INFORMATION AND INFORMED CONSENT FORM

RESEARCH PROJECT TITLE:
“Genetic characterization and genotype-phenotype correlation of a dementia cohort from central Portugal”

PROTOCOL N°

PROMOTOR

COORDINATOR INVESTIGATOR
Professor Isabel Santana, MD, PhD

STUDY SITE
Centro Hospitalar e Universitário de Coimbra,
Faculdade de Medicina da Universidade de Coimbra

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3000-548 Coimbra

TELEPHONE
239 400 448

PARTICIPANT’S NAME
(CAPITAL LETTERS)
You are invited to voluntarily participate in this study because you have a diagnosis of either a dementia syndrome (Alzheimer’s disease, Lewy bodies dementia, Frontotemporal dementia or other related syndrome) or a Mild Cognitive Impairment.

This procedure is called informed consent and describes the general aim of the study, its procedures and its potential risks and benefits. Your participation may contribute to improve the knowledge in genetics and other biomarkers of the disease onset, as well as progression biomarkers, which may be used in the planning of clinical trials destined to prevent or delay disease’s onset or progression.

You will receive a copy of this Informed Consent to review and search counselling of family and friends. The Investigator or other member of his team will clarify any of doubt about this consent and also any word or information that you may not fully understand.

After understanding the study and not having any doubt about itself, you may decide whether to participate or not. In the case you want to participate, you will be asked to sign and date this form. After you and the Investigator sign, you will be given a copy. In the case you do not want to participate, this will have no impact or loss in your care from that point onwards.

1. GENERAL INFORMATION AND STUDY AIMS

This study will take place in the Neurology Department of the Coimbra’s University and Hospital Center (Centro Hospitalar e Universitário de Coimbra), Faculty of Medicine of the University of Coimbra in collaboration with the Van Andel Research Institute - Guerreiro and Brás Laboratories. It is a research non-interventional study and therefore it will have no impact on your usual medication or care.

This study was approved by the Ethical Committee of the Faculty of Medicine of the University of Coimbra (Faculdade Medicina da Universidade de Coimbra), in order to guarantee the safety, well-being and protection of the data of every included participant and to guarantee a public evidence of that protection.

As a participant in this study, you will benefit of vigilance and support of your doctor, thus guaranteeing your safety.

This study intends to better understand the genetic changes underlying dementia syndromes in the Portuguese population. It involves collecting a blood sample for genetic studies (15ml). This study has the following aims:
1) To identify genetic mutations that cause disease and its relative frequency in the Portuguese population;

2) To search for new disease-causing mutations, possibly specific of our population and to thoroughly study its carriers at a clinical level and in terms of biomarkers (imaging, blood or CSF);

3) To describe genetic variants (which may confer risk or protection for the development of disease) present in the Portuguese population;

4) To correlate genetic data with other characteristics of the disease, namely clinical findings (physical and neurological examination findings, neuropsychological evaluation) or complementary diagnostic exams (MRI, lumbar puncture or others), if available.

We estimate we will include around 1500 individuals in this study.

2. PROCEDURES AND STUDY CONDUCTION

2.1. Procedures

There will be a collection of 15ml of blood sample by peripheral venous puncture. This collection will be integrated in the routine analysis everytime possible. This way, it will neither imply an additional venous puncture, nor any additional travel or expense.

2.1.1. Biochemical analysis

In each visit, we will collect blood samples for DNA analysis (up to 15ml of blood).

2.1.2. Genetic analysis

DNA will be extracted to perform genetic studies. This will be performed in two steps:

1) On a first phase, we will verify if the participant carries any of the known mutations associated with their disease.

There may be the case that you have already been submitted to this study. However, that study only screened the main mutations causing that disease. In this study, we will extend that study to many other genes related to neurodegenerative disorders in a general way. This will increase the odds of finding a pathogenic mutation, if you carry one; or increase the certainty that you do not carry one, what may have implications for your family.

In the case we find a mutation, this will also have implications to your relatives, namely the first-degree ones (siblings and children). In that case, they may be sent to an appointment of genetic counselling, so they can eventually do the same genetic study.
You have the possibility of refusing to know the result, but still allowing that your data is used for research on the disease.

You must also know that carrying a mutation does not, based on the current knowledge, alter the expected course of your disease.

2) On a second phase, we will screen for risk variants. These genetic variants are important in population studies. However, on an individual level they generally do not have clinical implications and, according to the current clinical practice, will not be communicated to you, unless you prefer to.

2.2. DATA TREATMENT AND RANDOMIZATION

The data will be kept at in the installations of the Higher Cortical Functions of the Neurology Department, under custody of the principal Investigator. Your records will always be kept confidential and anonymous, according to the current laws and regulations on this matter. All the clinical information will be reported in anonymized documents and identified by a code. Only your doctor, also an investigator in this project will know the correspondence between the code number and whom it identifies.

It is possible that information from analyses of your samples and your medical information will be shared with other investigators or put into an access controlled online database. These databases will not contain any identifying information about you, such as your name, address, telephone number, or social security number. Your personal identifying information will not be shared with other investigators. Your privacy is very important to us and we use many safety procedures to protect your privacy.

The genetic data collected in this study will be crossed with other clinical data of yours, namely family history, clinical history and complementary diagnostic exams, to better understand its interrelationship and impact on the disease.

If the results of this study are published, your identity will remain completely confidential.

In all this process, the maintenance of your privacy is a priority. It will not be possible, from the shared data, to reach the people they were collected from, unless through the Principal Investigator and only after strict consent from the person they were collected from or his legal representative.
2.3. **PERMISSION FOR THE USE OF THE DATA IN FUTURE STUDIES**

The data collected for the purpose of this study may be important information for other scientific research Studies in the future. If allowed, this contribution may, be very important in the understanding of your Disease. However, to participate in this study, you do not have to necessarily participate in future studies. If you allow that the gathered information may be, after anonymization, stored and used in future scientific research studies, please fill the section for this specific purpose in the end of this form.

The consent for this possible future use lays on the same principles, described for this specific study. You may withdraw your consent for these studies or ask for further information regarding these studies at any point, by contacting the principal investigator.

3. **POTENTIAL RISKS AND INCONVENIENCES FOR THE PARTICIPANT**

The collection of the blood sample (15m) will be performed by a peripheral venous puncture. The risks associated with any blood sample collection are very rare. The most common ones are local bruise, vasovagal reactions or syncope. Besides that, the collection will be, if possible, integrated on blood sample collection for routine analysis ordered in the clinic. This way, it will neither imply an additional venous puncture, nor any additional travel or expense.

4. **POTENTIAL BENEFITS**

The potential benefits will focus on the solid information about the identification of disease markers, namely genetic, and its relationship with clinical findings and complementary diagnostic exams. This will allow to deepen the knowledge of the natural history of the disease caused by each mutation.

This study has also the advantage of allowing the identification, as complete as possible, of the main genetic related dementias in Portugal. This would be useful in the planning of support and healthcare to the members of those families.

Finally, the mutation carriers may be invited to integrate trials of new medications under study, that are directed to specific mutation carriers. This invitation may also be extended to the relatives who carry mutations but are asymptomatic.
5. **NEW INFORMATION**

You will be given any information that may be relevant to your condition or that may influence your willingness of continue to participate in this study.

6. **ALTERNATIVE TREATMENTS**

This study does not foresee any change in the type or scheme of your medication.

7. **SAFETY**

We do not expect that due to your participation in this study will come any health problems, given the fact that the ordered exams are performed on a routine basis in the follow-up of your condition. However, if you may suffer any injury resulting from the participation in this research project, you will be assisted in the Coimbra’s University and Hospital Center, in order to get the necessary treatment of those injuries.

8. **PARTICIPATION/VOLUNTARY LEAVE**

You are entirely free of accepting or refusing to participate in this study. You may withdraw your consent at any time without any consequence for yourself, without the need to justify your decision, without any harm or loss of benefits and without compromising the relationship with the investigator that proposed you to enter in this study, You will be asked to inform the investigator to withdraw your consent.

The study investigator may decide to end your participation in this study if he understands that continuing on it is not in the best interest of your health. Your participation may also be terminated if you are not following the study plan, by an administrative decision or by a decision f the Ethical Committee. The study doctor will notify you in any of these circumstances and will talk to you personally about that.

9. **CONFIDENTIALITY**

Without violating the confidentiality rules, auditors and regulatory agencies will be granted access to the medical records to verify the procedures and the information obtained during the
course of this study, according to the laws and regulations that apply in these situations. Your records will always be kept confidential and anonymized, as determined by the laws and regulations that apply on these cases. If the results of these studies are published, your identity will also be kept confidential.

By signing this Informed Consent, you authorize this conditioned and restrict access.

You may also exercise your right of access to the information at any point. You may also have access to your medical information directly or through your doctor in this study. You also have the right to oppose to the transmission of data that are covered by professional confidentiality.

The medical records that identify you and the Informed Consent that you sign are verified for the purpose of the study by the investigators and, possibly, for regulatory agencies. The Ethical Committee responsible for the study may ask for the access to your medical records to assure that the study is occurring according to the protocol. We cannot guarantee absolute confidentiality due to the need of giving information to those entities.

By signing this informed consent, you allow that your information in this study are verified, processed and reported as needed for scientific legitimate purposes.

10. CONFIDENTIALITY AND PERSONAL DATA TREATMENT

The personal data of the study participants, including the medical information collected or created as apart of this study (eg. Medical records, test results) will be used for the conduction of this study, namely to scientific research purposes related with the diseases under study.

By giving consent to your participation in this study, the information that concerns you, namely the clinical information, will be used in the following ways:

1. The researchers and other people involved in the study will collect and use your personal data for the abovementioned purposes.

2. The study data, associated with a code number that does not identify yourself directly, will be communicated by the investigator to other people involved in the study, that will use it for the abovementioned purposes.

3. The study data, associated with a code number that does not allow to identify yourself directly, may be communicated to national and international health authorities.

4. Your identity will not be revealed in any reports or publications resulting from this study.

5. All the people and entities with access to your personal data will be obligated to professional confidentiality.

6. By giving your consent to participate in the study, you authorize the monitoring companies
of these type of studies specifically hired for the effect and its collaborators and/or health authorities to access the data in your medical records, to confer the collected and recorded information by the investigators, in order to assure the rigor of the data and to guarantee that the study is being developed correctly and that the data is reliable.

7. According to the law, you have the right of, through any of the doctors involved in the study, to ask for access to the data that are concerned with you, as well as to ask rectification of your identification data.

8. You also have the right to withdraw this consent at any point, through the notification of the investigator, what will imply that you stop participating in this study. However, the collected or produced data as part of the study until that point that do not identify yourself may continue to be used for the purposes of the study, namely to keep the scientific integrity of the study, and your medical information will be removed from the study archive.

9. If you do not give consent, by signing this document, you may not participate in this study. If the consent given now is not withdrawn and until that point, it will be valid and operative.

11. COMPENSATION

This study is of the investigator’s initiative and, because of that, your participation is asked without a financial compensation for its execution, as it happens to the investigators and the study site. The study site will support all the costs related to the performed procedures. Therefore there will be no costs for you as a participant in this study.

12. CONTACTS

If you have any questions regarding your rights as a participant in this study, you shall contact:

Ethical Committee of the Faculty of Medicine of the University of Coimbra
Azinhaga de Santa Comba, Celas – 3000-548 Coimbra
Telephone: 239 857 707
email: comissaoetica@fmed.uc.pt
If you have any questions about this study, you should contact:

Miguel Tábuas Pereira  
Neurology Department – Centro Hospitalar e Universitário de Coimbra  
Praceta Prof. Mota Pinto  
3000-045 Coimbra  
Telefone: 91 3166131  
Email: miguelatcp@gmail.com
DO NOT SIGN THIS INFORMED CONSENT FORM
UNLESS YOU HAVE HAD THE OPPORTUNITY TO ASK
AND HAVE RECEIVED SATISFYING ANSWERS
TO ALL OF YOUR QUESTIONS.

INFORMED CONSENT

According to the World Medical Association Helsinki Declaration and their updates:

1. I declare that I have read this form and accept to voluntarily participate in this study.

2. I was properly informed about the nature, aims, risks, probable duration of the study, as well as what is expected from me.

3. I had the opportunity to ask questions about the study and I have understood the answers and information I was given.

At any point I may ask further questions to the doctor responsible for the study. During the study and anytime I want, I may receive information about its progression. The responsible doctor will give all the important information that comes during the study that may affect my will to continue in the study.

4. I accept that the information about my clinical history is used in the strict respect of medical secrecy and anonymity. My data will be kept strictly confidential. I authorize the access to my data only by the people designated by the promotor and by regulatory agencies representatives.

5. I accept to follow the instructions given to me during this study. I accept to collaborate with the doctor and inform him or her immediately about changes in my health status and well-being and about any unexpected symptoms that may occur.

6. I authorize the use of the results of exclusively scientific purposes and, in particular, I accept that these results are disclosed to the competent health authorities.
7. I accept that the data generated during this study will be computerized by the promotor or someone designated by.

I may use my right of rectification and/or opposition.

8. I know that I am free to quit the study at any point, without having to justify my decision and without compromising the quality of my medical care. I know that my doctor has the right of deciding about my premature leave of the study and that he will inform me about it.

9. I was informed that the study may be interrupted by the investigator’s, promotor’s or regulatory agencies’ decision.

Participant’s name____________________________________________________________
Signature: ____________________________ Date: ______/_____/____

Name of the witness /Legal representative:__________________________________________
Signature: ____________________________ Date: ______/_____/____

I confirm that I have explained the abovementioned participant about the nature, aims and potential risks of the abovementioned study.

Investigator’s name:____________________________________________________________
Signature: ____________________________ Date: ______/_____/____
I consent that the genetic data collected for the purpose of this study, may be stored and used by the investigators of this study in future research on the genetics of Alzheimer’s disease or other neurodegenerative disorders.

☐ Yes  ☐ No

Participant’s name____________________________________________________________
Signature:___________________________________________ Date:_______/_____/____

Name of the witness /Legal representative:
Signature:___________________________________________ Date:_______/_____/____

I confirm that I have explained the abovementioned participant about the nature, aims and potential risks of the abovementioned study.

Investigator’s name:____________________________________________________________
Signature:___________________________________________ Date:_______/_____/____