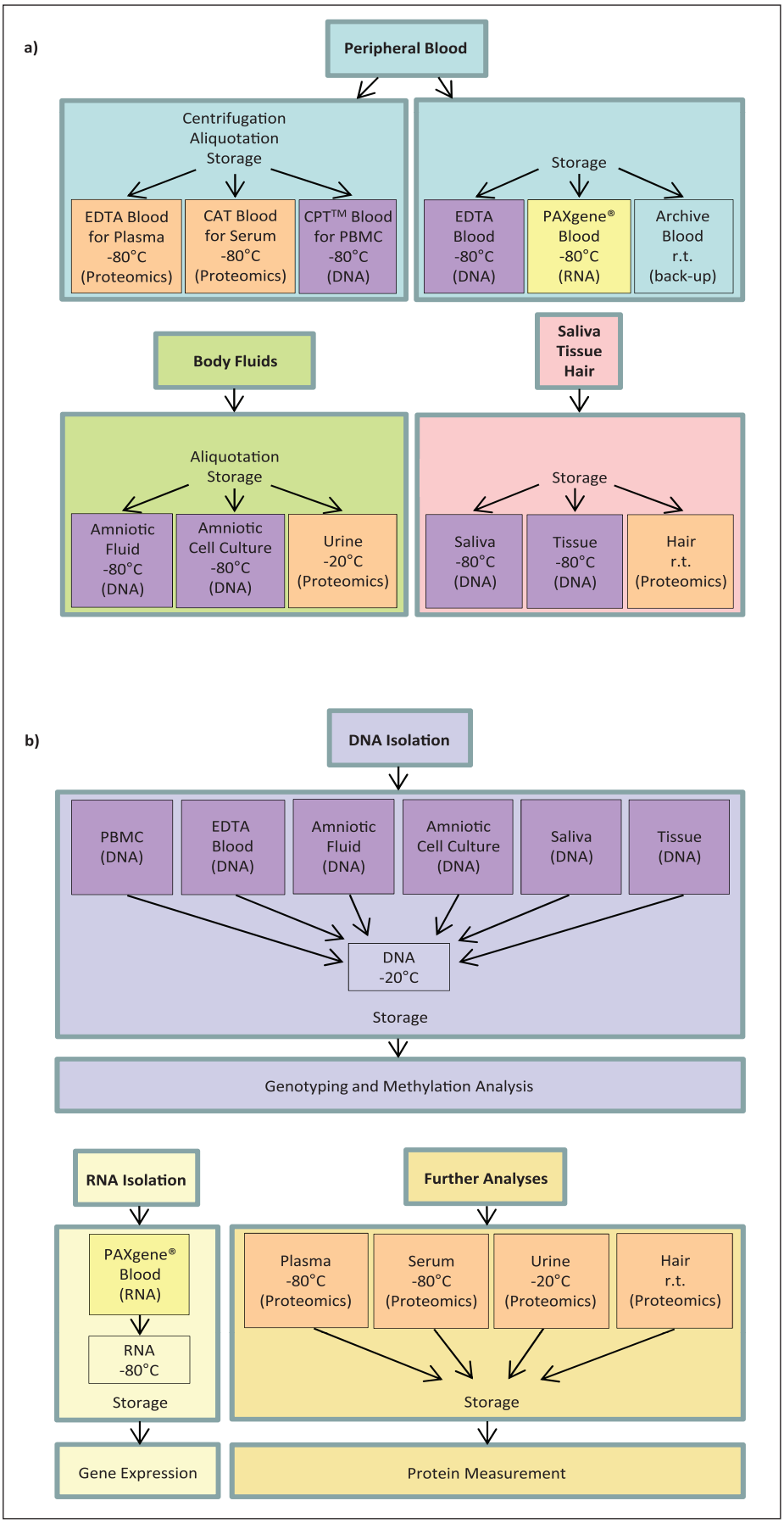

Figure 1: Workflow overview of the Biobank of Psychiatric Diseases Mannheim – BioPsy. a) Pre-analysis of BioPsy workflow. b) Processing and analysis of BioPsy workflow (Abbreviations: EDTA = Ethylenediaminetetraacetic acid; CAT = Clot Activator Tube; CPT™ = Cell Preparation Tube; PBMC = peripheral blood mononuclear cell; DNA = Deoxyribonucleic acid; RNA = Ribonucleic acid; r.t. = room temperature).

Context

Spatial coverage

Description: Dept. of Genetic Epidemiology in Psychiatry, Molecular Genetic Laboratory, Central Institute of Mental Health (CIMH), Mannheim, Germany
Latitude: 49 Degrees, 29 Minutes, 34 Seconds
Longitude: 8 Degrees, 27 Minutes, 56 Seconds

Temporal coverage

Collection ongoing since 2007.

Temporal coverage for accessibility

N/A.

(2) Methods

Steps

BioPsy collects biospecimens according to Standard Operating Procedures (SOPs), which are available upon request (www.zi-mannheim.de/biobank). The facility operates a laboratory information management system (LIMS); a controlled automated liquid-handling system; and an automated DNA/RNA extraction system. Access to biospecimens is possible in collaboration with the responsible principal investigators. Requests for access should be forwarded to the BioPsy manager. **Table 1** provides an overview of collected biospecimen.

Stabilization/preservation

- Peripheral blood in EDTA (for plasma and DNA preparation)
- Peripheral blood in PAXgene® (PreAnalytiX GmbH tubes for RNA preparation)
- Peripheral blood in CPT™ (Cell Preparation Tube) Sodium Citrate (Becton Dickinson, for PBMC preparation; PBMC = peripheral blood mononuclear cell)
- Peripheral blood in CAT (Clot Activator Tube for serum preparation)
- Saliva in Oragene™ (DNA Genotek Inc., for DNA preparation)
- Cell lines in DMSO (Dimethyl sulfoxide) and Medium (for cryopreservation)

Type of long-term preservation

Freezing. All samples are stored in locked, temperature-monitored freezers, and are accessible by BioPsy personnel only.

Storage temperature

–80°C; –20°C; 4°C; room temperature (18–25°C).

Shipping temperature from patient/source to preservation or research use

–80°C (on dry ice); 0–4°C (on ice); room temperature (18–25°C).

Shipping temperature from storage to research use

–80°C (on dry ice); 0–4°C (on ice); room temperature (18–25°C)

Quality assurance measures

All BioPsy procedures are subject to rigorous quality control. The principal measures for ensuring sample quality include procedures to:

- Guarantee the integrity of nucleic acids using NanoDrop 1000 (peqlab); infinite M200PRO (Tecan); 2100 Bioanalyzer (Agilent Technologies); and agarose gel analysis
- Ensure immediate intervention in the event of a power-cut and thus safeguard samples through use of appropriate alarm systems for all freezers
- Up-date local and online databases

Source of associated data

- Extensive phenotypic assessment, including data from questionnaires, psychopathology evaluation, psychometry, (functional) magnetic resonance imaging
- Clinical records

In accordance with data protection guidelines and laws, no personal, phenotypic-, genetic-, or clinical data are stored in the biobank.

Phenotypic and genetic data are stored in secured environments, in separate dedicated data bases. This involves fine grained data access control for authorized personnel only.

Data are stored in pseudonymized form without personally identifiable information. Personal data are saved in a closed environment and are not accessible over network.

Ethics Statement

BioPsy applies appropriate ethical and data security measures on various levels:

- Sample pseudo- or anonymization
- High data privacy standards
- Confidentiality and data protection by restricting access to BioPsy personnel only and the use of security systems
- Written informed consent for collection, storage, and distribution
- Regulation of distribution to the scientific community by evaluation and approval of all projects for which samples are requested

For all ethical, legal, and societal issues, BioPsy adheres to German and European data protection laws and the recommendations of the following organizations and guidelines:

Technology, Methods, and Infrastructure for Networked Medical Research (TMF e.V.); the Permanent Working Party of Research Ethics Committees in Germany (AMK); the European Network of Research Ethics Committees (EUREC); the OECD Guidelines on Human Biobanks and Genetic Research Databases; and the OECD Best Practice Guidelines for Biological Resource Centres.

The clinicians who were responsible for subject recruitment evaluate all access requests to ensure compliance with the respective informed consent documentation. If indicated, the opinion of the respective ethics committee is also requested.

Biomaterial collection for scientific medical research is approved by the Medical Ethics Committee II of the Medical Faculty Mannheim/Heidelberg University, and the ethics committees of the collaborating recruiting centers.

Constraints
N/A.

(3) Bioresource description

Object name
Biobank of Psychiatric Diseases Mannheim.

Bioresource name
Biobank of Psychiatric Diseases.
Bioresource acronym: BioPsy.

Bioresource location
Dept. of Genetic Epidemiology in Psychiatry, Molecular Genetic Laboratory, Central Institute of Mental Health (CIMH), Mannheim, Germany.

Bioresource contact
Staff: Helene Dukal: helene.dukal@zi-mannheim.de
Christine Hohmeyer: christine.hohmeyer@zi-mannheim.de
Head: Dr. Stephanie Witt: stephanie.witt@zi-mannheim.de

Bioresource URL
www.zi-mannheim.de/biobank

Identifier used
All samples are barcoded in accordance with universal standard identifier standards.

Bioresource type
Disease-based, epidemiological samples, and control samples.

Type of sampling
Population, family, disease based, longitudinal cohorts, sampled in clinical care, sampled in a research protocol context.

Anatomical site
N/A.

Disease status of patients/source
Psychiatric Diseases.

Clinical characteristics of patients/source
Patients and probands stem from various projects, each of which has specific characteristics.

Size of the bioresource
To date, approximately 180,000 biospecimens from around 78,000 individuals have been collected within 56 ongoing projects. The average sample accrual is 16,000 per year. The average number of requested samples is 9,000 per year.

Vital state of patients/source
Alive at the time of sampling.

Clinical diagnosis of patients/source
Psychiatric Diseases: e.g., Major Depression, Schizophrenia, Bipolar Disorder, Substance Use Disorders, Personality Disorders, Attention Deficit and Hyperactivity Disorder, Autism Spectrum Disorders, Dementia.

Pathology diagnosis
N/A.

Control samples
Controls are either population based or selected according to project-specific criteria.

Biospecimen type

Biospecimen Type	Biospecimen Processing	Number of Aliquots	Size (mm) / Volume (ml)	Storage Temperature
Peripheral Blood	Whole blood (EDTA)	1–3	9 ml	–20°C short term / –80°C long term
	PAXgene®blood	1	9 ml	–80°C
	Plasma	Up to 7	0.5 ml	–80°C
	Serum	Up to 7	0.5 ml	–80°C
	Archive	1	20 × 60 mm	18–25°C
Saliva	Oragene™	1	4 ml	–80°C
Tissue	Placenta	1	50 ml	–80°C
Hair	Hair	1	40 × 120 mm	18–25°C
Body fluids	Amniotic fluid	5	0.5 ml	–80°C
	Amniotic cell culture	1	0.3 ml	–80°C
	Urine	5	1 ml	–20°C
Processed	DNA	2	1 ml	–20°C
	RNA	5	0.03 ml	–80°C
	PBMC	1	1 ml	–80°C

Table 1: Overview of type, processing, aliquot number, volume and storage temperature of collected biospecimen.

Release date
N/A.

Access criteria
External collaborators are granted access to samples and/or data after the provision of consent by the respective principle investigators and the manager of BioPsy, who must be contacted directly by the applicant. A prerequisite for access is that the intended research is compatible with the respective informed consent documentation. Compatibility with the informed consent is evaluated by the recruiting clinician, who might also request the opinion of the Ethical Committee. Reimbursement for shipping expenses may be required.

(4) Reuse potential

Sample and/or data may be reused for further laboratory and/or data analyses, replication of previous findings, or meta-analyses. Reuse is possible on a collaborative basis, with the permission of the respective principle investigators and the manager of BioPsy, who must be contacted directly by the applicant.

Acknowledgements
We thank the host institute, the Central Institute of Mental Health Mannheim, Germany, for its support. We also thank our numerous collaborators for the recruitment of probands and patients, and all participating individuals.

MR and SHW received funding from the German Research Foundation (DFG; grant FOR2107; RI908/11-1 to MR and WI3439/3-1 to SHW), and the German Federal Ministry of Education and Research (BMBF; D.BU.0006.004).

Competing Interests
The authors declare that they have no competing interests.

Author Information
The Biobank was established by MR. SHW is the head and manager; HD, CH, SR-B, DS, FS, JS and JT collect data and samples; ML and JF are the biobank curators.

How to cite this article: Witt, S, Dukal, H, Hohmeyer, C, Radosavljevic-Bjelic, S, Schendel, D, Frank, J, Lang, M, Streit, F, Strohmaier, J, Treutlein, J and Rietschel, M 2016 Biobank of Psychiatric Diseases Mannheim – BioPsy. *Open Journal of Bioresources* 3: e2, DOI: http://dx.doi.org/10.5334/ojb.18

Published: 08 July 2016

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