Genoma España

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The Spanish National DNA bank infrastructure: promoting disease-oriented genetic/genome research

ESF-UB Conference

Biobanks: Introduction and Next Steps

Sant Feliu de Guixols, 5th November 2008

Genoma España

GENOME SPAIN INITIATIVE

The **National DNA Bank of Spain** is a technological platform created in March 2004 by a collaboration agreement between *Fundación Genoma España*, *Universidad de Salamanca* and *Consejería de Sanidad de la Junta de Castilla y León*, with the aim of promoting genomic research in Spain.

NATIONAL DNA BANK of SPAIN

GENERAL GOAL

To promote and support research on genetic/genomic diversity associated with HEALTH, disease pathogenesis and therapy, and human evolution, with special emphasis on the population living in Spain.

- To identify genes in complex diseases.
- To dissect the role of environmental, social, nutritional and lifestyle factors in complex diseases.
- To promote research in pharmacogenomics (interaction between genes, phenotype and drug response).

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National DNA Bank of Spain

Major roles

- To obtain, process and store biological samples and their associated data.
- To provide DNA samples to research groups.
- To ensure a rational, effective, ethical and legal use of the available resources.

The real value of a biobank lies on the existence of "cooperative research projects of excellence".

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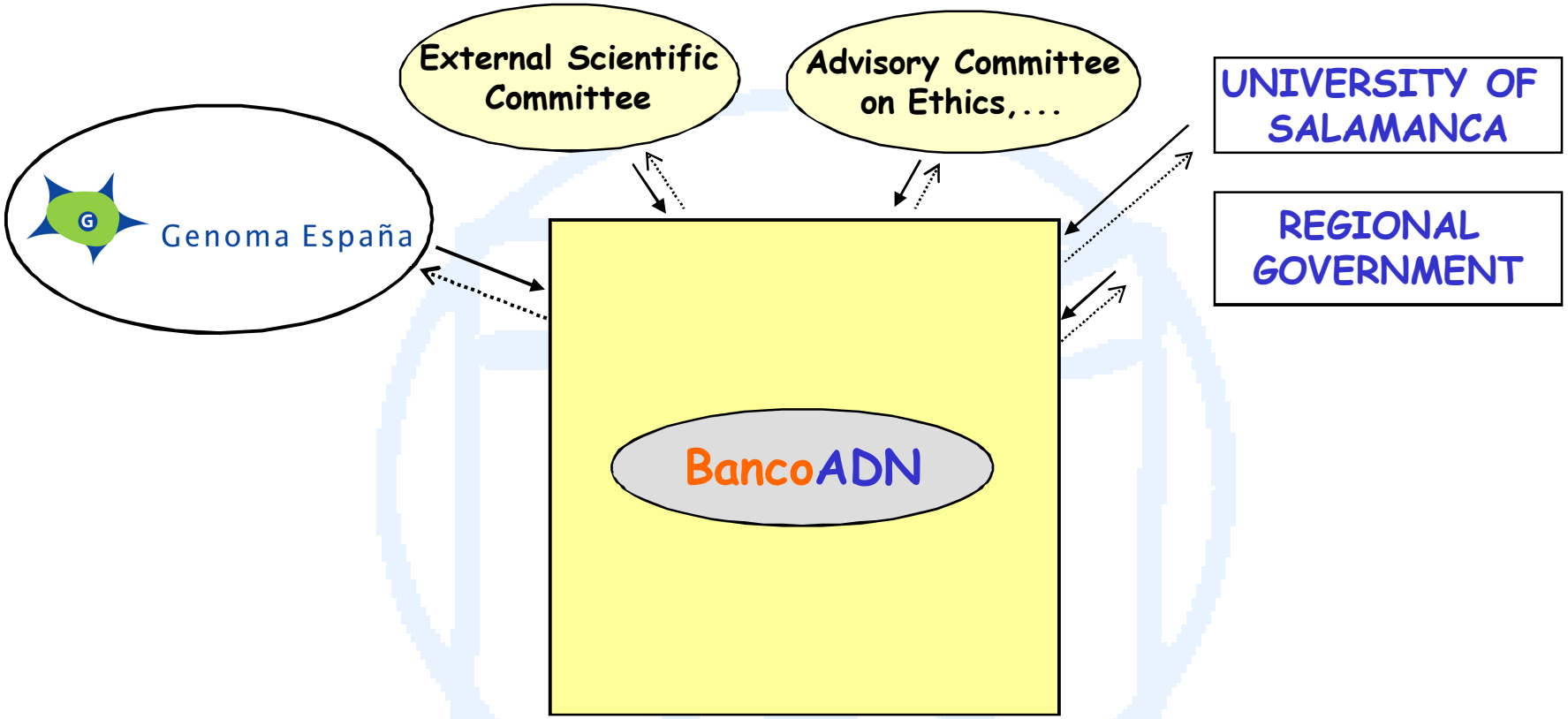
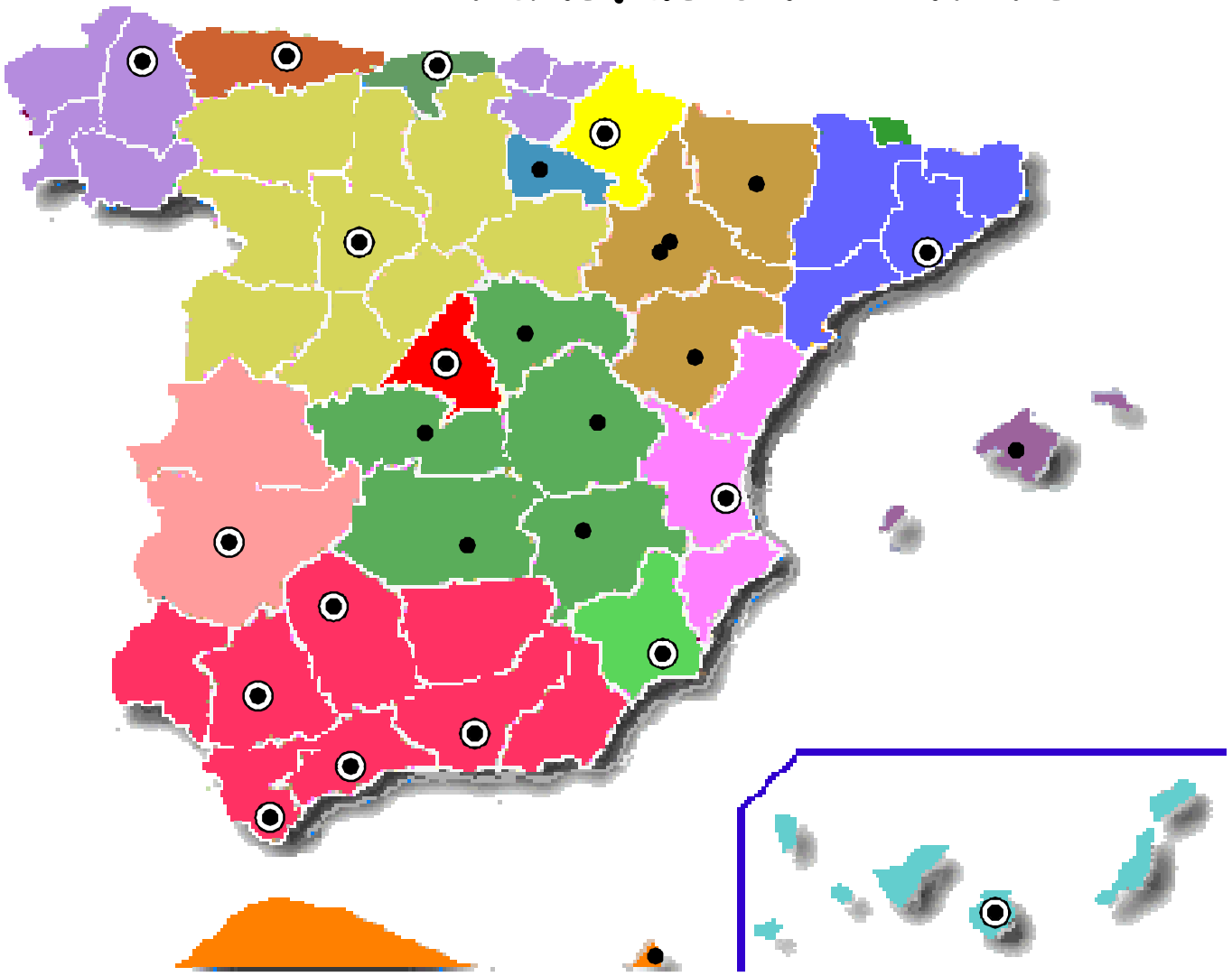
STRUCTURE (until October 2006)



National DNA Bank of Spain
Network of Blood Banks and Regional Transfusion Centers



◉ REGIONAL BLOOD TRANSFUSIÓN CENTERS • BLOOD BANK

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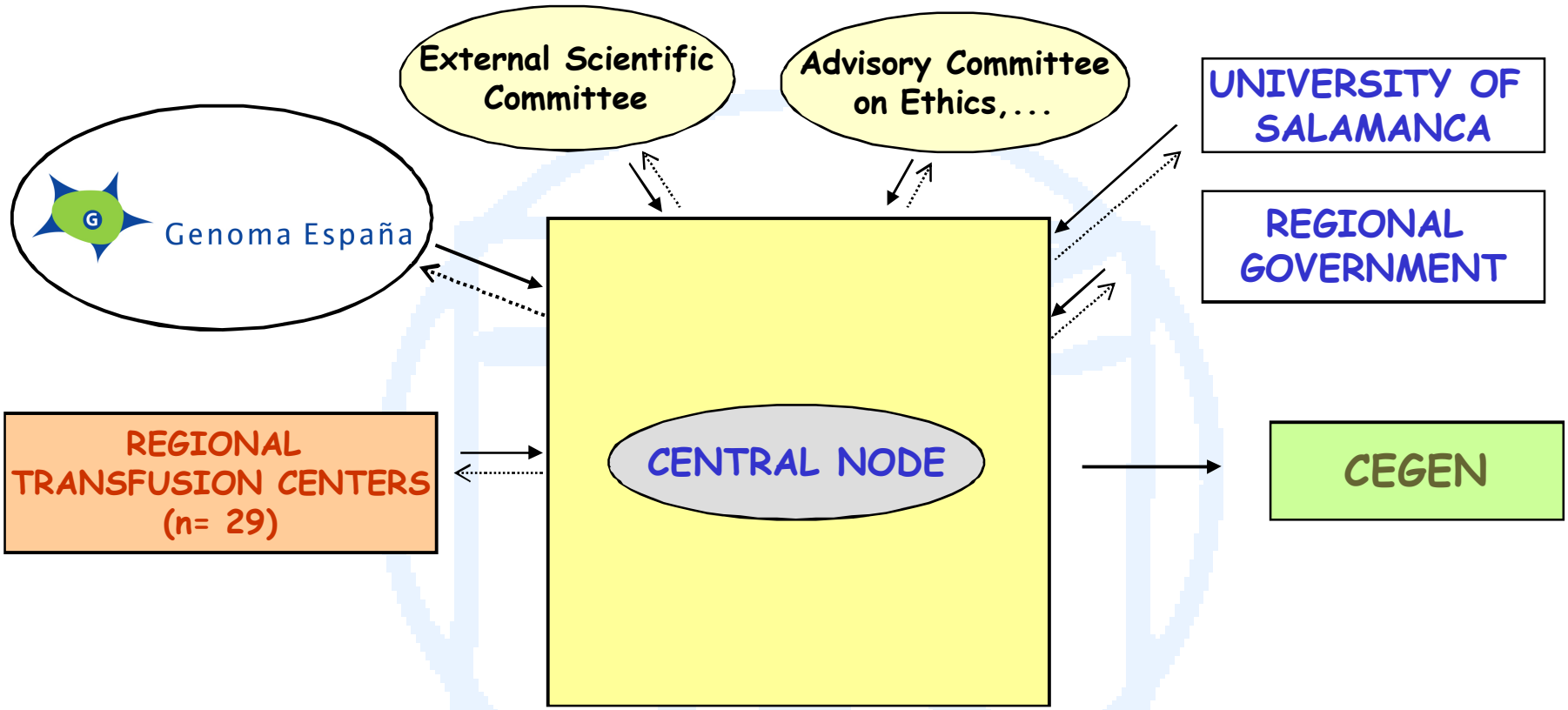
STRUCTURE (until October 2006)



COHORT OF SAMPLES OF REFERENCE OF THE SPANISH POPULATION

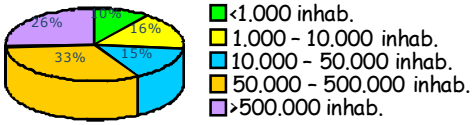
All samples stored at the National DNA Bank of Spain contain associated information & informed consent.

N. of samples: **1003**

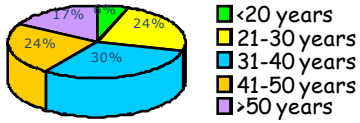
Status: **AVAILABLE**

Region (CCAA)	N. of samples received
Andalucía	154
Aragón	26
Asturias	25
Baleares (Islas)	26
Canarias	22
Cantabria	25
Castilla la Mancha	32
Castilla y León	69
Cataluña	157
Ceuta	10
Comunidad Valenciana	97
Extremadura	25
Galicia	94
La Rioja	25
Madrid	149
Melilla	12
Murcia	30
Navarra	25
Subtotal number of stored samples	**1003**

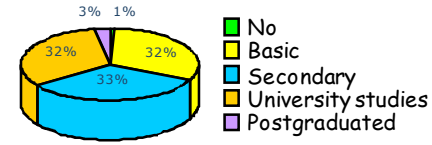
DISTRIBUTION ACCORDING TO SIZE OF PLACE OF BIRTH



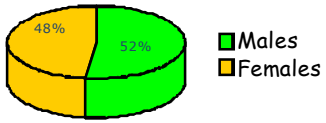
AGE DISTRIBUTION



DISTRIBUTION ACCORDING TO EDUCATION STUDIES



GENDER DISTRIBUTION



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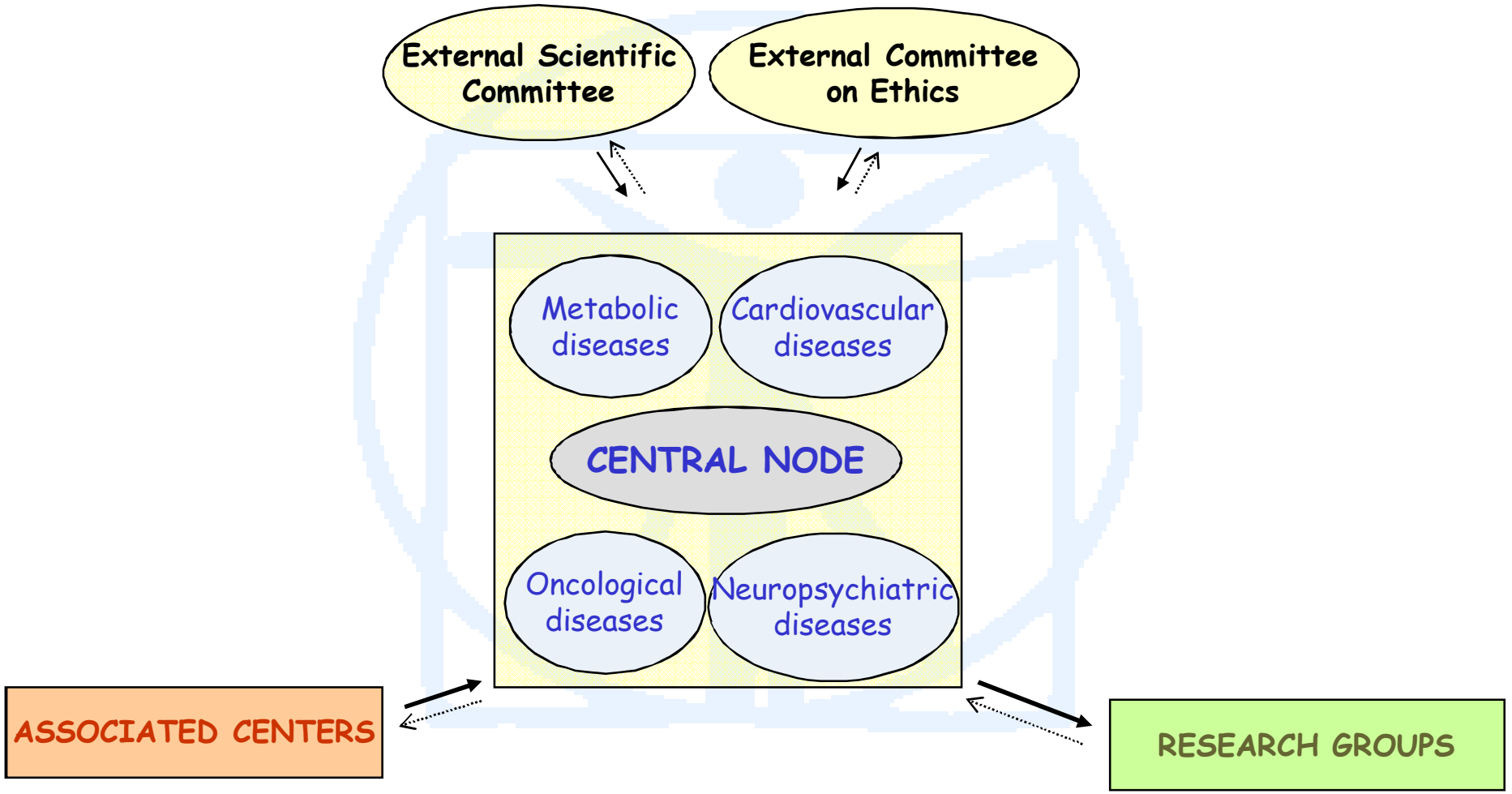
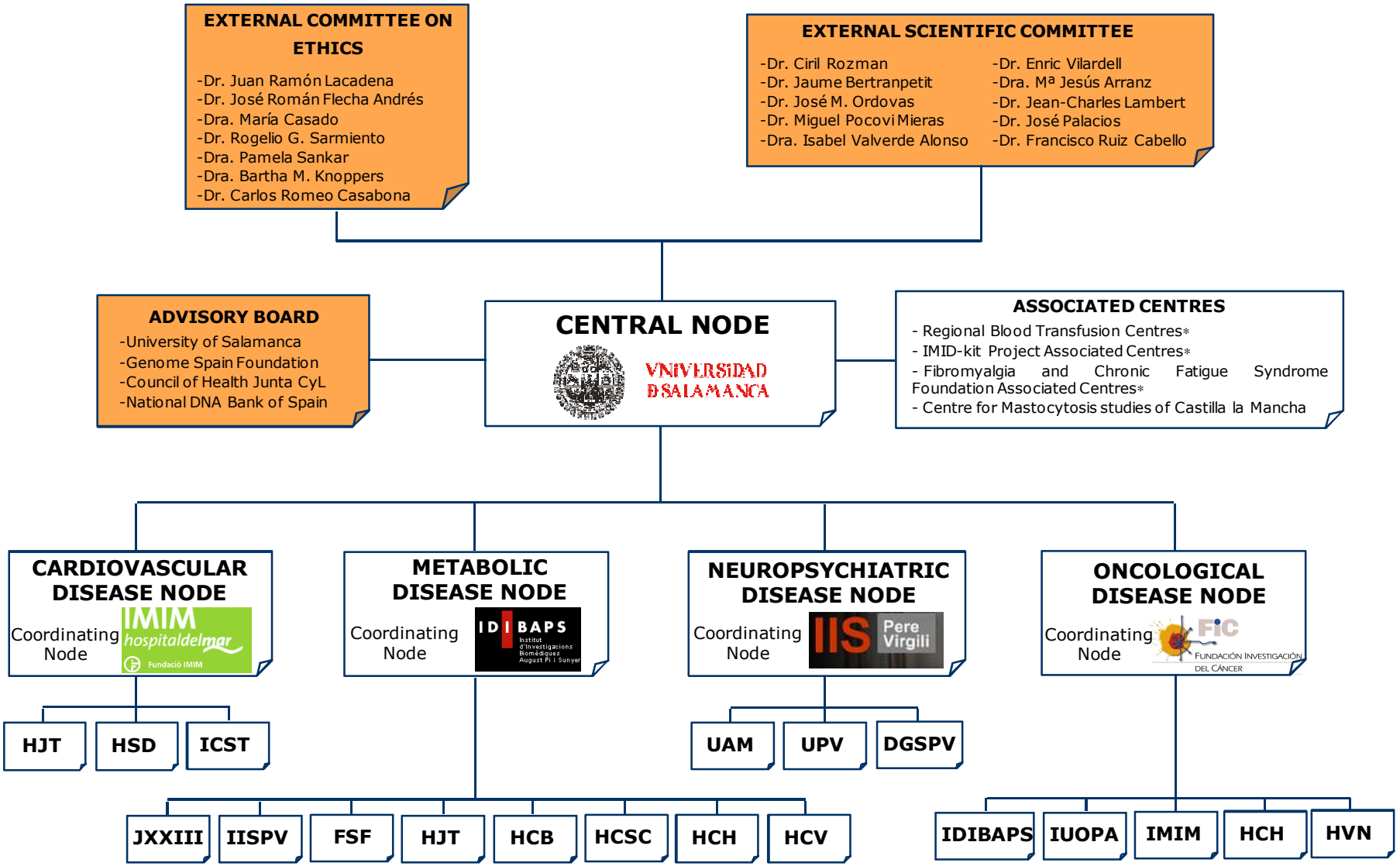
STRUCTURE (since October 2006)



National DNA Bank of Spain

STRUCTURE



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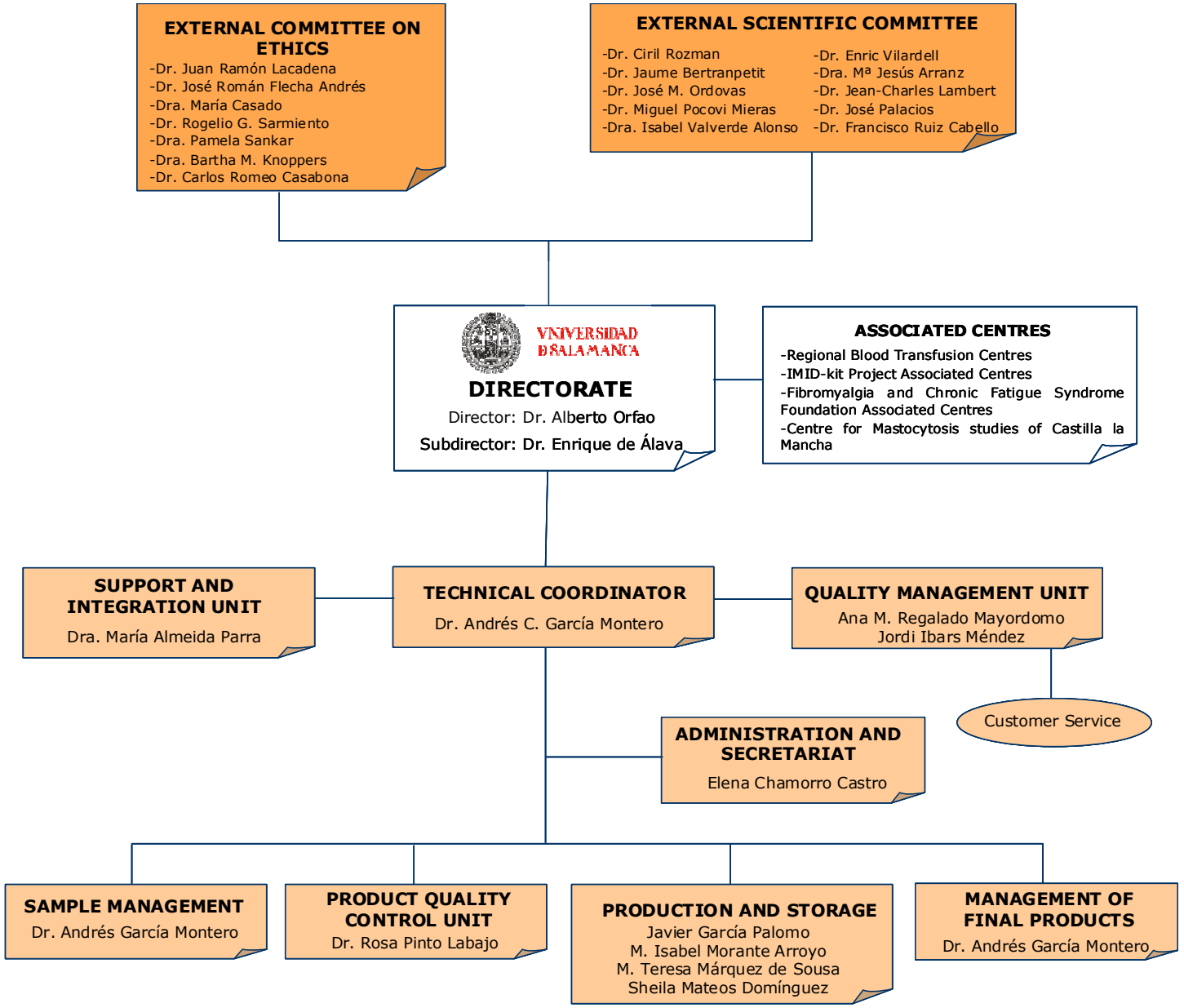
NATIONAL DNA BANK of SPAIN
CENTRAL NODE STRUCTURE



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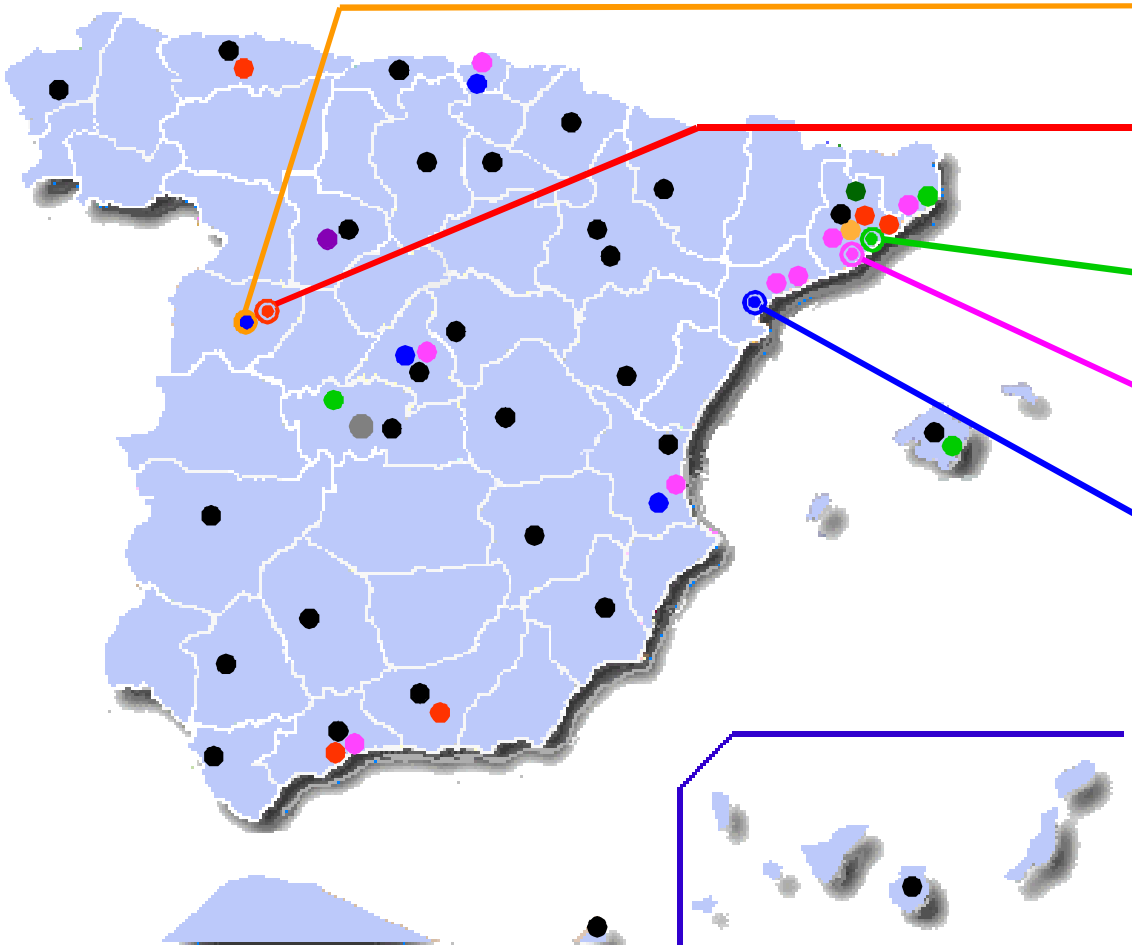
National DNA Bank of Spain

NETWORK STRUCTURE



Central Node
Coordinating center: **Universidad de Salamanca**
Director: **Dr. Alberto Orfao**

Oncological Node
Coordinating center: **Centro de Investigación del Cáncer (Salamanca)**
Coordinator: **Dr. Enrique de Álava**

Cardiovascular Node
Coordinating center: **Fundación IMIM (Barcelona)** Coordinator: **Dr. Jaume Marrugat**

Metabolic Node
Coordinating center: **IDIBAPS-Hospital Clinic (Barcelona)** Coordinator: **Dr. Ramón Gomis**

Neuropsychiatric Node
Coordinating center: **Institut d'Investigació Sanitària Pere Virgili (IISPV) (Reus)**
Coordinator: **Dra. Elisabet Vilella**

- Regional Blood Transfusion Centers
- Consejería de Sanidad JCyL
- Foundations for Fibromialgy and Chronic Fatigue Syndrome
- Hospital Vall d'Hebron
- Centro de Estudios de Mastocitosis de Castilla la Mancha

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ONCOLOGICAL DISEASES:

SOLID TUMORS:

Colorectal, breast, head & neck, lung and prostate

HEMATOLOGIC MALIGNANCIES:

Chronic lymphocytic leukemia, chronic myeloproliferative disorders, acute leukemias, Non-Hodgkin lymphomas

N. of estimated samples: **4,350**

N. of samples stored: **3,011**

CARDIOVASCULAR DISEASES:

Hypertension, myocardial infarction, ictus, heart failure, auricular fibrillation

N. of estimated samples: **2,500**

N. of samples stored: **1,514**

NEUROPSYCHIATRIC DISEASES:

Schizophrenia, Alzheimer, Parkinson, multiple sclerosis, amyotrophic lateral sclerosis, idiopathic cervical dystonia

N. of estimated samples: **2,300**

N. of samples stored: **871**

METABOLIC DISEASES:

Diabetes Mellitus (type I), Diabetes Mellitus (type II), obesity, morbid obesity, dyslipemias, controls

N. of estimated samples: **2.500**

N. of samples stored: **1,899**

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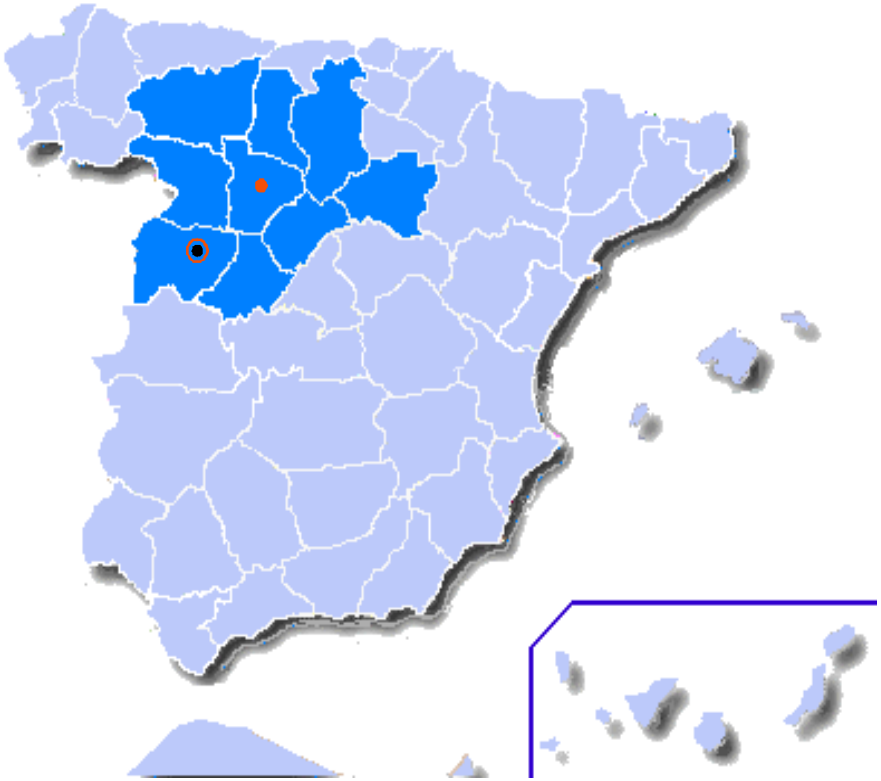
POPULATION OF CASTILLA Y LEÓN: STUDY OF CARDIOVASCULAR RISK



COORDINATING NODE: **Banco Nacional de ADN**

Director: Prof. Alberto Orfao de Matos

Consejería de Sanidad, JCyL: (Valladolid)

Project coordinator: Dr. Tomás Vega Alonso

N. of samples: **3,488**

Status: **Available**

All samples have written informed consent restricted to research projects related to cardiovascular risk.

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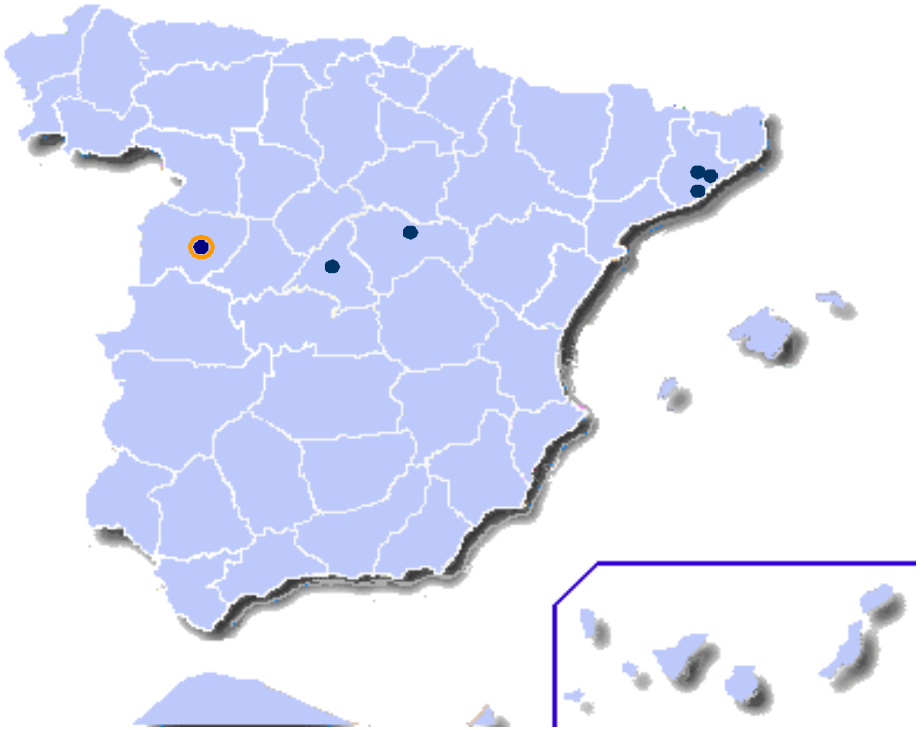
FIBROMIALGY AND CHRONIC FATIGUE SYNDROME



COORDINATING NODE: National DNA Bank of Spain Director: Prof. Alberto Orfao de Matos

Fundación de Fibromialgia y Síndrome de Fatiga Crónica:

Project coordinator: Dr. Antonio Collado

Supporting Institution: Fundación de Afectados y Afectadas de Fibromialgia y Síndrome de Fatiga Crónica

N. of estimated samples: **3000**

Available in October 2008: 989

The **National DNA Bank of Spain** and the **Foundation for Fibromialgy and Chronic Fatigue Syndrome** collaborate to support scientific research on patients with fibromialgy and chronic fatigue syndrome.

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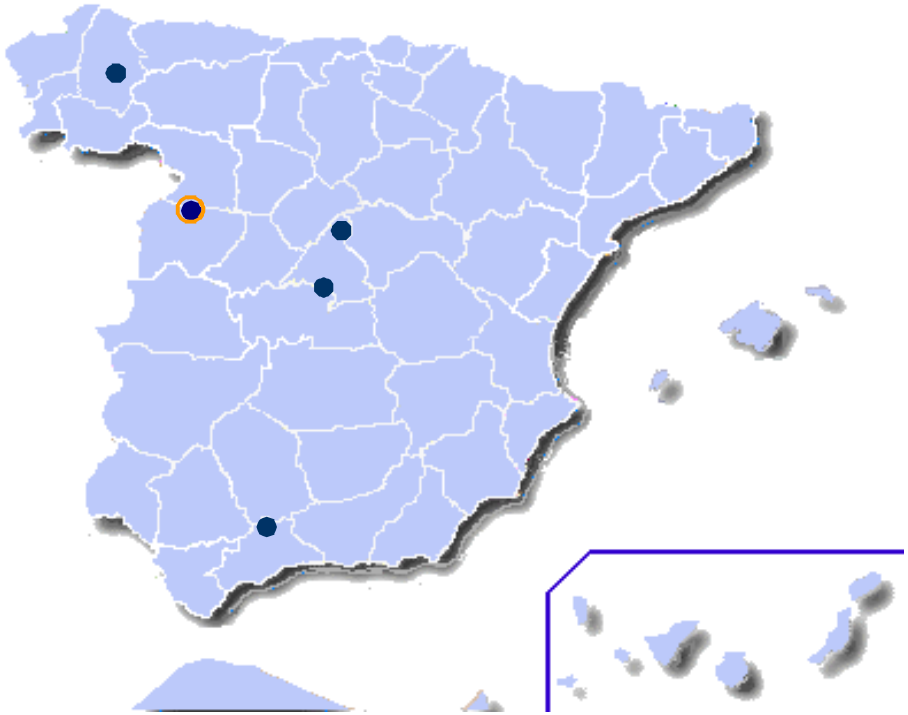
SPANISH NETWORK ON MASTOCYTOSIS: DNA/CELL BANK



COORDINATING NODE: Banco Nacional de ADN
Director: Dr. Alberto Orfao de Matos

Red Española de Mastocitosis (REMA):
Project Coordinator: Dr. Luis Escribano

N. of estimated samples: **3000 (patients and family members).**

Available in October 2008: 167

The **National DNA Bank of Spain** and the **REMA (Spanish Network on Mast cell disorders)** cooperate to promote scientific research on mastocytosis.

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"Singular and Strategic Projects" of the Ministry of Education and Science

"Determination of genetic predictors and therapeutic targets in immune mediated inflammatory diseases (IMID) using a whole genome strategy"

Principal Investigator: **Dra. Sara Marsal**
(Fundación Institut de Recerca del Hospital Universitari Vall d'Hebron)

Project duration: **2007-2010**

DISEASES:	N. SAMPLES:
Rheumatoid Arthritis	3.000
Psoriasis	3.000
Crohn disease	3.000
Controls	3.000
TOTAL:	**12,000***

ASSOCIATED INSTITUTIONS:

- Fundación Institut de Recerca del Hospital Universitari Vall d'Hebron
- Schering-Plough S.A.
- Universidad de Salamanca (Banco Nacional de ADN)
- Fundació Centre de Regulació Genòmica
- Universitat Pompeu Fabra CCT
- Hospital General Universitario Gregorio Marañón
- Fundación Privada Clinic per la Recerca Biomedica
- Barcelona Supercomputing Center
- Centro Nacional de Investigaciones Oncológicas
- Hospital Universitario de la Princesa

***3,388 collected samples**

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BNADN: AVAILABLE SAMPLES (2008)

	N.of samples	Cell lines
Control population:		
- Spanish population	1.840	1.000
- Population of Castilla y León	3.488	
- Nonagenarians	30	
Prevalent diseases:		
- Neuropsychiatric diseases	871	157
- Metabolic diseases	1.899	
- Cardiovascular diseases	1.514	238
- Oncological diseases	3.011	
Other diseases:		
- Fibromialgy and Chronic Fatigue Syndrome	1.231	
- Mastocytosis	167	
- Immune-mediated inflammatory diseases and controls	3.388	
Total:	**17.438**	**1.395**

BNADN: OVERALL PROGRESS IN PROVIDING SERVICES

2004 - Creation of the BNADN

2005 - Collection representative of the Spanish healthy population (n=1,003).

2006 - Incorporation of 4 nodes on major/frequent diseases
- Population based collection of Castilla y León (n=3,488)
- Fibromyalgia & chronic fatigue syndrome (n=242)

2007 - New bank on Mastocytosis (August)
- New bank on IMID (August)
- New collection on population-based controls (November)
- New extended bank on FM & CFS (January 2008)
- New collections on major diseases (October 2006)

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BNADN: OVERALL PROGRESS IN PROVIDING SERVICES

2008 - Bank on Mastocytosis (n=167)
- Bank on IMID (n=3,388)
- New population-based controls (n=837)
- New extended bank on FM & CFS (n=1.231)
- New collections on major diseases (n=7.295)

- **New banks with Working Groups of:**
  Spanish Society of Internal Medicine (July)
  Spanish Society on Atherosclerosis

	Year				
	2004	2005	2006	2007	2008
N. of samples	160	1,003	4,733	10,435	17,438

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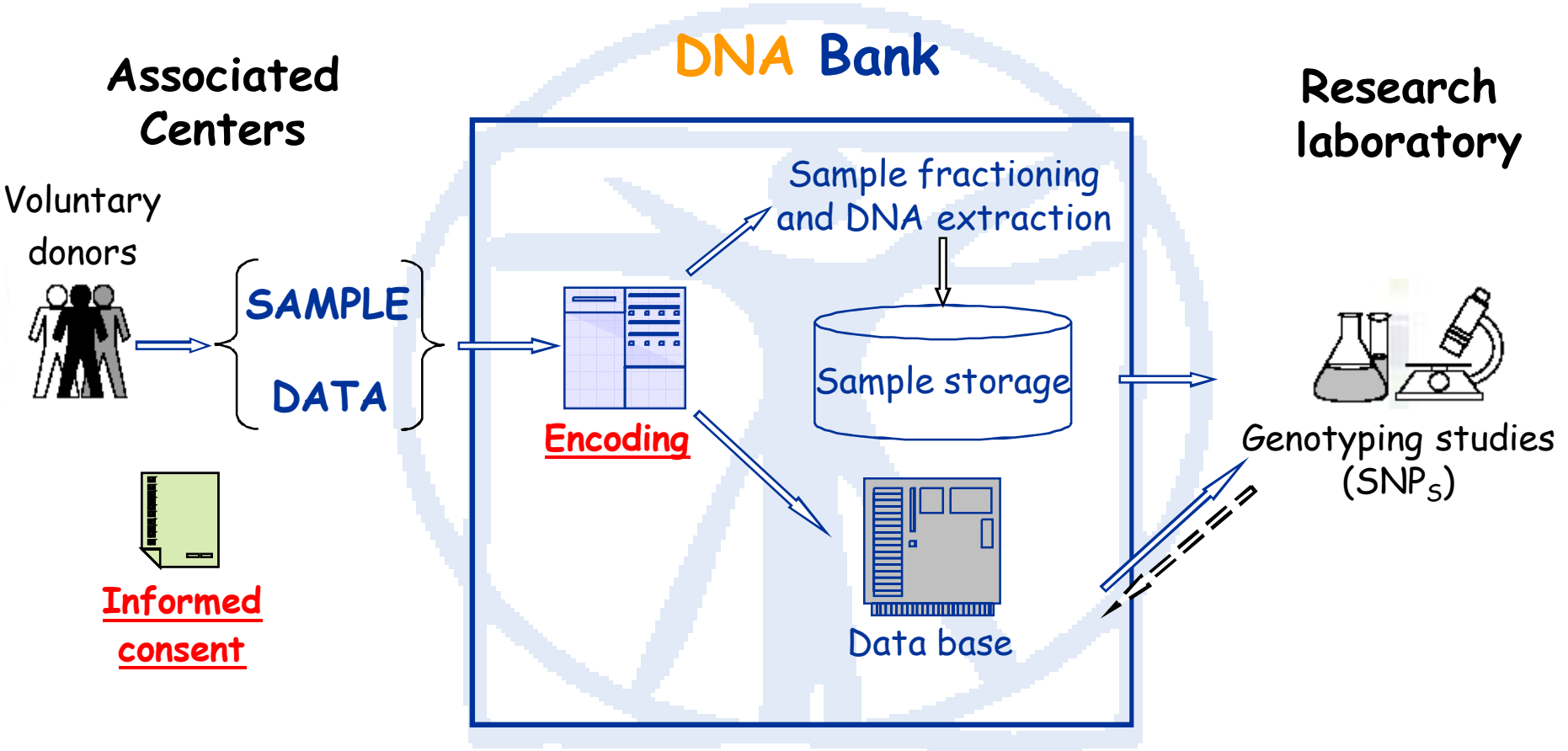
Laboratory Integrated Management System



1st Donation code → 2nd Internal code → 3rd Send out code

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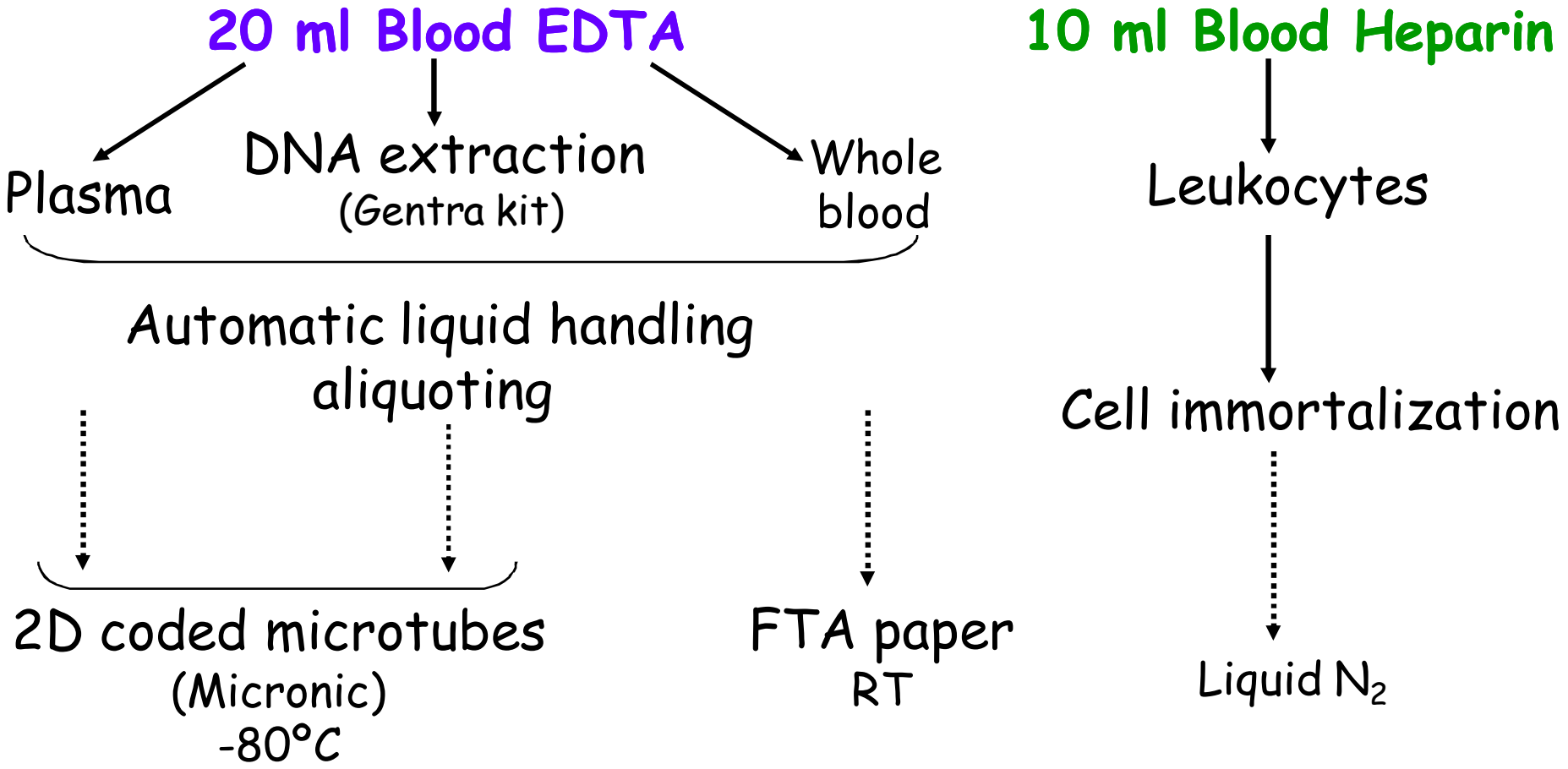
SAMPLE* FRACTIONING



STORAGE

* Also tumour tissues, urine, mRNA, miRNA, depending on disease type

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ASSOCIATED DATA

Epidemiologic questionnaire:

- **General Health**
  (familiar antecedents)
- **Nutritional and lifestyle habits**
  (smoking, alcohol, physical activity…)
- **Demographic data**
  (family, place of living, culture…)
- **Genealogic data**
  (two generations)
- **Phenotypic data**
  (biochemical analysis, virology, anthropometrical measurements)

Disease questionnaire:

(Specific for each type of disease)

Data always included:

- **Clinical data**
- **Diagnostic data**
- **Outcome data**
- **Associated diseases**

EQUIPMENT RESOURCES

INTEGRATION SOFTWARE:

LIMS (*VITRO S.A.*) specifically developed by Vitro SA and the BNADN

AUTOMATION:

Automatic DNA extraction **Robot**, ***Autopure LS (GENTRA)***

Spectrophotometers and fluorimeter, *Nanodrop (Nanodrop Technologies) and* GENios (TECAN)

Liquid handler **robots**, *GENESiS 150 and freedom EVO* (*TECAN*): aliquoting

2D code microtube aliquoting system (***Micronic®***)

Programmable cell fridge, ***Criomed*** (*Thermo*)

BIOSAFETY:

Biosafety **Level III** laboratory (50m^2): Cell line production

Biosafety cabinets (Bio IIA): Sample processing and cell culture

STORAGE:

Stabilized freezer **4°C** (*Thermo*): DNA (short term storage)

Mechanical freezers **-80°C**: plasma and DNA (long term storage)

Vapor phase **liquid nitrogen** (*CBS Scientific*): lymphocytes and cell lines

QUALITY MANAGEMENT SYSTEM

The **National** DNA **Bank** has developed, documented and implemented a **quality management system (QMS)** according to **UNE-EN-ISO 9001:2000** model, as a basic strategy for increasing the user's and other interested parties satisfaction by guarantying the fulfillment of the requirements.

Certified: **February 2006,**

ISO 9001
BUREAU VERITAS
Certification

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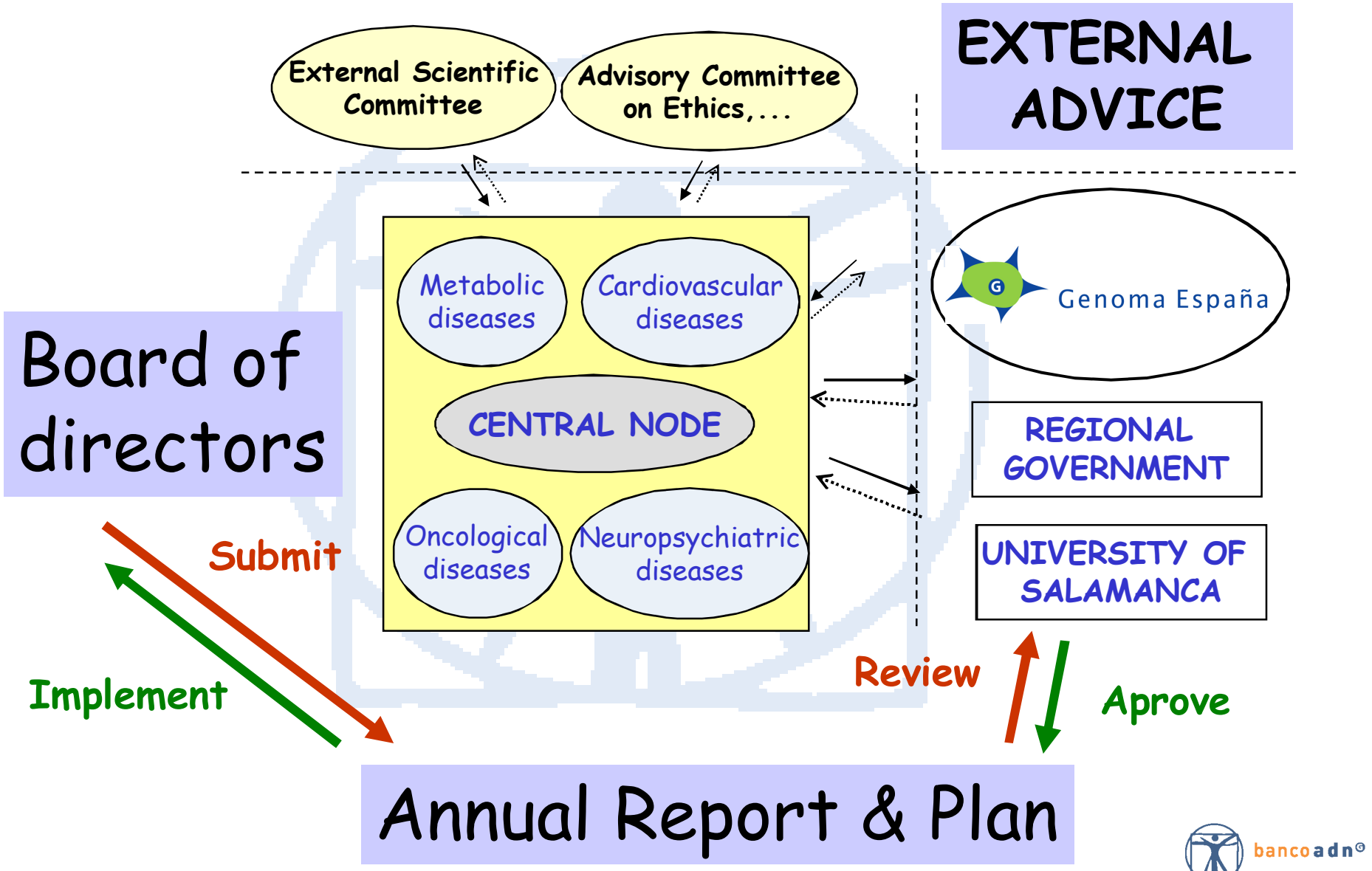
National DNA Bank of Spain

STRUCTURE (since October 2006)



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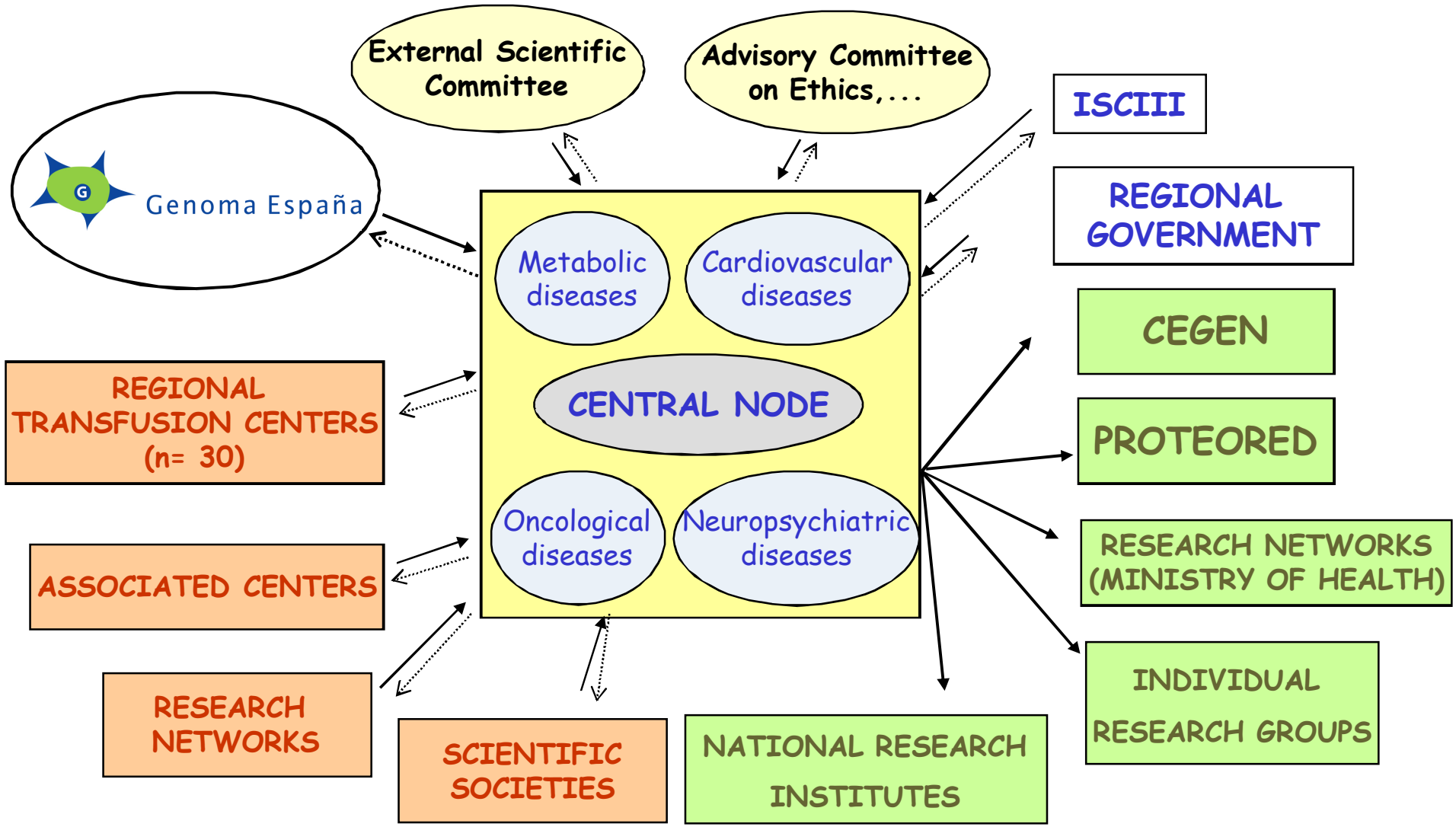
STRUCTURE (since October 2006)



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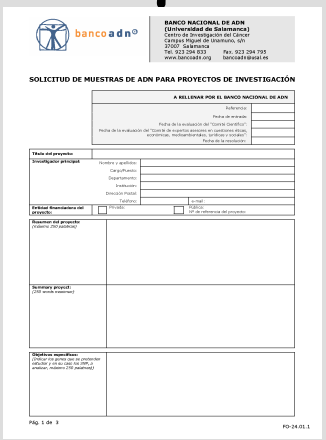
Access to DNA samples

Research groups: National, European and International (in collaboration projects with Spanish groups)

Research projects: "of scientific interest" and favorable evaluated by the External Committees.

DNA samples request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BANCO NACIONAL DE ADN
[Universidad de Salamanca]
Centro de Investigación del Cáncer
Campus Miguel de Unamuno, s/n
37007 Salamanca
Tel.: 923 294 810 Fax: 923 294 795
www.bancoadn.org bancoadn@usal.es

SOLICITUD DE MUESTRAS DE ADN PARA PROYECTOS DE INVESTIGACIÓN

A RELLENAR POR EL BANCO NACIONAL DE ADN

Título del proyecto

Investigador principal

Nombre y apellidos
Cargo/Puesto
Departamento
Institución
Dirección Postal
Teléfono
e-mail

Entidad financiadora del proyecto

Nº de referencia del proyecto

Resumen del proyecto

Summary project

Objetivos específicos

Pág. 1 de 3

FO-24.01.1

Evaluation of the request

External Committees

<30 days

Delivery of the samples

Anonymous samples (n> 100)

<30 days

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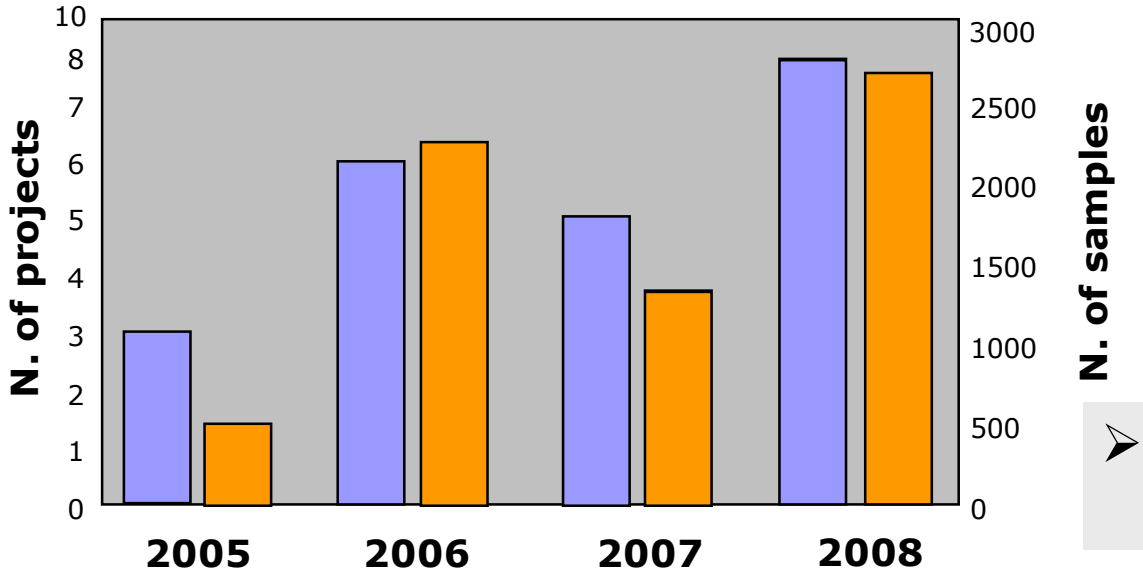
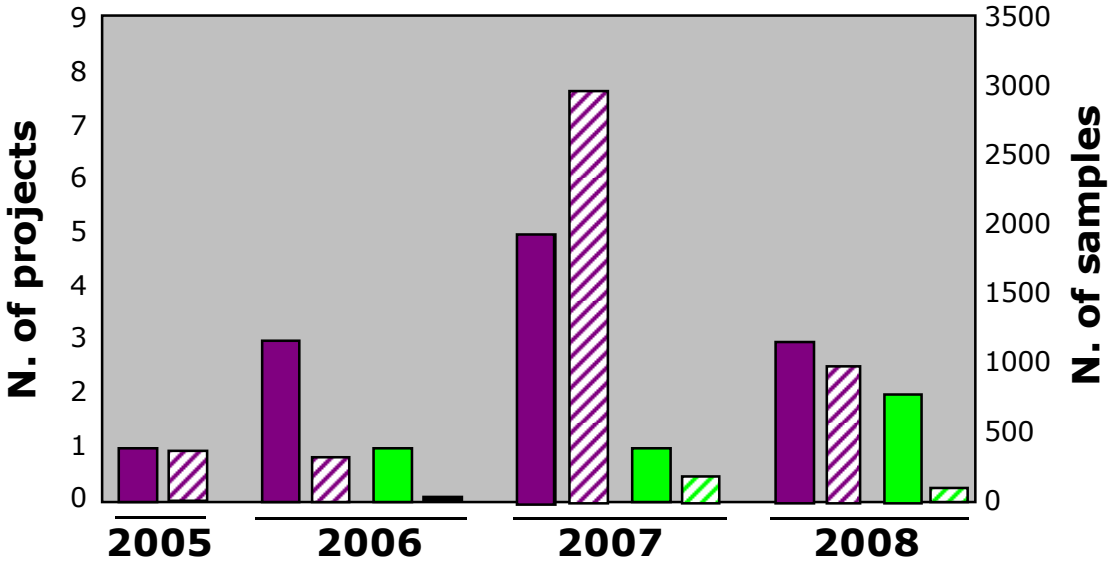
EXTERNAL ACCESS TO DNA SAMPLES



- 9.303 samples distributed
- 25 research projects

OTHER SERVICES



- 4.686 samples
- 16 service requests

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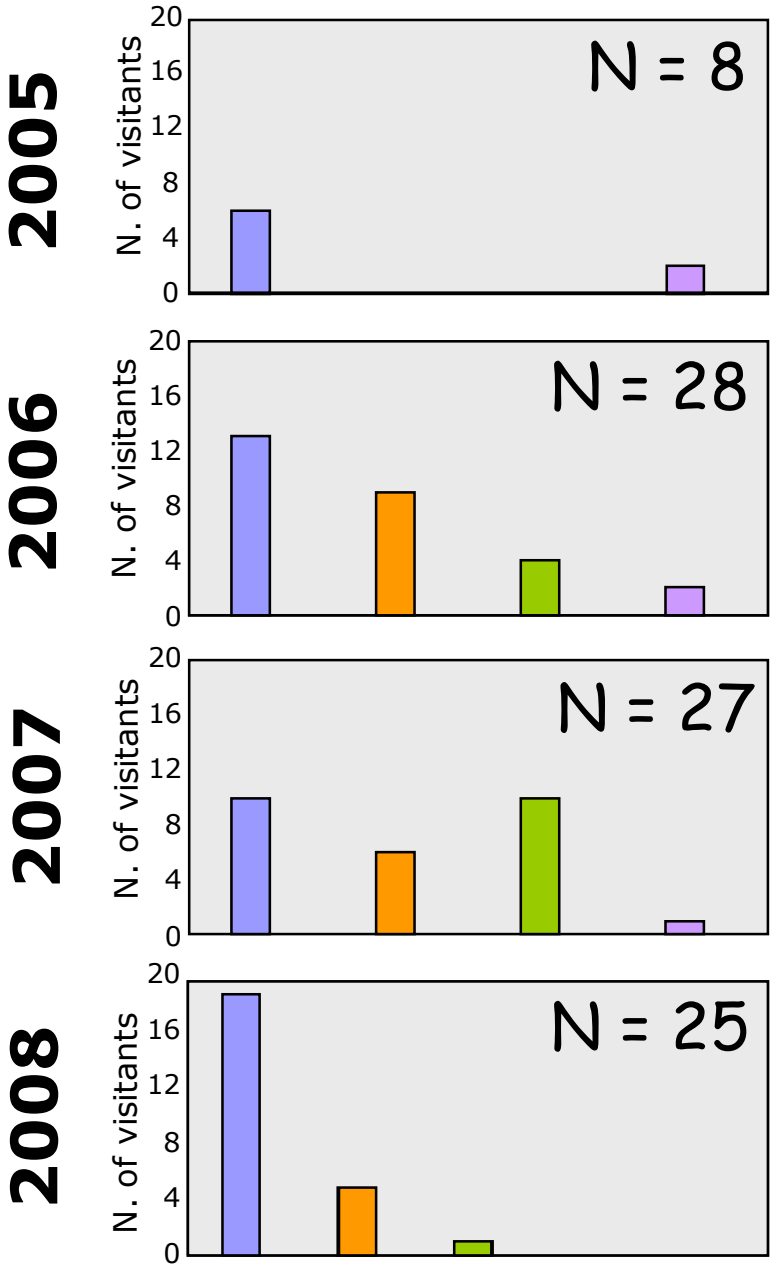
VISITS AND TRAINING COURSES



- 88 Visitors
- Mean stay of: 5 days

Academic Qualification

PhD	Laboratory Technician
Bachelor	Laboratory Technician on Practice

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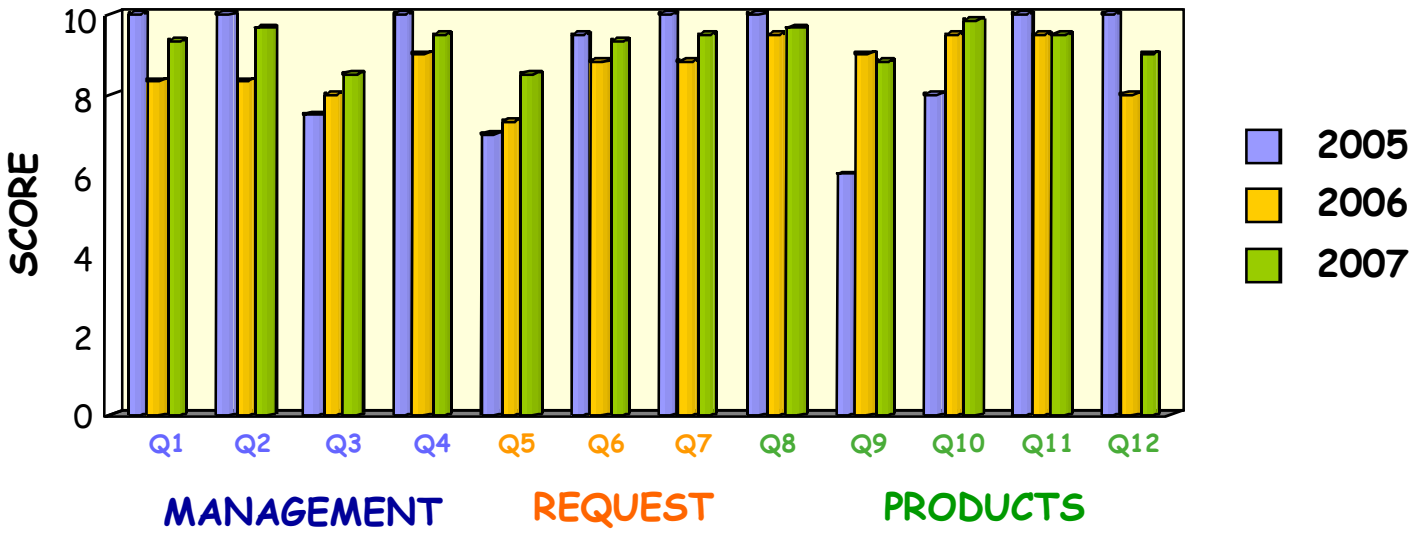
BNADN: EVALUATION OF SERVICES BY USERS



Users overall rating (scale 0-5): **4,7**

Q1. The communication between the DNA Bank and the researcher is fluid
Q2. The DNA Bank answers satisfactorily all the technical questions proposed
Q3. The information given in the DNA Bank web is sufficient and clear
Q4. To contact with the DNA Bank is easy

Q5. The DNA Bank comply with the established periods for approving the project
Q6. The researcher agrees with the commitments acquired when requesting the products
Q7. Service rates are appropriate

Q8. The DNA Bank has delivered all the requested products.
Q9. The DNA Bank has complied with the established periods for delivering products.
Q10. The products have arrived in the appropriate conditions.
Q11. The DNA quality offered is adequate for the research project.
Q12. The DNA quantity received is sufficient.

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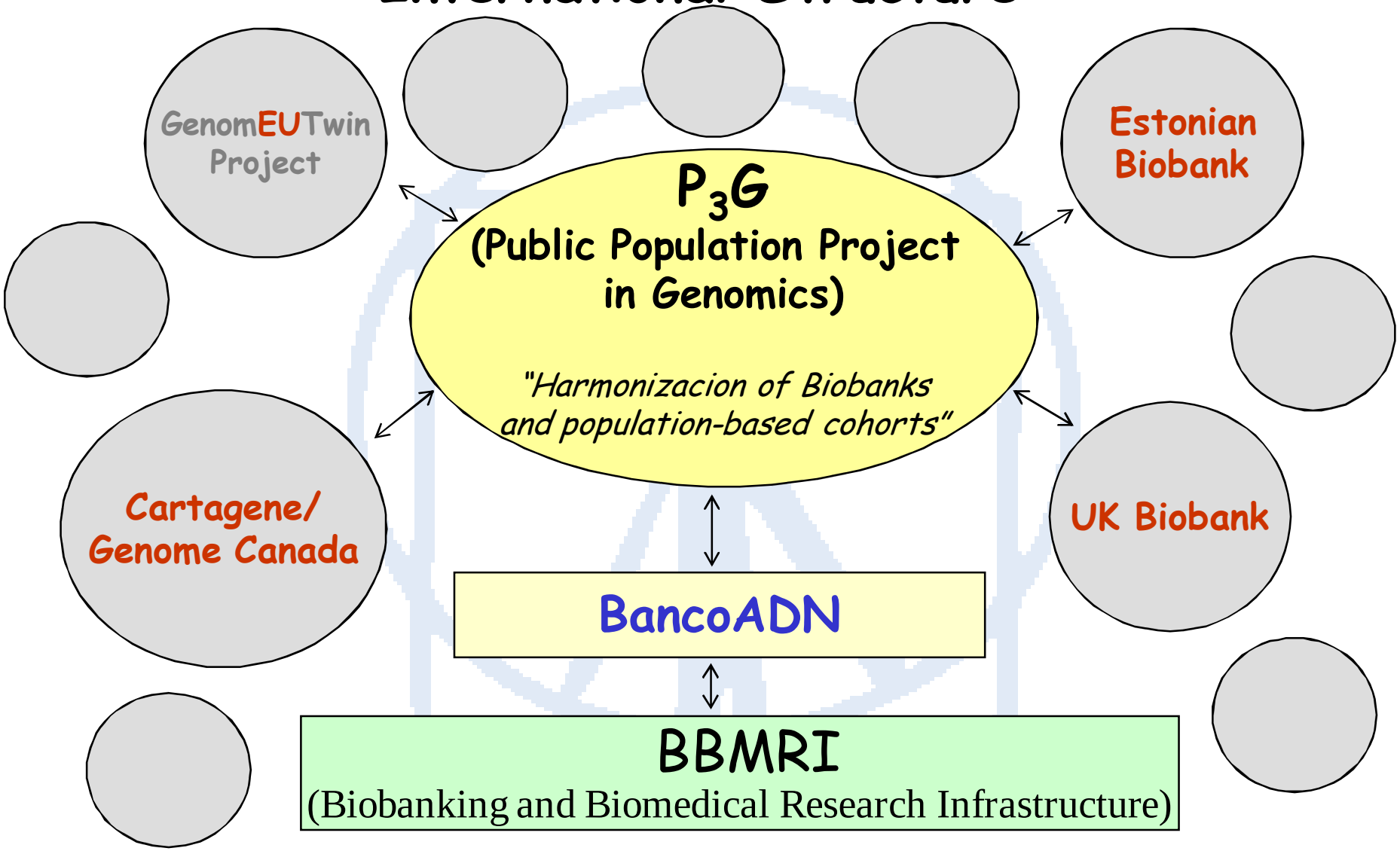
International Structure



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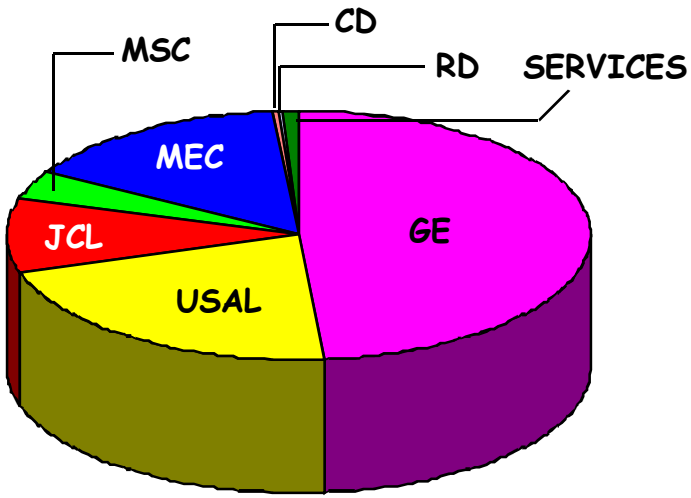
National DNA Bank

FUNDING ENTITIES 2004/08

ENTITIES	AMOUNT
FUNDACIÓN GENOMA ESPAÑA (GE)	1.583.441,05 €
UNIVERSIDAD DE SALAMANCA (USAL)	701.888,78 €
JUNTA DE CASTILLA Y LEÓN (JCL)	316.033,75 €
MINISTERIO DE SANIDAD Y CONSUMO (MSC)	115.184,39 €
MINISTERIO DE EDUCACIÓN Y CIENCIA (MEC)	498.760,00 €
CAJA DUERO (CD)	7.468,75 €
ROCHE DIAGNOSTICS (RD)	15.000,00 €
INTERNAL RESOURCES (SERVICES)	25.399,96 €
TOTAL	**3.263.176,68 €**



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LEGAL DEFINITION AND REGULATION OF BIOBANKS IN SPAIN

Ley de Investigación Biomédica (Law for Biomedical Research):

1.- Genetic Analyses
2.- Use of Biological samples
3.- Biobanks
4.- (Others: research using embryonic stem cells)

Artículo 3.- Biobanco: establecimiento público o privado, sin animo de lucro, que acoge una colección de muestras biológicas concebida con fines diagnósticos o de investigación biomédica y organizada como una unidad técnica con criterios de calidad, orden y destino

INFORMED CONSENT (INFORMATION)

Purpose

Expected benefits

Potential inconveniences

ID responsible for the research

Site of analysis & destination*

Right to know the Genetic results (data)

Right to revoke the consent & consequences

Guarantee of confidenciality

Implications on donor's health

Familial implications

Further contact

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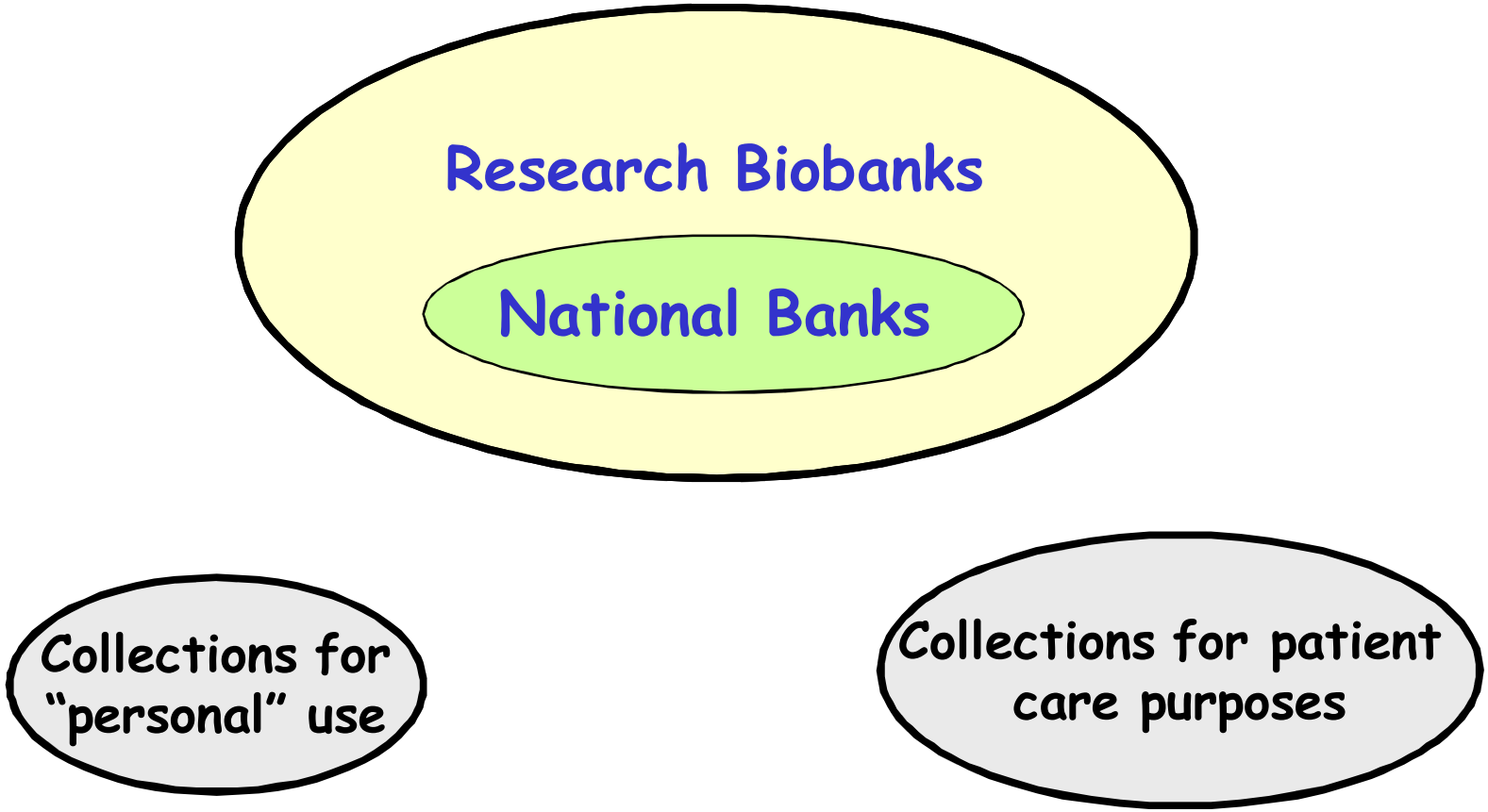
LEY DE INVESTIGACIÓN BIOMÉDICA
collections of samples vs biobanks



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SPANISH LAW ON BIOMEDICAL RESEARCH: obligations for the biobank

- **Authorized** by the regional governments (created by the Ministry of Health)
- **Structure** of the organization:
  - Scientific director & person responsible for "database"
  - External Committees
- **Activities:**
  - To ensure fulfilling all legal requirements
  - Registry of activities
  - Guarantee of quality, safety & traceability of samples, data y procedures
  - Attend to enquires & claims
  - Good-practice manual/documentation
  - Annual report

INSPECTED

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BIOBANK REGISTRY

for biomedical research

ISCiii

Regional Governments

Research Biobanks

Other collections

Collections for health care purposes

Collections for "personal" use

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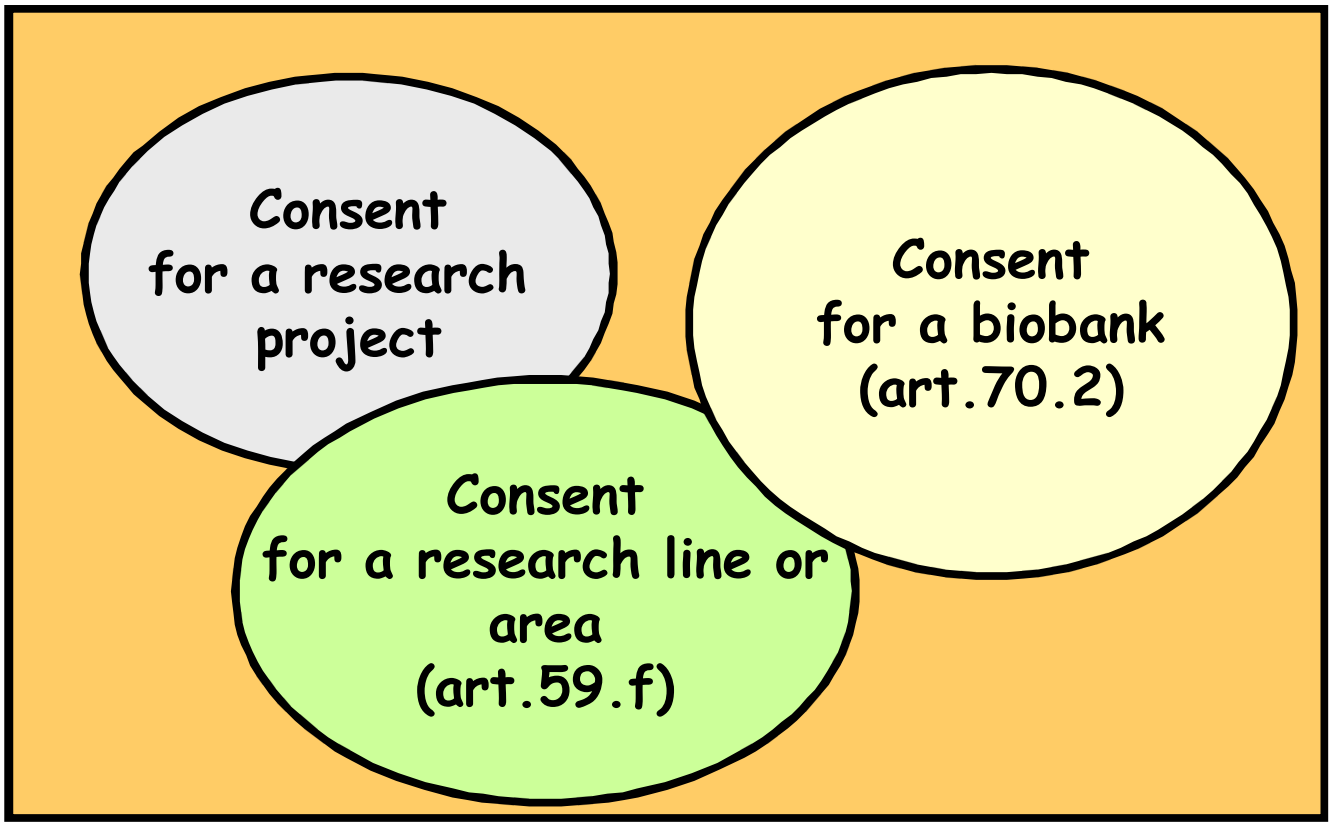
SPANISH LAW ON BIOMEDICAL RESEARCH:

Informed consent(s)



HAND OVER TO A THIRD PARTY

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National DNA Bank of Spain

FUTURE DEVELOPMENT

New legal frame (strategic plan)

EXPAND SERVICES

- -New technologies
- -New collaborations
- -New services
- -New nodes

NEW ACTIVITIES

Biobanking Research:

- Pre-analytical issues
- Cell purification
- Cryobiology

Biobanking Education:

- EQC program
- Master degree

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THANK YOU

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National DNA Bank

WEAKNESSES:

- Lack of an appropriate legal framework for the development of the DNA bank:
  - Low flexibility on hiring personnel
  - Difficulties on applying for grants
  - Impact on "corporate image" (e.g.: a scattered network)
- Lack of a stable financial support at medium/long-term (Currently: yearly plan)
  - Negative impact on adequate planning
- Lack of a medium/long term (approved) strategic plan
  - Imbalanced ratio between collaborations/laboratory facilities
  - Limited coordination with other initiatives
- Difficulties on donor recruitment

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National DNA Bank: Strengths

- Assumption of the acquired commitments
- Robustness of its structure and organization
- Strength of the networks and collaborations
- Specialized education of the BNADN professionals
- Ethical and legal frame/structure
- Quality of the samples and associated information
- Cost-effective project
- Strategic plan

MAIN FUTURE GOALS

SHORT TERM (2008)

- Integration of the four new nodes
- Implementation of an external quality control program for biobanks
- Development and implementation of a communication plan for users and donors

MEDIUM TERM (2008-2010)

NEW TECHNICAL IMPLEMENTATIONS:

- Whole genome amplification
- New immortalization approaches for different tissues
- Automated cell line generation facilities

OPTIMIZATION OF COLLECTIONS OF SAMPLES

- Population-based studies:
  - Representative of the population living on Spain
  - Minimum sample number (estimated): 60 per million inhabitants
- Disease-based studies:
  - Inflammatory diseases (n=9.000)
  - Thromboembolic diseases (to be determined)

LONG TERM (2007-2016)

INCREASE NUMBER AND TYPE OF SAMPLES: Rare diseases,

TRANSCRIPTOMICS (mRNA):

- cell separation and purification
- mRNA extraction

IMPLEMENTATION OF PHENOTYPIC STUDIES

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NEW EQUIPMENT AND STAFF REQUIREMENTS

MEDIUM TERM (3 years)

EQUIPMENT:

- New (larger) building facilities:
  - Storage laboratory and freezers
- Automation for whole genome amplification
  - Liquid handler PCR preparation robot
- Automation of cell line generation
  - Cell line production cabin
- Automation for whole genome amplification
  - Liquid handler PCR preparation robot

Additional STAFF:

- 2 laboratory technicians and 1 bachelor in science

LONG TERM (10 years)

EQUIPMENT:

- Equipment for phenotypic studies (e.g.: biochemical analyzer)
- Equipment for cell purification/isolation (e.g. AutoMACS)
- Automated mRNA extraction robot

Additional STAFF:

- 2 laboratory technicians and 2 bachelors in science

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