



Lifebrain

D2.5. Enrichment of existing cohorts by administration of buccal swabs for epigenetic analyses across WP4 tasks 2-6

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Executive summary

UzL has started generating DNA methylation data for all the 1445 cohort samples from the University of Oslo (UiO); around 280 more UiO samples arrived to Lübeck by 13th December 2018. BASE-II sampling is still ongoing, currently 243 samples have been received, DNA has been extracted successfully in all of these.

In addition, we are expecting up to 600 DNA samples from the CALM study (legal materials are currently being finalized before materials can be transferred).

The completion of certain parts of this task are delayed due to the late start of the BASE-II examinations and delays in finalising MTAs for other cohorts (e.g. CALM). However, this delay shall have no bearing on the scientific outcomes of this task or the results of related tasks in WP4 (D4.2-D4.6).

Table of contents

Executive summary	3
Table of contents.....	4
List of acronyms/ abbreviations	5
1. Introduction.....	6
1.1. Deliverable description	6
1.2. Objectives of the deliverable.....	6
1.3. Genetic data collection	7
2. Description of activities	8
2.1. LCBC cohort samples.....	8
2.2. BASE II cohort samples	8
2.3. Other samples	8
3. Conclusions.....	9

List of acronyms/ abbreviations

Lifebrain	Healthy minds from 0 to 100 years: Optimizing the use of European brain imaging cohorts
BASE II	Berlin Aging Study II
CALM	Centre for Attention, Learning and Memory, University of Cambridge
CamCAN	Cambridge Centre for Ageing and Neuroscience, University of Cambridge
DNA	Deoxyribonucleic acid
DTA	Data Transfer Agreement
EB	Executive Board
GA	Grant Agreement
LB	Lifebrain
LCBC	Centre for Lifespan Changes for Brain and Cognition
M	Month
MPIB	Max Planck Institute for Human Development
MTA	Material Transfer Agreement
NESDA	The Netherlands Study of Depression and Anxiety
UB	University of Barcelona
UiO	University of Oslo
UOXF	University of Oxford
UzL	University of Lübeck
VUmc	VU University Medical Centre Amsterdam
WP	Work Package

1. Introduction

1.1. Deliverable description

Task 2.5 Enrichment of existing cohorts by administration of buccal swabs for epigenetic analysis Lead: UzL; Participants: UiO, UmU, UOXF, MPIB, UB, REGIONH, MRC, VUMC (M6-M24)

Coordination of the sample collection, laboratory experiments and bioinformatic processing of the data for analysis in WP4. Buccal swabs will be collected by probands at home using the Catch-All Sample Collection Swabs (Epibio, Inc.) following standardized collection protocols and then mailed to the UzL site for DNA extraction, QC and subsequently DNA methylation profiling using the Infinium MethylationEPIC BeadChip array by Illumina, Inc. This array currently represents the most advanced product in the field and includes 850.000 methylation sites at single nucleotide resolution optimized for covering the most relevant gene regulatory sites in the genome. Overall, we propose to determine DNA methylation profiles from 2000 Lifebrain probands. These will be collected from at least four different participating centers (UiO, MPIB, MRC/ UOXF/ VUMC) to account for cohort and population specific variation in DNA methylation patterns. We will specifically select probands with maximally complete phenotype data (neuroimaging, cognitive testing and longitudinal follow-up data available) to allow the largest possible set of epigenome-wide association analyses. As DNA quality is insufficient for epigenome-wide / genome-wide profiling from buccal swab specimen in up to 25% of the cases, we propose to distribute 3,000 collection kits in order to ensure high-quality samples for DNA methylation profiling in 2000 samples.

1.2. Objectives of the deliverable

Coordination of the sample collection, laboratory experiments and bioinformatic processing of the data for analysis in WP4.

1.3. Genetic data collection

Table 1. summarises the Lifebrain cohorts contributing to the genetics-related tasks (T2.5. enrichment of existing cohorts by administration of buccal swabs for genetic analysis) and T2.6. Generation of new GWAS) and present an update on the sample collection.

Table 1. Genetic data from the Lifebrain cohorts (D2.5 and D2.6)

Cohort	Number of samples	GWAS data availability	Analysis site	Status
<i>Barcelona (ES)</i>	<i>n.a.</i>	<i>No</i>	<i>n.a.</i>	<i>Sample excluded</i>
RegionH (DK)	95	Yes (Illumina 660W Quad)	UzL	DTA pending
NESDA (NL)	2600	Yes (Affy 6.0)	NESDA	Ready to go
Whitehall II (UK)	800	No (Illumina HumanCore)	UzL	MTA in preparation
CamCAN (UK)	650	Yes (Illumina Omni Express)	CamCan	Ready to go
CALM (UK)	600	No	UzL	MTA pending
Betula (SWE)	355	Yes (OmniExpress & Exome)	UzL	DTA pending
LCBC (NO)	1445	Yes (GSA [ongoing])	UzL	Genotyping ongoing
BASE-II (DE)	1500	GWAS (Affy 6.0)	UzL	Sampling ongoing
TOTAL (with GWAS)	7800			

2. Description of activities

2.1. LCBC cohort samples

UzL has obtained human specimen for DNA extraction and further genomics and epigenomics processing from a total of 1,445 individuals from LCBC at UiO. These samples were divided as follows:

- 595 samples with DNA already extracted previously (from saliva),
- 416 saliva samples in Genotek-Oragen tubes,
- 339 buccal swabs (Isohelix SK-1),
- 95 buccal swabs (4N6 FLOQSwabs).

For all but the 595 previously extracted DNA samples, UzL extracted DNA followed by extensive laboratory quality control.

A total of 1,376 samples passed quality control and were subjected to both automated genome-wide SNP genotyping (using the “Global Screening Array” by Illumina; covered by non-Lifebrain funding) as well as manual genotyping of the e4-SNP in APOE (rs429358). For these, UzL were able to successfully generate genome-wide SNP genotyping data in 1,374 samples and APOE genotypes in 1,344 samples. The genome-wide data are currently being processed and QC’ed at the UzL site. All individuals who passed GWAS QC are currently being subjected to DNA methylation profiling using the Infinium Methylation EPIC microarray. The EPIC arrays for part of this task have already been purchased from the Lifebrain budget and are being stored in the UzL laboratory.

An additional 280 UiO samples arrived to Lübeck by 13th December 2018 for further analysis.

2.2. BASE II cohort samples

In addition to these UiO samples, UzL also received Isohelix SK-1 buccal swabs from 243 individuals from the BASE-II study from Berlin. For these, DNA extraction was successful in all of these individuals.

NB: the clinical examinations (including cognitive assessments and buccal swab sampling) of the BASE-II individuals started in May of 2018 and will be ongoing until the end of 2019.

2.3. Other samples

In addition to samples from UiO and BASE-II, we expect to collect up to 600 DNA samples from other Lifebrain cohorts which will be included in all GWAS (and partially EWAS) aims (see details under description of D2.6).

3. Conclusions

The completion of certain parts of this task are delayed due to the late start of the BASE-II examinations and delays with preparing legal documents for other cohorts (such as CALM or Whitehall II), however, this delays shall have no bearing on the scientific outcomes of this task or the results of related tasks in WP4 (D4.2-D4.6).