

**INSTITUT D'INVESTIGACIÓ EN CIÈNCIES DE LA SALUT GERMANS TRIAS I
PUJOL**

TECHNICAL SPECIFICATIONS DOCUMENT

**CONTRACTING SERVICES FROM A SPECIALIZED HIGH-THROUGHPUT
GENOMICS LABORATORY FOR THE CHARACTERIZATION OF METHYLATION
PATTERNS USING THE "Methylation Epic V2.0 BeadChip Kit" FOR THE
GERMANS TRIAS I PUJOL HEALTH SCIENCE RESEARCH INSTITUTE
FOUNDATION**

Exp. 12563/2024

NON-HARMONIZED PROCEDURE

1. OBJECT OF CONTRACTING

The purpose of this procedure is to invite suppliers to submit proposals for the contracting of services from a specialized high-throughput genomics company to perform DNA methylation analysis on the blood of participants from the GCAT cohort, part of the CUPID research project "Understanding the relationship between chrono-nutrition and cardiometabolic disorders: an epigenetic perspective," in accordance with the protocol attached as an Annex to the Specific Administrative Clauses Document.

2. OBJECTIVE OF THE STUDY

Alterations in the circadian rhythm associated with the activities of a modern 24-hour society, such as night work, late eating, or reduced sleep, can increase the risk of cardiometabolic diseases such as obesity, diabetes, and cardiovascular diseases. However, many aspects of circadian behaviors, particularly those related to "chrono-nutrition," need to be considered holistically to better understand their impact on health.

There is a lack of studies to better understand the molecular mechanisms explaining these associations. A possible hypothesis is that alterations in circadian rhythms affect epigenetics, specifically in how genes are expressed, particularly in a mechanism that can control gene expression without affecting genetic information, known as DNA methylation.

The CUPID project will investigate how this relates to cardiovascular health: if circadian epigenetic markers modified by chrono-nutritional behaviors are associated with differences in cardiometabolic disease risk, this would indicate a potential mediating effect of methylation in the role of nutritional circadian misalignment in these diseases. The project's objective is to identify DNA methylation patterns that may be associated with alterations in chrono-nutrition patterns as mediators of pathological processes and mechanisms involved in higher cardiovascular risk, as well as to serve for the identification of potential markers of cardiovascular events. These analyses will be combined with in-silico bioinformatics techniques in our laboratory.

3. OBJECTIVE OF THE SERVICE

IGTP is seeking a laboratory/supplier capable of performing DNA methylation analysis on at least N=540 blood samples using state-of-the-art methods within a period of 6 months.

The purpose is to contract the services of a specialized high-throughput genomics company for the discovery of methylation patterns using Illumina technology, specifically the "Methylation Epic V2.0 BeadChip Kit," for the CUPID research project "Understanding the relationship between chrono-nutrition and cardiometabolic disorders: an epigenetic perspective." The objective is to conduct an epigenome-wide association study (EWAS) between chrono-nutritional patterns and CpG methylation marks in the genome, subsequently defining the relationship.

4. PROJECT CHARACTERISTICS

Study Phase: Basic Research

Therapeutic Area: Human Molecular Epidemiology; Genomics, Epigenomics

Indication: Lifestyle habits, diet, chronotype, cardiovascular risk, diagnosis, and prognosis

5. MINIMUM ESSENTIAL CHARACTERISTICS REQUIRED

The service must include:

- State-of-the-art, large-scale techniques with arrays that allow the analysis of a high number of samples and CpG loci per reaction.
- High sensitivity and robustness in the quantitative detection of methylation levels.

6. CONDITIONS

The selected laboratory must meet these requirements:

- Specific experience in working with high-throughput epigenetic genomics platforms such as the "Methylation Epic V2.0 BeadChip Kit" (approximately 935K sites), with minimal sample volumes and high sensitivity of at least one year and at least 10 works carried out.

The following will be considered essential obligations of the awarded provider:

- Initial meeting at the beginning of the project and communication at the end of each stage: assay design, sample reception, quality control, sample preparation for assay (aliquoting), result control, final results, and on-demand at any time during the project. Ensuring that project partners' feedback is considered for solution development.
- Conducting cross-quality controls with previously analyzed GCAT samples.
- Ensuring all data is kept secure and compliant with legal regulations.
- Bimonthly progress reports on the work.
- Delivery of final results.

7. EXECUTION PERIOD

The execution period for the project and delivery of reports and results will be 6 months (from the delivery of DNA samples), unless otherwise agreed upon services modification, as established in the Specific Administrative Clauses Document, which will determine the execution period of the modification