



UNIVERSIDAD
DE SALAMANCA



Red Biobancos
Instituto de Salud Carlos III



EL BANCO DE ADN (BNADN) CUMPLE 10 AÑOS

**BANCO NACIONAL DE ADN CARLOS III
UNIVERSIDAD DE SALAMANCA, CIC E IBSAL**

Curso/Taller

**"Estructuras de apoyo a la investigación:
LOS BIOBANCOS DE CASTILLA Y LEÓN"**

Valladolid, 29 de octubre de 2014



bancó·adn

Plataforma en Red
Banco Nacional de ADN Carlos III



GENOME SPAIN INITIATIVES

Genoma España



banco adn[®]



www.bancoadn.org

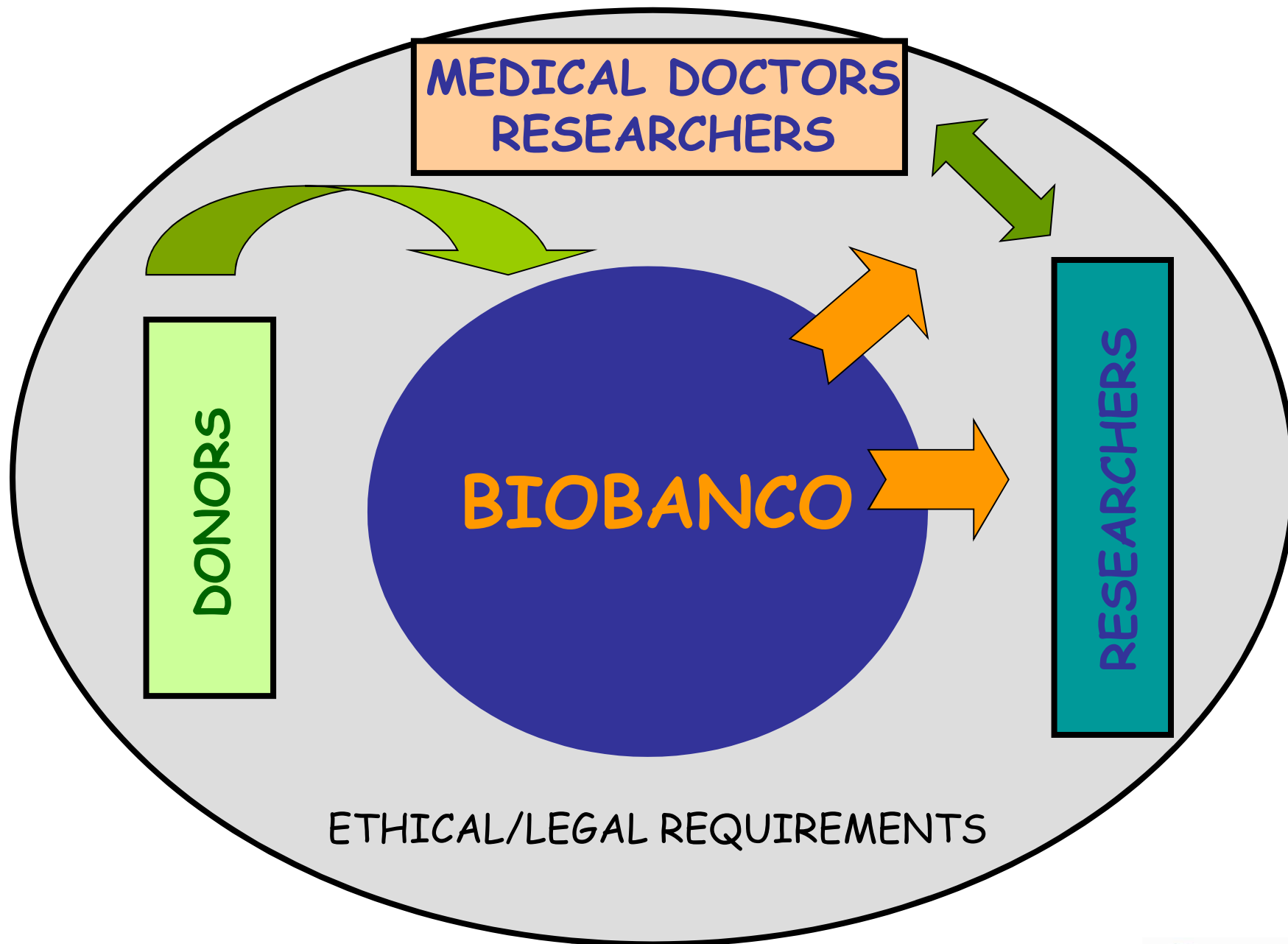


BIOBANKS & BIOMOLECULAR RESOURCE CENTRES

- 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"

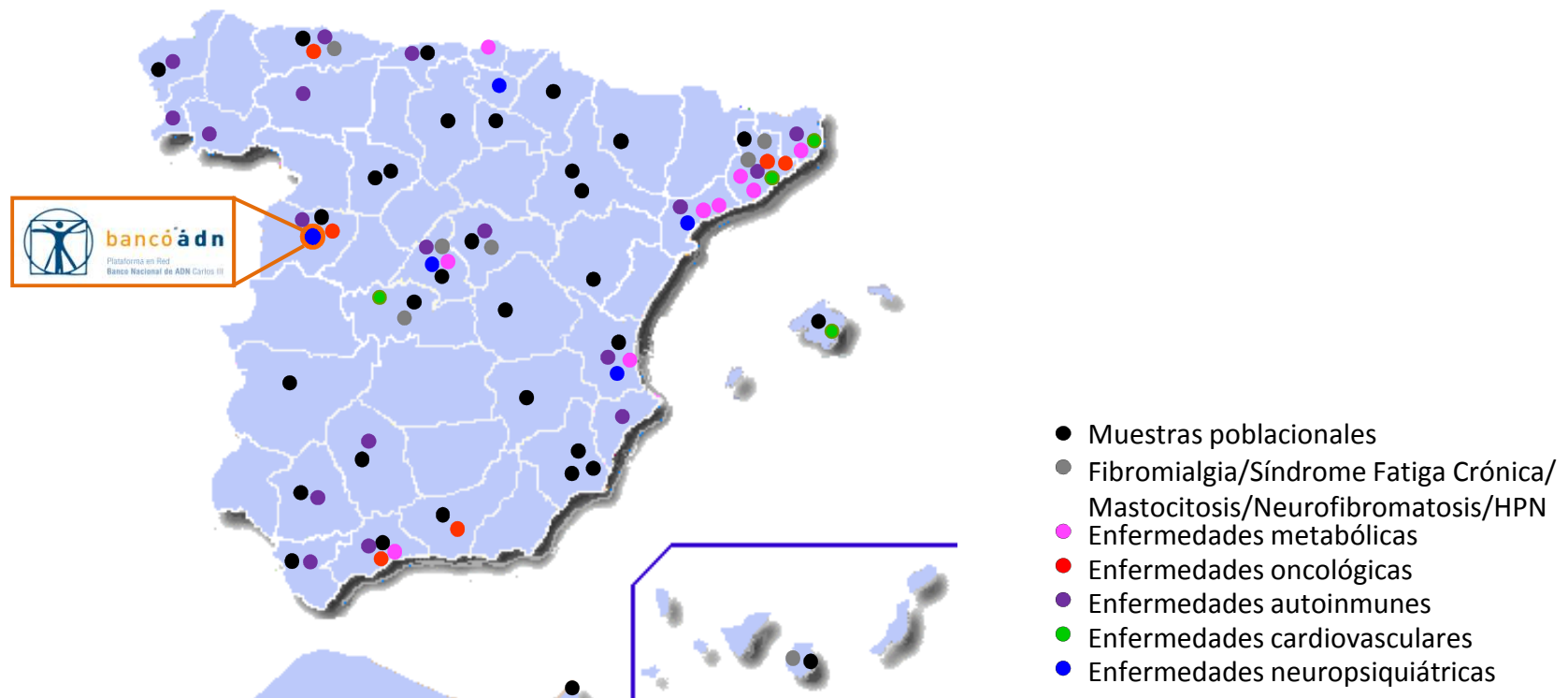
Predict usage of samples far in advance: decide on type of sample, sample conditions and manipulation (*sample fractioning, cell & fluid components of interest...*)



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UNA DÉCADA AL SERVICIO DE LA INVESTIGACIÓN

CENTROS COLABORADORES (n=83)



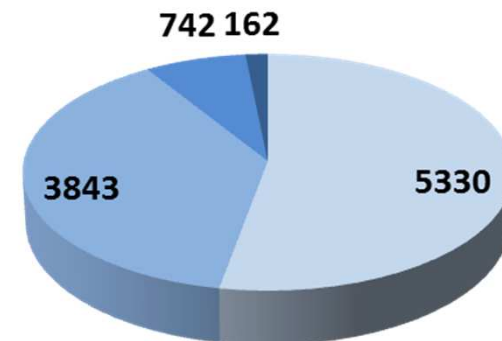
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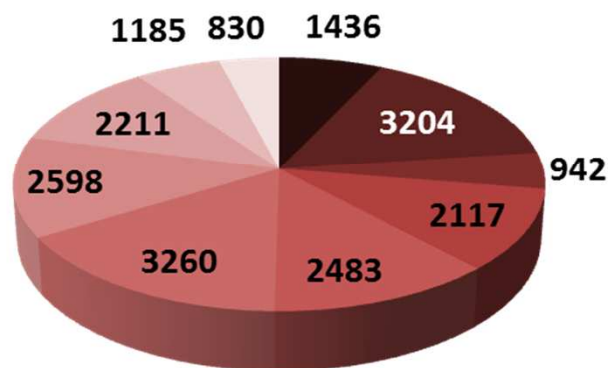
MUESTRAS DISPONIBLES

MUESTRAS POBLACIONALES (n=10 077)

- Muestras poblacionales
- Muestras de referencia de riesgo cardiovascular en Castilla y León
- Colección de gemelos de la región de Murcia
- Colección de nonagenarios



ENFERMEDADES PREVALENTES (n=20 266)



- Enf. cardiovasculares
- Enf. metabólicas
- Enf. neuropsiquiátricas
- Enf. oncológicas
- Fibromialgia y Síndrome de Fatiga Crónica
- Enfermedad de Crohn
- Psoriasis
- Artritis reumatoide
- Artritis psoriásica
- Lupus eritematoso

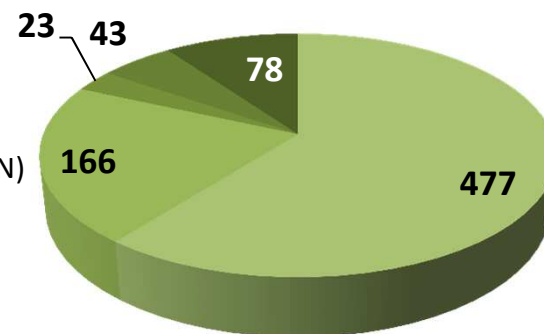
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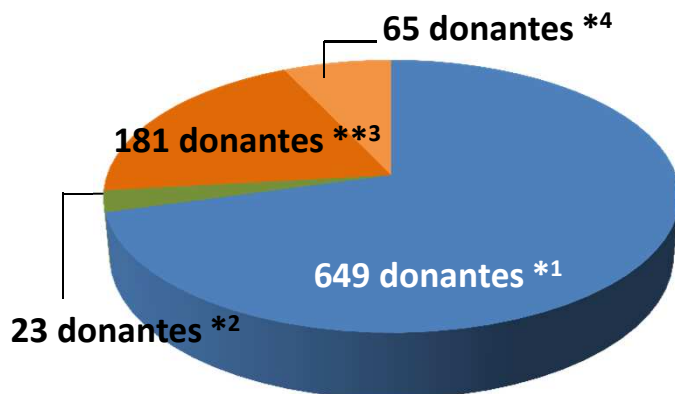
MUESTRAS DISPONIBLES

ENFERMEDADES RARAS (n=887)

- Mastocitosis
- Neurofibromatosis
- Hemoglobinuria paroxística nocturna (HPN)
- Esclerosis lateral amiotrófica
- Distrofia cervical idiopática



POBLACIONES CELULARES PURIFICADAS (n=918)



- Muestras poblacionales
- Pacientes diagnosticados HPN
- Pacientes tumores oncológicos
- Pacientes tumores oncológicos

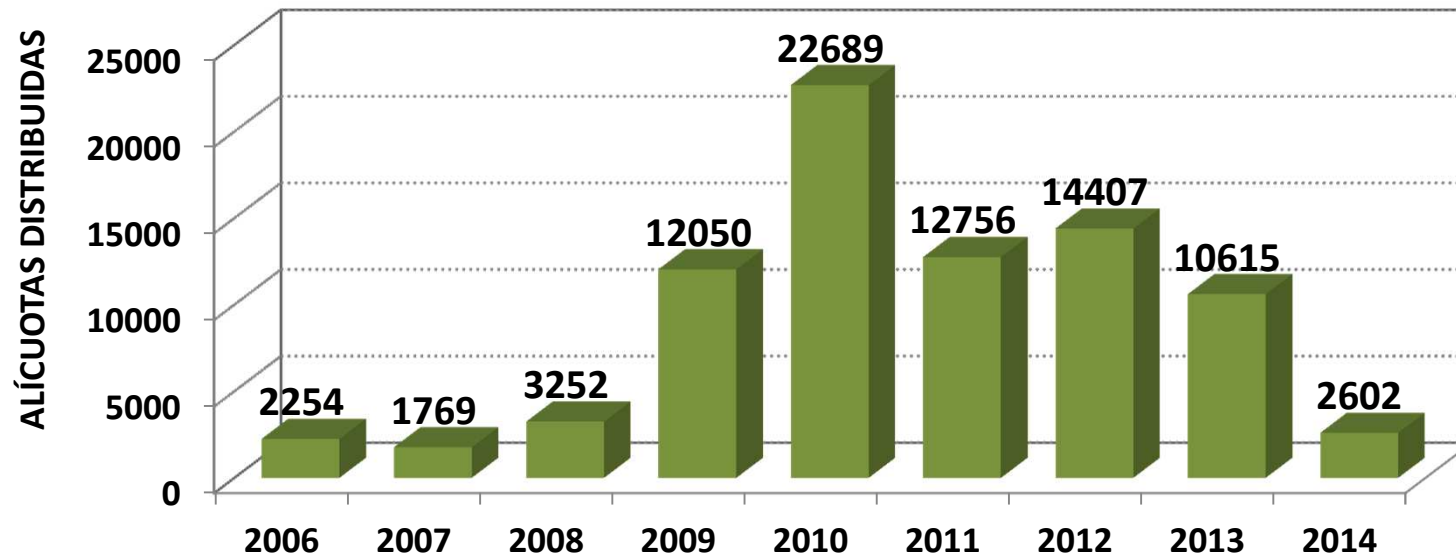
.. ** células

* muestras de ADN y ARN

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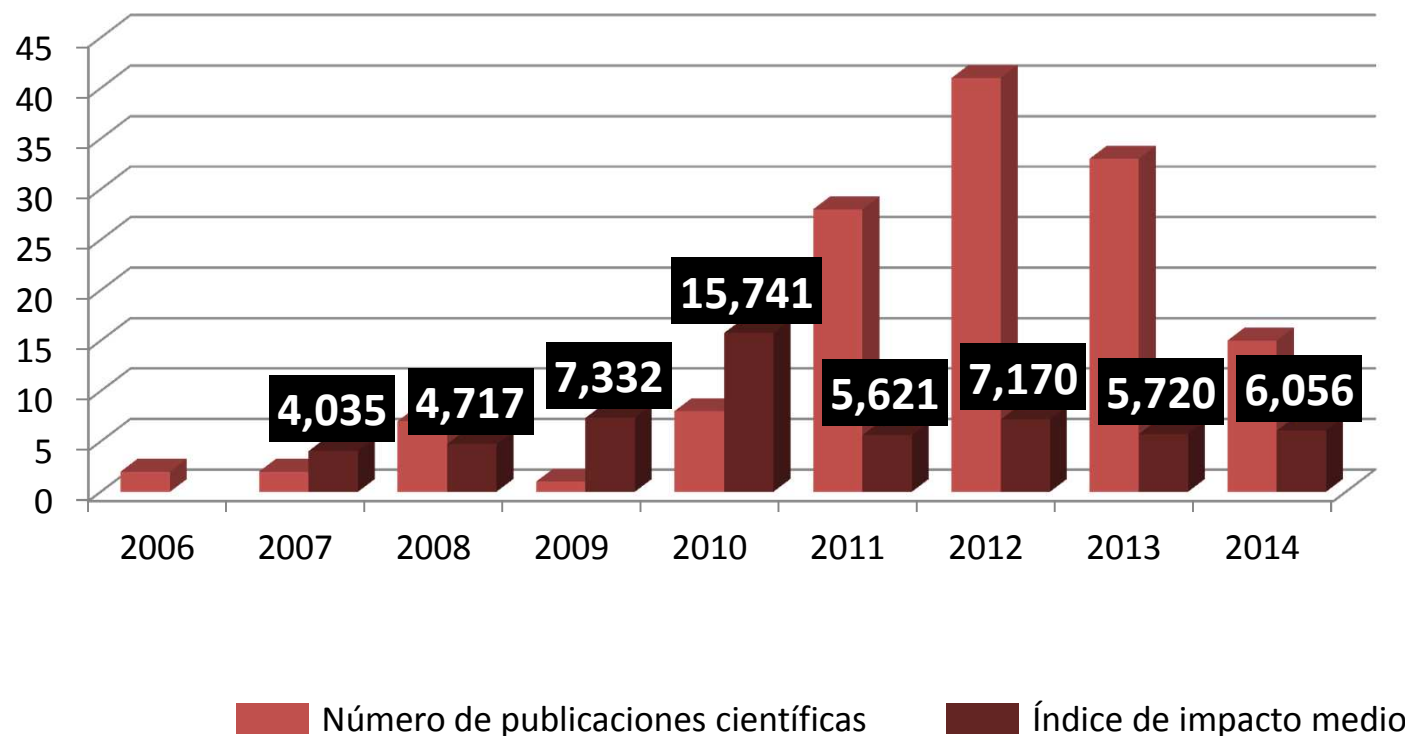
ALÍCUOTAS DISTRIBUIDAS PARA PROYECTOS DE INVESTIGACIÓN



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PUBLICACIONES CIENTÍFICAS (n=128)



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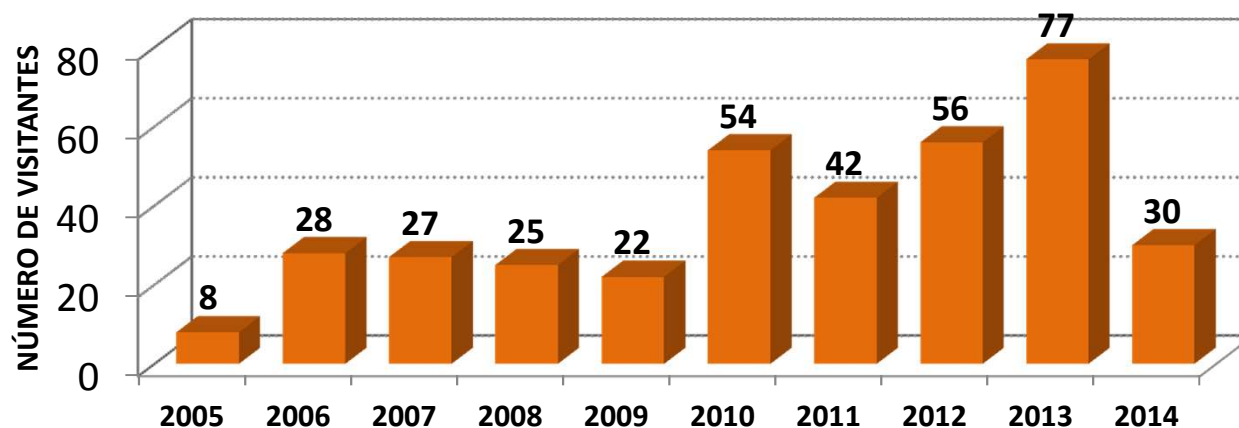
CARTERA DE SERVICIOS

- **EXTRACCIÓN DE ÁCIDOS NUCLEICOS**: extracción de ácidos nucleicos a partir de sangre periférica (fresca o congelada).
- **ESTABLECIMIENTO DE LÍNEAS LINFOBLASTOIDES**: inmortalización de células mediante infección con EBV en laboratorios de seguridad biológica, garantizando la esterilidad de las muestra.
- **SERVICIOS DE FORMACIÓN**: cursos de formación impartidos por el personal del biobanco personalizados en función de las necesidades del solicitante.
- **ASESORAMIENTO EN IMPLANTACIÓN DE SGC**: servicio de consultoría para el diseño, desarrollo e implantación de un SGC conforme a la norma internacional ISO 9001:2008.

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ASISTENTES A LOS CURSOS DE FORMACIÓN (n= 369)



DIFERENTES CURSOS DE FORMACIÓN:

- cursos presenciales en el biobanco
- título de experto/máster en biobancos
- cursos de formación continua de la Universidad de Salamanca
- cursos de formación a través de acuerdos con fundaciones y/o asociaciones

BANCO NACIONAL DE ADN CARLOS III

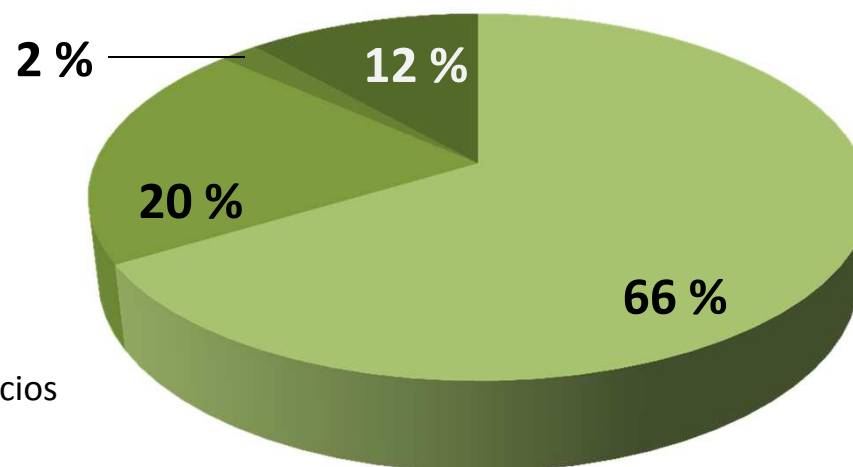
UNA DÉCADA AL SERVICIO DE LA INVESTIGACIÓN

SATISFACCIÓN DE LOS USUARIOS

A cada uno de los usuarios que solicitan por primera vez alguno de los servicios ofrecidos por el BNADN se le envía un cuestionario de satisfacción con el fin de detectar posibles áreas de mejora. La valoración global media de los usuarios en relación a la satisfacción de los servicios ofrecidos por el BNADN de los últimos cinco años es de **8,95** puntos sobre 10.

FIDELIZACIÓN DE USUARIOS

- Investigadores que han solicitado un servicio
- Investigadores que han solicitado dos servicios
- Investigadores que han solicitado tres servicios
- Investigadores que han solicitado cuatro o más servicios



BANCO NACIONAL DE ADN CARLOS III
UNA DÉCADA AL SERVICIO DE LA INVESTIGACIÓN

PROYECTOS INTERNACIONALES



**PUBLIC
POPULATION
PROJECT IN
GENOMICS
AND SOCIETY**

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WHAT IS P3G?

➤ P3G is a not-for-profit organization that provides the international research community with access to the expertise, resources and innovative tools for health and social sciences research.



IPAC

International Policy interoperability and data Access Clearinghouse



TOOLKIT

SEARCHING, ANALYSING, VISUALISING
BY NAME, CATEGORY OR TYPE



LIFESPAN

BRIDGING THE GAP BETWEEN
DIFFERENT PHASES AND STAGES
OF THE RESEARCHER'S CAREER



HUB

EXCHANGING KNOWLEDGE AND
COLLABORATING WITH EXPERTS
IN YOUR RESEARCH AREA



TRAINING

ACROSS THE RESEARCH AND
INFORMATION SCIENCES




CATALOGUES

PERSONAL AND COLLECTIVE
APPLICATIONS-BASED DATABASES



BRIEF

RESEARCH BRIEFING FOR A
BROADENING OF ACCESS
AND IMPACT



1000 Genomes

A Deep Catalog of Human Genetic Variation

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LATEST ANNOUNCEMENTS

WEDNESDAY OCTOBER 31, 2012

An integrated map of genetic variation from 1092 human genomes

The Phase 1 publication, *An integrated map of genetic variation from 1092 human genomes* is now available from Nature and can be downloaded directly from the [ftp site](#). The paper is distributed under a Creative Commons Attribution-NonCommercial-ShareAlike 3.0 Unported license. Please share our paper appropriately.

All the data files associated with this paper can be found in our [phase 1 analysis results directory](#).

THURSDAY FEBRUARY 20, 2014

Recent project announcements





1000 Genomes Project and Beyond
24-26 June 2014
Churchill College, Cambridge, UK


This Wellcome Trust conference will focus on advances enabled by the 1000 Genomes Project, including the new directions in genomics and genomics that it has facilitated. It is the latest in the successful series of community meetings for the HapMap and 1000 Genomes Project, marking the end of the 1000 Genomes Project this summer.

NAVIGATION

- [Frequently Asked Questions](#)


LINKS


-  [All Project Announcements](#)
-  [Sample and Project Information](#)
-  [Media Archive](#)
-  [Download the 1000 Genomes Plot Paper](#)




[Data Portal](#)
[Get Cancer Data](#)

[Data Access Compliance Office](#)
[Apply for Access to Controlled Data](#)


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Cancer Genome
Consortium


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[Media](#)


ICGC Cancer Genome Projects


Committed projects to date: [71](#)


Sort by: [Alphabet](#) ▼


Biliary tract cancer
Singapore 


Bladder Cancer
United States 


Bladder cancer
China 


Blood Cancer
United States 

Blood cancer
China 

Blood cancer
South Korea 

Blood cancer
United States 

Bone Cancer
United Kingdom 

Brain Cancer
Canada 

ICGC Goal: To obtain a comprehensive description of genomic, transcriptomic and epigenetic changes in 50 different tumor types and/or subtypes which are of clinical and societal importance across the globe.

[Read more >](#)

[Launch Data Portal >](#)

[Apply for Access to Controlled Data >](#)

Announcements

31February/2014 - The ICGC Data Coordination Center



BBMRI
 Biobanking and
 Biomolecular
 Resources Research
 Infrastructure

Managing resources for the future of research


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- Stakeholder's Forum
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- Catalog of European Biobank
- WIKI Legal Platform
- HSERN

BBMRI during the transition phase

BBMRI (Biobanking and Biomolecular Resources Research Infrastructure) was one of the first projects joining the European Research Infrastructure preparatory phase of the ESFRI roadmap funded by the European Commission (EC). The preparatory phase of BBMRI came to its end in January 2011. Over the past 3 years BBMRI has grown into a 54-member consortium with more than 225 associated organisations (largely biobanks) from over 30 countries, making it one of the largest research infrastructure projects in Europe.


When the preparatory phase of BBMRI came to its end on January 31, 2011, also the Governance and Management Structures which were based on the Grant Agreement came to end. In its final meeting on Jan 25, 2011, the BBMRI Steering Committee agreed that the Coordinator, the Executive Manager as well as the Steering Committee of the preparatory phase continued to function as interim bodies of BBMRI until the preparatory (governance) body (as described in the MoU) was established.





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Linking up rare disease research across the world

An integrated platform connecting databases, registries, biobanks and clinical bioinformatics for rare disease research

About RD-Connect

Fragmentation of research data makes rare disease research more difficult. RD-Connect links it all together, globally. [\[read more\]](#)

News

The award of 38 million EUR for rare disease research is highlighted at an international press event at Camp Nou, home of FC Barcelona. [\[read more\]](#)

Contribute your data!

The RD-Connect platform will accept data from IRDiRC research projects worldwide. Find out how to contribute your data to our system. [\[read more\]](#)



ARTICLE

doi:10.1038/nature11632

An integrated map of genetic variation from 1,092 human genomes

The 1000 Genomes Project Consortium*

By characterizing the geographic and functional spectrum of human genetic variation, the 1000 Genomes Project aims to build a resource to help to understand the genetic contribution to disease. Here we describe the genomes of 1,092 individuals from 14 populations, constructed using a combination of low-coverage whole-genome and exome sequencing. By developing methods to integrate information across several algorithms and diverse data sources, we provide a validated haplotype map of 38 million single nucleotide polymorphisms, 1.4 million short insertions and deletions, and more than 14,000 larger deletions. We show that individuals from different populations carry different profiles of rare and common variants, and that low-frequency variants show substantial geographic differentiation, which is further increased by the action of purifying selection. We show that evolutionary conservation and coding consequence are key determinants of the strength of purifying selection, that rare-variant load varies substantially across biological pathways, and that each individual contains hundreds of rare non-coding variants at conserved sites, such as motif-disrupting changes in transcription-factor-binding sites. This resource, which captures up to 98% of accessible single nucleotide polymorphisms at a frequency of 1% in related populations, enables analysis of common and low-frequency variants in individuals from diverse, including admixed, populations.

Recent efforts to map human genetic variation by sequencing exomes¹ and whole genomes^{2–4} have characterized the vast majority of common single nucleotide polymorphisms (SNPs) and many structural variants across the genome. However, although more than 95% of common (>5% frequency) variants were discovered in the pilot phase of the 1000 Genomes Project, lower-frequency variants, particularly those outside the coding exome, remain poorly characterized. Low-frequency variants are enriched for potentially functional mutations, for example, protein-changing variants, under weak purifying selection^{5,6}. Furthermore, because low-frequency variants tend to be recent in origin, they exhibit increased levels of population differentiation^{6–8}. Characterizing such variants, for both point mutations and structural changes, across a range of populations is thus likely to identify many variants of functional importance and is crucial for interpreting

individual genome sequences, to help separate shared variants from those private to families, for example.

We now report on the genomes of 1,092 individuals sampled from 14 populations drawn from Europe, East Asia, sub-Saharan Africa and the Americas (Supplementary Figs 1 and 2), analysed through a combination of low-coverage (2–6×) whole-genome sequence data, targeted deep (50–100×) exome sequence data and dense SNP genotype data (Table 1 and Supplementary Tables 1–3). This design was shown by the pilot phase¹ to be powerful and cost-effective in discovering and genotyping all but the rarest SNP and short insertion and deletion (indel) variants. Here, the approach was augmented with statistical methods for selecting higher quality variant calls from candidates obtained using multiple algorithms, and to integrate SNP, indel and larger structural variants within a single framework (see

Table 1 | Summary of 1000 Genomes Project phase 1 data

	Autosomes	Chromosome X	GENCODE regions*
Samples	1,092	1,092	1,092
Total raw bases (Gb)	19,049	804	327
Mean mapped depth (×)	5.1	3.9	80.3
SNPs			
No. sites overall	36.7 M	1.3 M	498 K
Novelty rate†	58%	77%	50%
No. synonymous/non-synonymous/nonsense	NA	4,765/0/097 K	199/293/6.3 K
Average no. SNPs per sample	3.60 M	105 K	24.0 K
Indels			
No. sites overall	1.38 M	59 K	1,867
Novelty rate†	62%	73%	54%
No. inframe/frameshift	NA	19/14	719/1,066
Average no. indels per sample	344 K	13 K	440
Genotyped large deletions			
No. sites overall	13.8 K	432	847
Novelty rate†	54%	54%	50%
Average no. variants per sample	717	26	39

NA, not applicable.

*Autosomal genes only.

†Compared with dbSNP release 135 (Oct 2011), excluding contribution from phase 1 1000 Genomes Project (or equivalent data for large deletions).

*Lists of participants and their affiliations appear at the end of the paper.



RESEARCH ARTICLE SUMMARY

Integrative Annotation of Variants from 1092 Humans: Application to Cancer Genomics

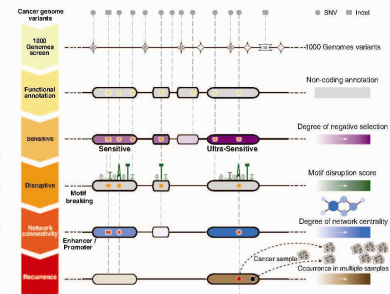
Ekta Khurana, Yao Fu, Vincenza Colonna, Ximeng Jasmine Mu, Hyun Min Kang, Tuuli Lappalainen, Andrea Sboner, Lucas Lochovsky, Jieming Chen, Arif Harman, Jishu Das, Aleksey Abysov, Suganthi Balasubramanian, Kathryn Beal, Dimple Chakravarty, Daniel Challis, Yuan Chen, Declan Clarke, Laura Clarke, Fiona Cunningham, Uday S. Evans, Paul Flícek, Robert Fragoza, Erik Garrison, Richard Gibbs, Zeynep H. Gümlüs, Javier Herrero, Naoki Kitabayashi, Yong Kong, Kasper Lage, Vaja Liliashvili, Steven M. Lipkin, Daniel G. MacArthur, Gabor Marth, Donna Muzny, Tune H. Pers, Graham R. S. Ritchie, Jeffrey A. Rosenfeld, Cristina Sisu, Xiaomu Wei, Michael Wilson, Yali Xue, Fuli Yu, 1000 Genomes Project Consortium, Emmanouil T. Dermizakis, Haiyuan Yu, Mark A. Rubin, Chris Tyler-Smith,* Mark Gerstein*

Introduction: Plummeting sequencing costs have led to a great increase in the number of personal genomes. Interpreting the large number of variants in them, particularly in noncoding regions, is a current challenge. This is especially the case for somatic variants in cancer genomes, a large proportion of which are noncoding.

Methods: We investigated patterns of selection in DNA elements from the ENCODE project using the full spectrum of variants from 1092 individuals in the 1000 Genomes Project (Phase 1), including single-nucleotide variants (SNVs), short insertions and deletions (indels), and structural variants (SVs). Although we analyzed broad functional annotations, such as all transcription-factor binding sites, we focused more on highly specific categories such as distal binding sites of factor ZNF274. The greater statistical power of the Phase 1 data set compared with earlier ones allowed us to differentiate the selective constraints on these categories. We also used connectivity information between elements from protein-protein-interaction and regulatory networks. We integrated all the information on selection to develop a workflow (FunSeq) to prioritize personal-genome variants on the basis of their deleterious impact. As a proof of principle, we experimentally validated and characterized a few candidate variants.

Results: We identified a specific subgroup of noncoding categories with almost as much selective constraint as coding genes: “ultra-sensitive” regions. We also uncovered a number of clear patterns of selection. Elements more consistently active across tissues and both maternal and paternal alleles (in terms of allele-specific activity) are under stronger selection. Variants disruptive because of mechanistic effects on transcription-factor binding (i.e. “motif-breakers”) are selected against. Higher network connectivity (i.e. for hubs) is associated with higher constraint. Additionally, many hub promoters and regulatory elements show evidence of recent positive selection. Overall, indels and SVs follow the same pattern as SNVs; however, there are notable exceptions. For instance, enhancers are enriched for SVs followed by nonallelic homologous recombination. We integrated these patterns of selection into the FunSeq prioritization workflow and applied it to cancer variants, because they present a strong contrast to inherited polymorphisms. In particular, application to ~90 cancer genomes (breast, prostate and medulloblastoma) reveals nearly a hundred candidate noncoding drivers.

Discussion: Our approach can be readily used to prioritize variants in cancer and is immediately applicable in a precision-medicine context. It can be further improved by incorporation of larger-scale population sequencing, better annotations, and expression data from large cohorts.



Prioritization of candidate noncoding cancer drivers based on patterns of selection. (Step 1) Filter somatic variants to exclude 1000 Genomes polymorphisms; (2) retain variants in noncoding annotations; (3) retain those in “sensitive” regions; (4) prioritize those disrupting a transcription-factor binding motif and (5) residing near the center of a biological network; (6) prioritize ones in annotation blocks mutated in multiple cancer samples.

The list of author affiliations is available in the full article online.

*Corresponding author. E-mail: cts@sanger.ac.uk (C.T.-S.); mark.gerstein@yale.edu (M.G.)

READ THE FULL ARTICLE ONLINE
<http://dx.doi.org/10.1126/science.1235587>

Cite this article as E. Khurana *et al.*,
Science 342, 1235587 (2013).
DOI: 10.1126/science.1235587

FIGURES IN THE FULL ARTICLE

Fig. 1. Fraction of rare (DAF < 0.5%) SNPs.

Fig. 2. Fraction of rare SNPs in noncoding categories.

Fig. 3. SNPs in protein-protein interaction (PPI) network.

Fig. 4. Functional annotations of indels and SVs.

Fig. 5. Functional implications of positive selection.

Fig. 6. Functional interpretation of disease variants.

SUPPLEMENTARY MATERIALS

Materials and Methods

Supplementary Text

Fig. S1 to S29

Tables S1 to S12

References (49–90)

Data S1 to S7

BANCO NACIONAL DE ADN CARLOS III

UNA DÉCADA AL SERVICIO DE LA INVESTIGACIÓN

RESUMEN

La Plataforma en red Banco Nacional de ADN Carlos III (BNADN) cumple **10 años** desde que se constituyó oficialmente (16 de marzo de 2004) mediante un convenio de colaboración entre la Universidad de Salamanca, la Fundación Genoma España y la Consejería de Sanidad de la Junta de Castilla y León.

El Banco Nacional de ADN Carlos III es un biobanco sin ánimo de lucro cuya función principal es **proporcionar muestras, e información asociada**, de donantes voluntarios (sanos y/o enfermos) **a los investigadores** que las soliciten para desarrollar un proyecto de investigación. Con esta actividad se **promueve y facilita la investigación biomédica**, asegurando simultáneamente el **uso racional, eficaz, ético y legal de las muestras** que custodia para garantizar los derechos de los donantes.

Desde su creación son muchos los logros alcanzados, logros que han conducido al Banco Nacional de ADN Carlos III a convertirse en un **biobanco de referencia nacional y con gran proyección internacional**.

PROPUESTA DE PLATAFORMA DE BIOBANCOS 2014-2017

WP 1: Promoción de colecciones de valor estratégico.

WP 2: Gestión de servicios en red.

WP 3: Investigación + Desarrollo + Innovación.

WP 4: Aspectos Éticos y Legales.

WP 5: Formación y coordinación.

ESTRUCTURA FUNCIONAL DEL PROGRAMA

>50 biobancos

CUATRO LÍNEAS DE TRABAJO:

1.- Muestras poblacionales.

(J Martínez y AC García-Montero)

5 biobancos

2.- Muestras de enfermedades prevalentes.

(A Bosch y M Pocovi)

46 biobancos

3.- Muestras de enfermedades raras.

(I Novoa y M Posada)

14 biobancos

4.- Muestras de enfermedades en niños.

(MA Muñoz-Fernández y V Cusi)

12 biobancos

OBJETIVO

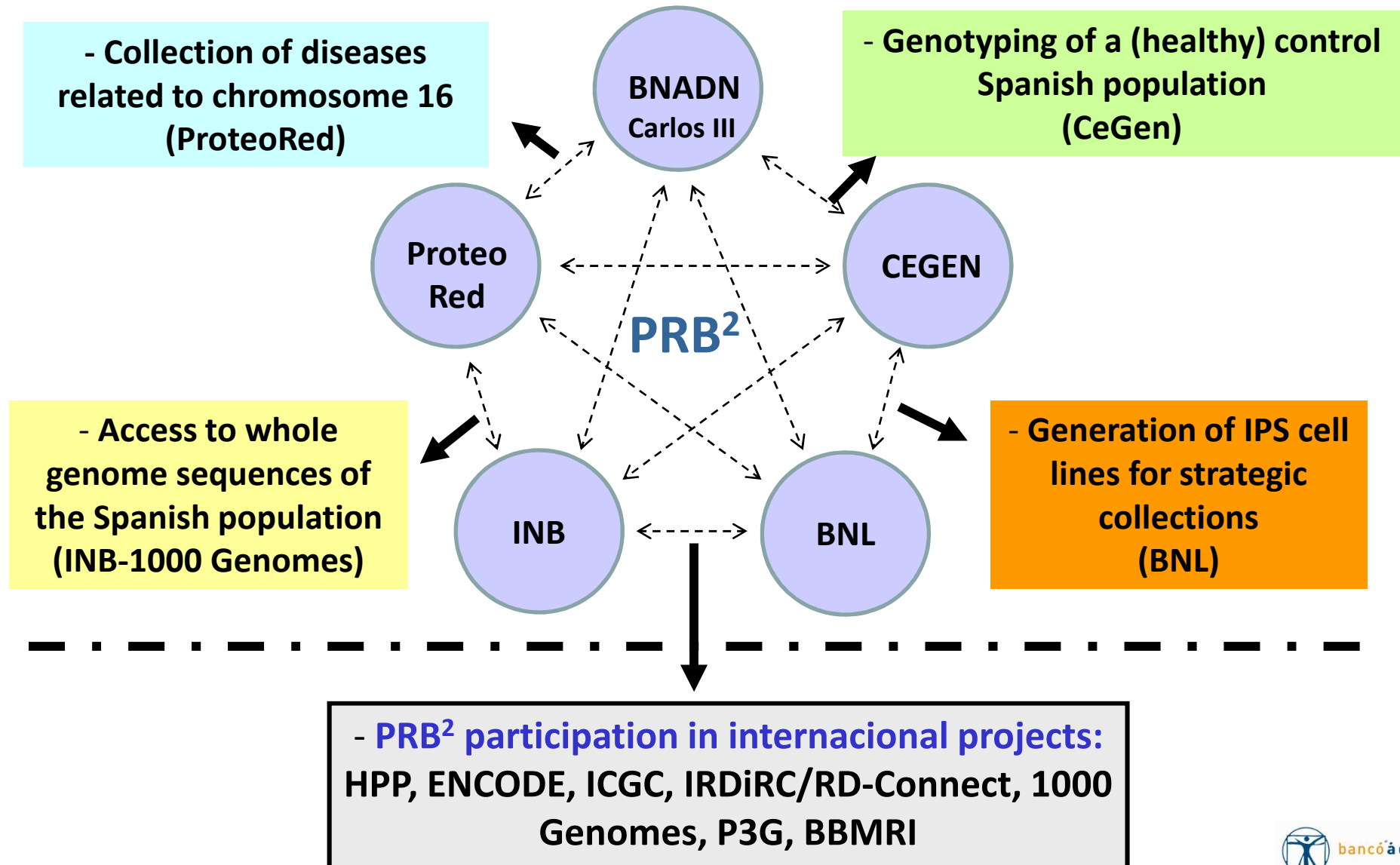
Construir y poner a disposición de los investigadores un catálogo común de colecciones de muestras biológicas humanas de carácter estratégico.

- i) Diseñar, desarrollar e implementar un plan de recogida
- ii) Desarrollar un control de calidad de muestras e información asociada.
- iii) Recogida de toda la información en una plataforma de gestión en red que permita la consulta directa al catálogo de mu

WP2

Biomolecular and Bioinformatic Resource Platform

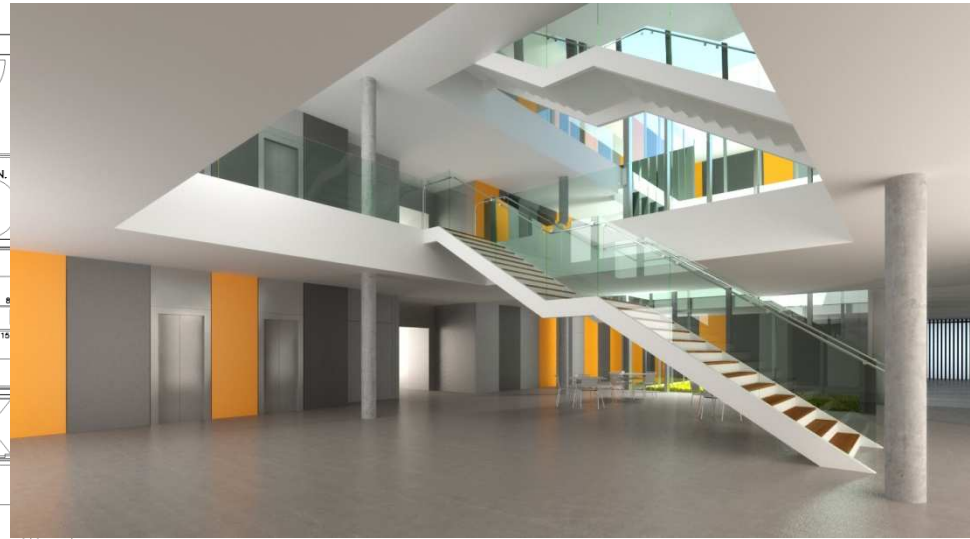
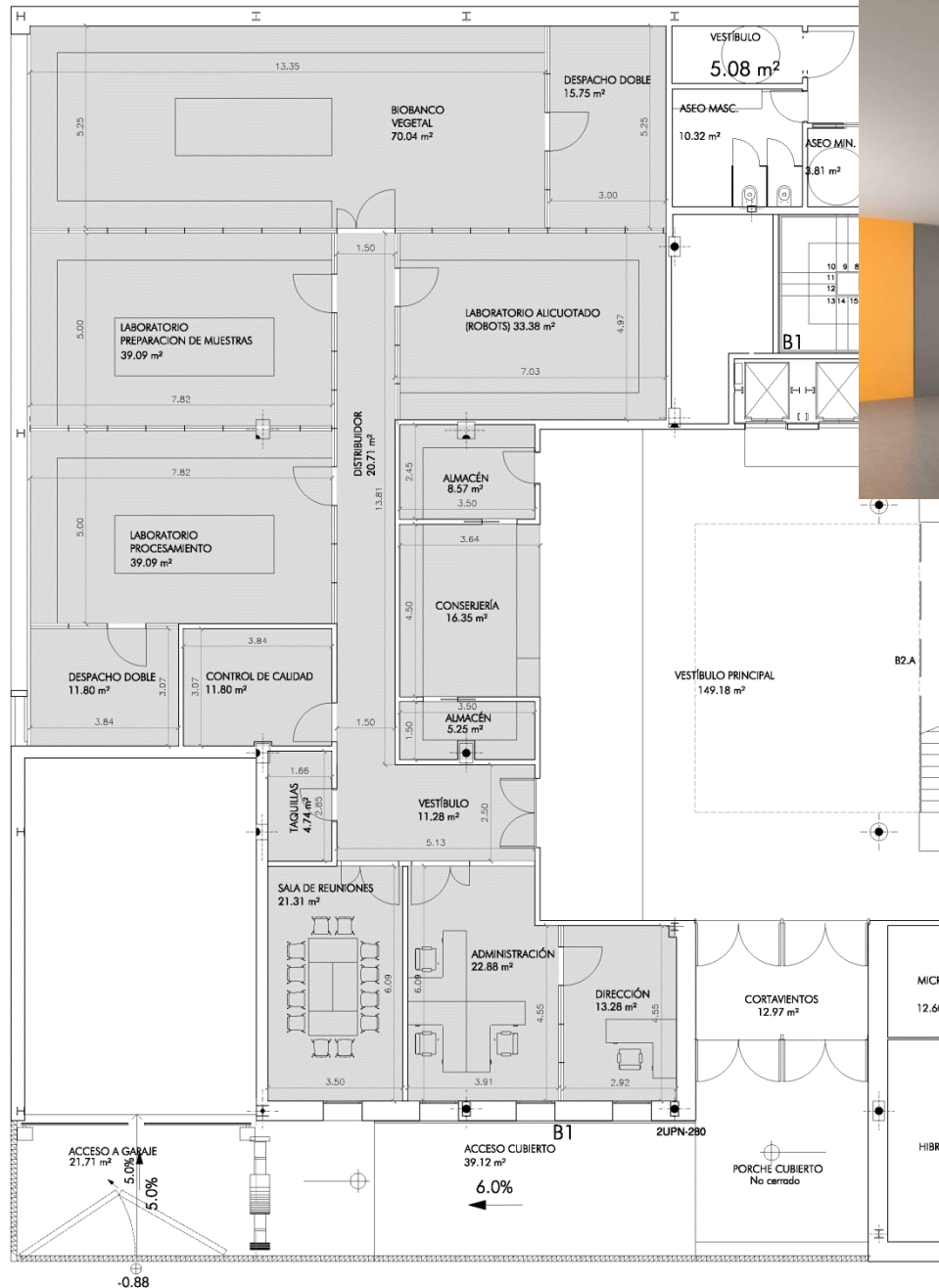
PRB²



Centro de Caracterización de Recursos Biológicos

- Ampliación del BancoADN
- Otras especies animales y vegetales
- Inversión en innovación en un área de retorno tangible
- Referencia internacional para:
 - Investigación tecnológica en biobancos
 - Tecnologías de caracterización de muestras biológicas*
 - Tecnologías de fraccionamiento y purificación celular
 - Difusión y formación en biobancos
- 100 personas
- Nuevo edificio de aprox. 5.000m²

Proyecto aprobado por la Comisión Interministerial el día 21.09.2010



650.61 m²

Administration: 69.27 m²

Laboratories: 128.94 m²

P3 Lab: 104.52 m²

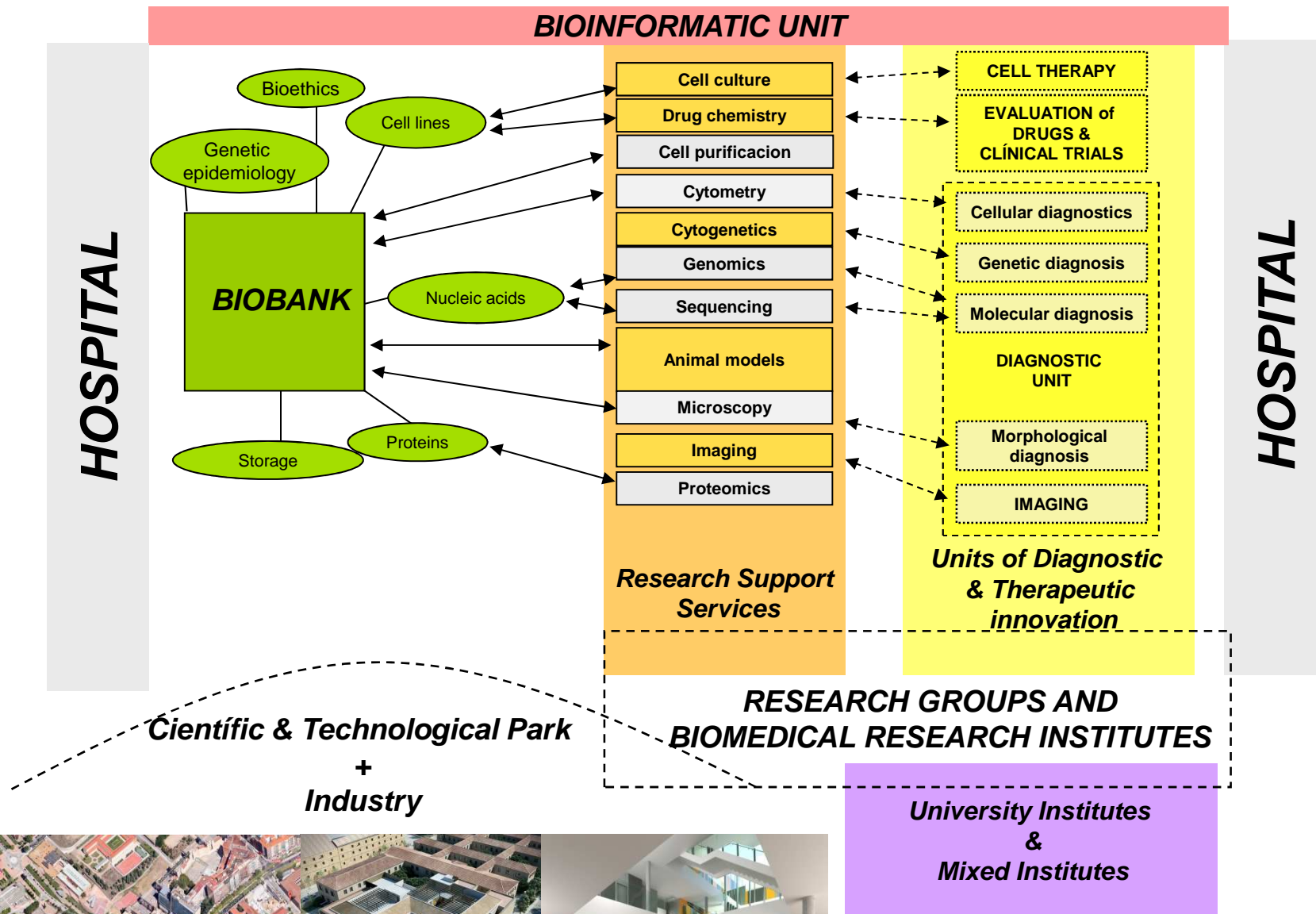
Storage:

-80°C: 216.04 m²

Liq N2: 70.71 m²

Qther: 61.13 m²

BIOMOLECULAR & BIOINFORMATIC RESOURCES



BANCO NACIONAL DE ADN CARLOS III

UNA DÉCADA AL SERVICIO DE LA INVESTIGACIÓN

AGRADECIMIENTOS

Con motivo del X ANIVERSARIO el personal del Banco Nacional de ADN Carlos III desea transmitir un agradecimiento especial a:

- todos los donantes que de manera desinteresada han cedido las muestras creyendo en este proyecto
- al personal sanitario (técnicos, enfermeras y médicos) que ha colaborado altruistamente con el biobanco en la recogida de muestras
- los grupos de investigación que han confiado en nuestro trabajo y han solicitado las muestras almacenadas haciendo partícipe al biobanco y a los donantes de los logros científicos alcanzados.

Y por último, agradecer a las instituciones públicas que han financiado este proyecto y que continúan confiando en su futuro.



VNIVERSIDAD
D SALAMANCA



Red Biobancos
Instituto de Salud Carlos III



GOBIERNO
DE ESPAÑA

MINISTERIO
DE ECONOMÍA
Y COMPETITIVIDAD



MUCHAS GRACIAS

bancoadn@usal.es

<http://www.bancoadn.org>



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