Biomaterial collection for neurodegenerative disease research (ND collection)

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What is this biomaterial collection about?

You are invited to donate samples to a collection of biological material. Before you decide whether or not to take part, it is important for you to understand why the collection is being done and what it will involve, also concerning the processing of your personal data. Please take time to read the following information carefully. This collection received a favourable opinion from the National Committee of Ethics and Research.

What is the purpose of the collection?

Research is fundamental to advance patient care as it improves the understanding of the mechanisms of disease and allows the development of new tests and new treatments, that not only control symptoms but may also help to stop the disease progression. To investigate the causes of disease, researchers need access to biomaterial and clinical data from patients and healthy control individuals to define disease markers and study mechanisms causing premature neuronal ageing. It takes substantial efforts to collect a large number of samples to be able to answer the most urgent research questions. Here, pseudonymised participants' clinical data and biosamples from this collection will help numerous research organisations in Luxembourg and abroad[1] to advance the understanding and treatment of common neurodegenerative diseases, such as Alzheimer's and Parkinson's diseases, epilepsy and chronic inflammatory brain diseases. The IBBL (Integrated BioBank of Luxembourg) part of the Luxembourg Institute of Health (LIH) and the LCSB

[1] Simons JA, et al. Multilingual Validation of the First French Version of Munich Dysphagia Test-Parkinson's Disease (MDT-PD) in the Luxembourg Parkinson's Study. *Front Neurol*. 10, 1180 (2019).

Hipp G, et al. The Luxembourg Parkinson's Study: A Comprehensive Approach for Stratification and Early Diagnosis. *Front Aging Neurosci*. 2018;10:326.

Baldini F, et al. Parkinson's disease-associated alterations of the gut microbiome predict disease-relevant changes in metabolic functions. *BMC Biology*. 2020;18(62).

Bobbili DR, et al. Excess of singleton loss-of-function variants in Parkinson's Disease. *J Med Genet*. 2020;jmedgenet-2019-106316.

Ohnmacht J, et al. Missing heritability in Parkinson's disease: the emerging role of non-coding genetic variation. *J Neural Transm (Vienna)*. 2020;127(5):729-748.

(Luxembourg Centre for Systems and Biomedicine), part of the University of Luxembourg are co-sponsors of the Collection.

Why have I been invited to participate?

You have been invited to participate either because you are affected by a neurodegenerative disease, such as Parkinson's disease, because you are a person with an increased risk to develop a neurogenerative disease, or because you are a healthy individual and you would like to support research. We are inviting all people with a neurodegenerative disease treated by Luxembourg hospitals and or in private practices to participate in this collection. As research is often done by comparing affected individuals to healthy ones, participants who do not suffer from without neurodegenerative disease(s) – "control participants" – are also essential, and therefore invited to donate to this collection.

If you agree to participate, you will be asked to donate biological samples, answer questionnaires and perform neuropsychological tests.

Do I have to take part?

It is up to you to decide whether or not to take part. If you do decide to take part, you will be given this Subject Information Sheet to keep and will be asked to sign an Informed Consent Form. If you choose to take part, you are still free to withdraw at any time and without giving a reason. If you decide not to take part in this study, your decision will not affect your medical care.

What will happen to me if I take part?

If you agree to take part in this collection, you will be asked to annually:

- visit a neurologist;
- undergo a neurological examination and perform neuropsychological tests (incl. questionnaires and self-declared responses);
- donate blood;
- donate urine;
- donate saliva;
- allow access to your medical record and neuroimaging information.

Depending on your health condition and other tests you may have to do for your medical care, you may be asked to contribute with the following materials, if you agree:

- hair
- nasal washes;
- nasal brushes;
- stool;
- skin biopsy;
- cerebrospinal fluid;
- additional colorectal tissue biopsy (only in the context of a colonoscopy required for a medical purpose).

Additionally, you will have a possibility (subject to your explicit consent) to:

- participate in device-based assessments using wearable sensor technology (e.g. eGaIT), in which case you consent to your coded data being transferred from a device or phone to the collection database for the use in future research,

If you are a hospital patient, you will have samples collected for medical reasons, e.g., for diagnosis. Whenever possible, samples for research will be collected together with the samples for your routine medical care. Also, surplus materials remaining after the diagnosis may be used for research. This will include the material which would otherwise be discarded.

Summary:

	Initial consultation	Visit 1	Follow up visits
MANDATORY FOR ALL PARTICIPANTS			
Eligibility assessment	*x*		
Informed consent		*x*	
Data collection		*x*	*x*
Neurological examination and basic neuropsychological assessment (level A) (approx. 145mins)		*x*	*x*
Blood sample (up to 50.5ml per visit)		*x*	*x*
Urine sample (up to 100 ml per visit)		*x*	*x*
Saliva collection (up to 6ml)		*x*	*x*

	Initial consultation	Visit 1	Follow up visits
OPTIONAL FOR ALL PARTICIPANTS			
Neuropsychological, visual and detailed motor exam (level B)		*x*	*x*
Hair collection – optional			
Nasal washes – optional		*x*	*x*
Nasal brushes – optional		*x*	*x*
Stool sample (small quantity) – optional		*x*	*x*
Skin biopsy – optional		*x*	*x*
Cerebrospinal fluid sample – lumbar puncture (up to 12ml per puncture) – optional		*x*	*x*
Colorectal tissue sample – colonoscopy (two small biopsies) – optional, only if a colonoscopy is required for a medical purpose		*x*	*x*
MRI imaging – optional		*x*	*x*
Polysomnography or equivalent modality – optional		*x*	*x*
Optical Coherence Tomography (OCT) – optional		*x*	*x*
Mobile application use – optional	*Usage frequency at personal preference*		

If you agree to donate specimens, they will be collected and stored at the IBBL (Integrated BioBank of Luxembourg), part of the LIH. Your samples may be used for other medical research projects carried out by the study sponsors (IBBL/LIH and LCSB) or other duly authorised national or international research organisations or biobanks for academic and/or commercial purposes after obtaining ethical approval.

The principles described in this document shall apply to future medical research projects in as far as they are relevant, except for future research projects by third parties:

- information on this future medical research is perhaps not available, and the Data Controller, the principal investigator, the sponsor and the authority providing authorisation may be different;
- in case of withdrawal of consent, you will not be able to request the destruction of samples or data that has already been provided to biomedical research projects.

Your samples and data will only be used for research projects that have received the formal approval from ethics committee (in Luxembourg, from the Comité National d'Ethique de Recherche – CNER – and the Ministry of Health), and that do not contradict the choices you have expressed in the informed consent form. In any case, the recipients of the data will not have access to information that allows your identity to be associated with these samples and data.

What are the possible risks?

There are no major risks associated with the collection of biospecimens. The table below presents all potential risks associated with the donation procedures, but these risks remain **rare**.

Procedure – Sample collected	Risks associated
Blood collection	Pain, bruise, faintness, infection
Urine collection	There are no known risks
Saliva collection	There are no known risks
Hair collection	There are no known risks
Nasal washes	Local irritations of the mucosa
Nasal brushes	Discomfort during the procedure, bleeding, infection
Stool collection	There are no known risks
Skin biopsy	Bleeding, bruising, scarring, infection, allergic reaction to the topical antibiotic applied before the biopsy
Cerebrospinal fluid collection – lumbar puncture	Bleeding into the spinal canal, discomfort during the procedure, headache after the procedure, hypersensitivity (allergic) reaction to the anaesthetic, infection introduced by the needle going through the skin
Colorectal tissue sample – colonoscopy	Discomfort during the procedure, abdominal pain, bleeding, perforation of the colon
Mobile application use	Minimal risks associated with the use of healthcare mobile phone applications
MRI imaging	Discomfort during the stay in the scanner, inconvenience due to the short-intended OFF-state, accidents during the transport
Polysomnography or equivalent modality (PSG)	PSG and sleep assessment are a non-invasive tool with no known side effects or complication except for possible slight discomfort while being branched to the cables during the sleep
Optical Coherence Tomography (OCT)	OCT is a non-invasive test with no known side effects or complications

When possible, the samples collected for this collection are collected together with the samples for the routine medical care. In some cases (when there is no sample collection for medical care or if you are a healthy control participant), you could have a specific visit for this collection.

Are there any benefits of taking part in the study?

You should not expect to benefit from this collection directly. The main reason you may want to participate is to help researchers find better treatments for neurodegenerative diseases, such as Parkinson's disease, and to better understand their development. Therefore, your valuable contribution may help to identify new therapies for these still incurable diseases.

There are no costs for you to donate your samples. You will also not be paid to donate your biospecimens.

What are genetic analyses?

You are being asked to allow genetic analyses of your samples. Genes are in every cell of the body. They provide the instructions for the body to operate and repair itself, and they are passed from parents to children and then from cell to cell as new cells are created in the body. The entirety of your heritable genetic information is called the genome.

Scientists want to understand how diseases might be linked to the genes that we all carry in our genomes. If these links can be understood, it would mean that more effective tests and treatments could be developed that would be personalised to each patient. For this kind of research to be carried out, the genomes from both healthy people and people with disease need to be analysed and compared. In this context, the application of modern Next Generation Sequencing (NGS) techniques allows an analysis of genomes at a very precise and complete level helping to discover even subtle genetic changes.

Will I receive any information in return?

While the ultimate goal of this collection is to support future research in the field of neurodegenerative diseases, there is a possibility that genetic information will be discovered that may be of relevance to your personal healthcare or that of your family. If this should happen, the researchers will inform the Principal Investigator of the collection who will evaluate the information and decide what to do, which may be to contact you through your doctor based on your informed consent.

You will be explicitly asked whether you agree to receive information about incidentally discovered germline mutations (mutations or aberrations that could affect not only my future health but also the health of your children, brothers/sisters, parents…) through your treating physician / the study responsible physician / a geneticist, to discuss the implications and to be referred to a local geneticist if needed.

In taking this decision, you confirm that you have been well informed and that you understand that the researcher has no obligation to actively search for genetic mutations in your sample(s) and that the discovery of such mutations does not in any way constitute a diagnostic. If such a finding occurs, it will occur at the time of analysis and in the frame of this current collection (i.e. not in the frame of future projects which could make secondary use of your pseudonymised sample(s)/data later on). It will also be at that moment that you will be recontacted if you have agreed to be informed. You can reconsider this decision at any time.

If you decide “not to be informed”, you will not receive any information regarding that/these incidental finding(s), and neither will your relatives.

Will I be contacted to provide further information?

As new scientific discoveries are continually being made, it may be important to collect additional information about health or lifestyle of participants that were not considered to be of importance when the collection was designed.

A possible scenario, for example, is that it could be suggested in an independent study that a specific genetic modification is only associated with a higher risk if the person also demonstrates a certain behaviour (e.g. consumption of coffee). If it can then be known how much coffee the donors drink (e.g. via an internet-based survey), the samples could be compared based on the coffee-drinking behaviour of their donors to see whether there is a link between the two.

If you consent, we shall contact you by e-mail or phone for new scientific questions no more than every six months. You will receive an e-mail from your doctor that will contain information about the general character of the survey and a web-link to the survey.

The LCSB internet portal offers the possibility of gathering information from collection participants for future research questions. This is less time- and organisation-consuming alternative to a telephone or written contact or repeated hospital appointments.

Please be assured that no third parties will receive your e-mail account details. Should you wish to protect your anonymity further, please indicate an e-mail address that does not contain your name.

The data collected via the LCSB internet portal (results of online questionnaires) will then be added to the samples stored at the IBBL or to the electronic data stored at the LCSB.

How will my personal data be collected? What type of personal data will be processed?

Once you give us your consent, we will collect information from multiple sources: hospital files and records, primary and secondary results of neurological and neuropsychological assessments, which include questionnaires and self-declared responses. The data collected will include age, gender, ethnicity, demographic data, contact data, diagnosis, associated medical conditions, treatment, risk factors, family history of disease, test results, imaging data, related diseases and concomitant medication.

On which legal basis will my personal data be collected and processed?

The use of your personal data is necessary to enable us to achieve the aims of the ND collection, which we are conducting in the public interest and for the purposes of scientific research (art. 6.1e and art. 9.2j of the GDPR.

Who is responsible for the processing of my personal data?

The Data Controller in respect of the processing of your data is the Université du Luxembourg, a Public Institution of Higher Education and Research, having its registered office at 2 avenue de l'Université, L-4365 Esch-sur-Alzette, Luxembourg, acting for its **Luxembourg Centre for Systems Biomedicine**, having its seat at 6, avenue du Swing L-4367 Belvaux.

For any request for information concerning the processing of your personal data as a result of this collection, you can contact the Data Protection Officer by e-mail at dpo@uni.lu, or by post at the following address:

UNIVERSITÉ DU LUXEMBOURG
Protection des données
Maison du Savoir
2, Avenue de l'Université
L-4365 Esch-sur-Alzette

Who will have access to my data?

Only the following categories of people may access your data:

- The Principal Investigator of this collection and a restricted number of authorised members of the team, of the LCSB and the IBBL/LIH, acting under his responsibility.

  Only the PI of this collection and the clinical team members authorized by him will be able to match your name with your samples and data.

- Other researchers or research organisations in the private or public sector will have access to your pseudonymised data for future scientific research purposes (in no case will data revealing your identity be provided). The transfer of data to third parties is subject to strict assessment by the sponsors.

We may also provide access to your pseudonymised data to service providers who perform services on our behalf. For example, GaitLab (previously eGaIT) is a sensor-based biometric gait-analysis that enables assessment of gait symptoms.

Data collected during the GaitLab analysis during the visit will be downloaded locally on the collection sites. This data will be coded and then securely transferred to the original developer of the sensor technology for analysis.

Finally, in the context of certain controls or audits, the competent authorities may also have access to your personal data if necessary, to control the quality of data.

Scientific studies of biomaterials can only be correctly interpreted if the research results are connected to disease data. Some clinical data about yourself (e.g. demographics, diagnosis, disease profile, treatment, laboratory results) will be entered into an electronic database. Your name is replaced by a combination of figures from which identification is impossible. Your samples will, therefore, be provided to the IBBL without your name on them, and this makes it very unlikely that anyone could identify you.

Results from future scientific studies will only be made public only in a way to ensure that no participant can be identified. Your name and identity will never appear in published materials.

Will my samples be stored and used for other research programs?

All samples for this collection will be stored at the IBBL (Integrated BioBank of Luxembourg) and/or at the LCSB for an indefinite period. A biobank (as the IBBL) is a place that collects, stores, processes and distributes biological materials (such as tissue or blood) and the data associated with those materials (such as medical information about the participant). The purpose of the IBBL is to support a diverse range of research intended to improve the prevention, diagnosis and treatment of illness, and the promotion of health throughout society. These research programs are subject to receiving ethics committee approval and may be carried out by either academic (non-commercial) or industrial (commercial) organisations.

If you agree to participate, this means that your samples and associated coded data may be used for other medical research programs, and sent to other countries in Europe and beyond, where the data protection laws may not be as strict. Some of your unused samples may also be used for quality control purposes.

What will happen to the results of future research studies?

Results may come from future research studies which may help to develop new treatments or tests for diseases. It is intended that the results of these studies will be published in medical and scientific journals.

IBBL will, from time to time, publish information concerning its activities regularly. IBBL will also take this opportunity to remind research participants that the consent given may be withdrawn at any time.

What are my rights?

In this context, you have the following rights:

- **access**: you have the right to access your personal data which are processed by LCSB.
- **rectification**: you have the right to obtain rectification of inaccurate or incomplete data concerning you.
- **erasure**: you have the right to obtain the erasure of your personal data in the following situations: (i) your data are no longer necessary for the purposes for which we collected them; (ii) you withdraw your consent where the processing is based on consent and there is no other legal basis for such processing; (iii) you object to the processing of your personal data and there is no compelling legitimate reason justifying the processing; (iv) the data is subject to unlawful processing; (v) the data must be erased due to a legal obligation.
- **opposition**: you can oppose the processing of your personal data: (i) where the processing concerned is based on your consent, without having to provide any particular reasons; (ii) where the processing is based on the legitimate interests of LCSB, you can oppose it for reasons related to your particular situation unless there are

legitimate grounds and imperative reasons for such processing which prevail, or else for the verification, exercise or defence of our rights in Court.

- **limitation**: you have the right to suspend the processing of personal data while verification is being carried out (verification of the accuracy of information, of the legal basis of processing, and of the legitimate reasons that LCSB opposes to their erasure).
- **transfer** to another provider. This right applies when the processing is based on your consent or the performance of a contract and is performed using automated processes.

If you wish to exercise your rights, you may contact the principal investigator or his designated representative.

Finally, you have the right to lodge a complaint with the National Commission for Data Protection (CNPD) concerning the processing of your personal data.

How do we protect your personal data?

The LCSB implements appropriate security measures, depending on the sensitivity of the data concerned, to protect your data against the risk of unauthorised access, loss, fraudulent use, disclosure, alteration, or destruction of your data.

Your data will be treated in a strictly confidential manner. They will be pseudonymised, i.e., a confidential reference code will be used instead of your name. This code alone does not allow you to be directly identified and will only be used for the scientific processing of your data. At no time will your identity appear in a document intended for the public or other institutions. The correspondence table establishing the link between the reference code and your name will be kept by the Principal Investigator in a confidential manner.

The LCSB also applies the principle of data segregation, i.e., identification data on the one hand and research data, on the other hand, are stored on different secure servers to minimise the potential risks of re-identification. Despite all security efforts, the risk of a data breach is not zero but can be described as very low.

The LCSB makes sure that all the data processors or other partners that might process your data according to the present Subject Information Sheet take all the necessary measures to protect your data.

How long do we keep your data?

Your personal data that are not directly identifiable (pseudonymised data) will be kept indefinitely since this is an open-end collection of samples to be used in different research projects.

If you no longer wish to participate in the study, your samples collected before the withdrawal of your consent may be retained and used in the study unless you object. In this case, they will be destroyed. However, if any of your samples have already been used in the study, they can no longer be removed from the study.

The national ethics committee (Comité National d'Ethique de Recherche – CNER) may be called to decide whether the provisions on storing the samples and data will be maintained or changed. You will be informed in case of changes.

Data transfers outside the European Union

Your data may be transferred outside the European Union when this is necessary for the implementation of the research or the exploitation of its results. Only anonymous data or data that does not allow you to be directly identified (coded or pseudonymised data) will be transmitted outside the European Union.

It is possible that certain countries outside the European Union/European Economic Area do not offer the same level of privacy protection as your country. In such cases, LCSB and IBBL/LIH will put in place appropriate measures to ensure

the protection of your personal data (for example, by including standard data protection clauses in its contracts, by complying with codes of conduct or by complying with a certification scheme) or will rely on your explicit consent.

For more detailed information on the appropriate measures implemented by the LCSB, you can send a written request to the Data Protection Officer of the University of Luxembourg by e-mail to dpo@uni.lu.

Can I withdraw from the collection?

You can withdraw your samples and clinical data from the collection at any time without giving a reason by contacting the Principal Investigator or the DPO. If any part of your sample has already entered a research study, it cannot be removed from it. You may also withdraw your consent to participate in the online surveys at any time.

Who is organising and funding the research?

This research is sponsored and paid for by the IBBL (Integrated Biobank of Luxembourg) and the LCSB (Luxembourg Centre for Systems Biomedicine) of the University of Luxembourg.

The Principal Investigator is **Prof Dr Rejko Krüger**, tel: +352 44 11 - 4848, e-mail: Parkinson@chl.lu.

Who has reviewed the collection?

This collection has been approved by the National Ethics Research Committee (CNER) on 2 July 2014.

Should you have any concerns about how the collection has been conducted, you should contact Comité National d'Ethique de Recherche (CNER), 1a-b rue Thomas Edison, L-1445 Strassen, Luxembourg.

Thank you for taking the time to read and consider this information.