Medicina Personalizada en Andalucía

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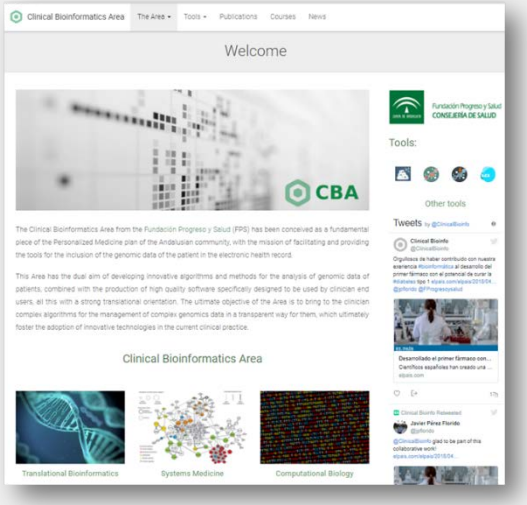
XII CONFERENCIA ANUAL
DE LAS PLATAFORMAS TECNOLÓGICAS
DE INVESTIGACIÓN BIOMÉDICA

The clinical bioinformatics area



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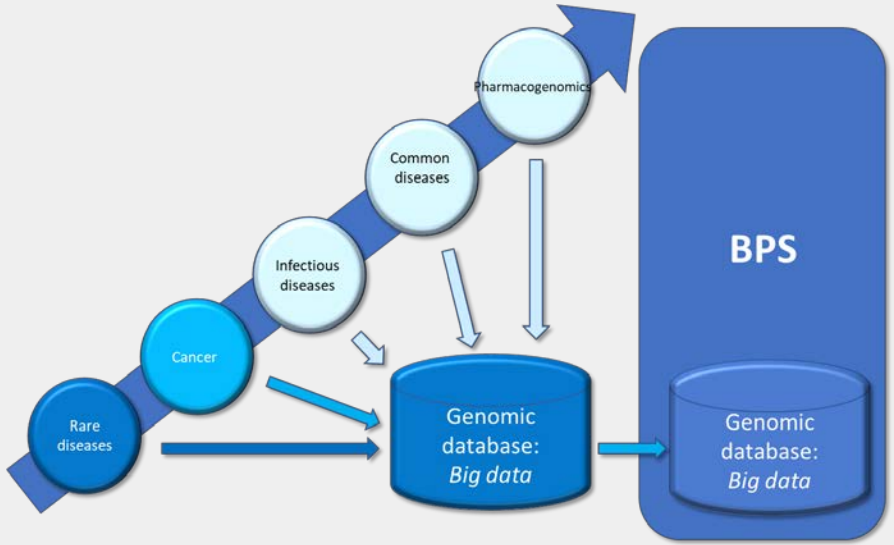
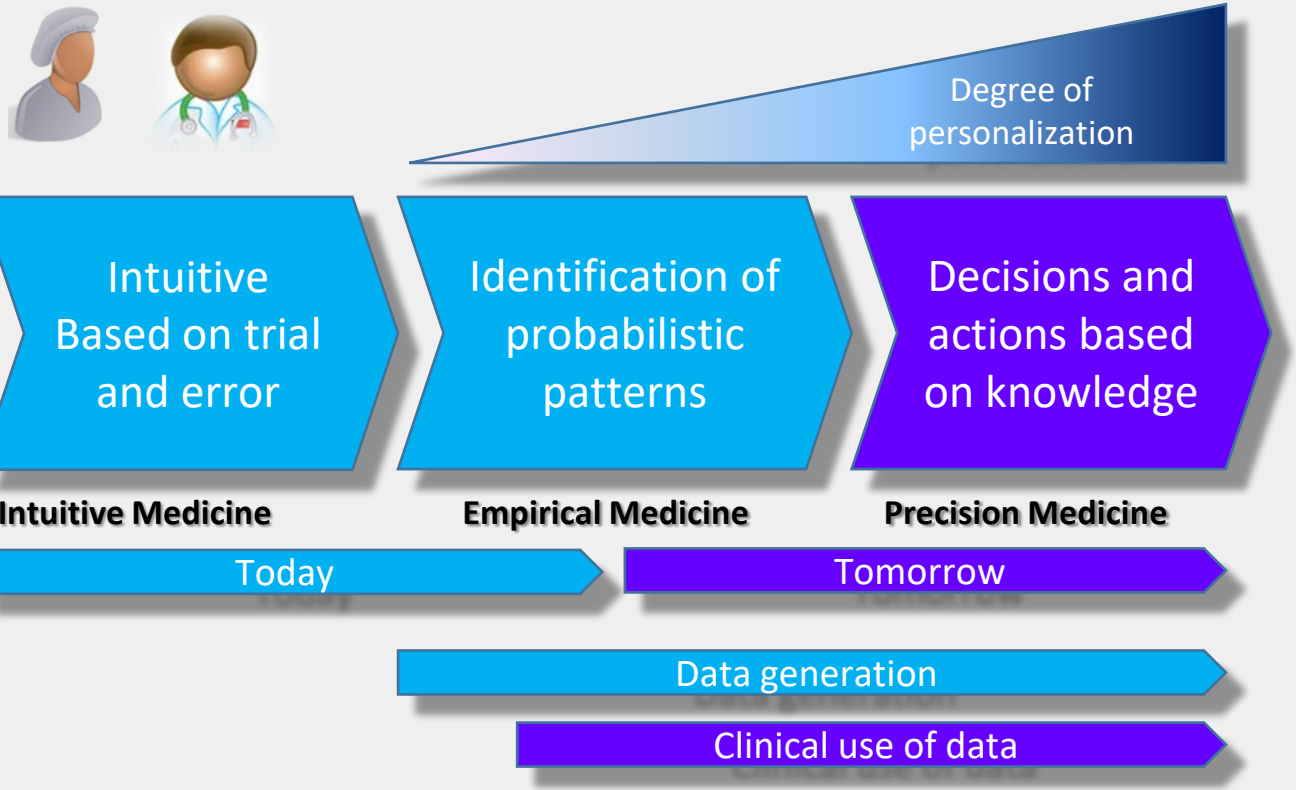


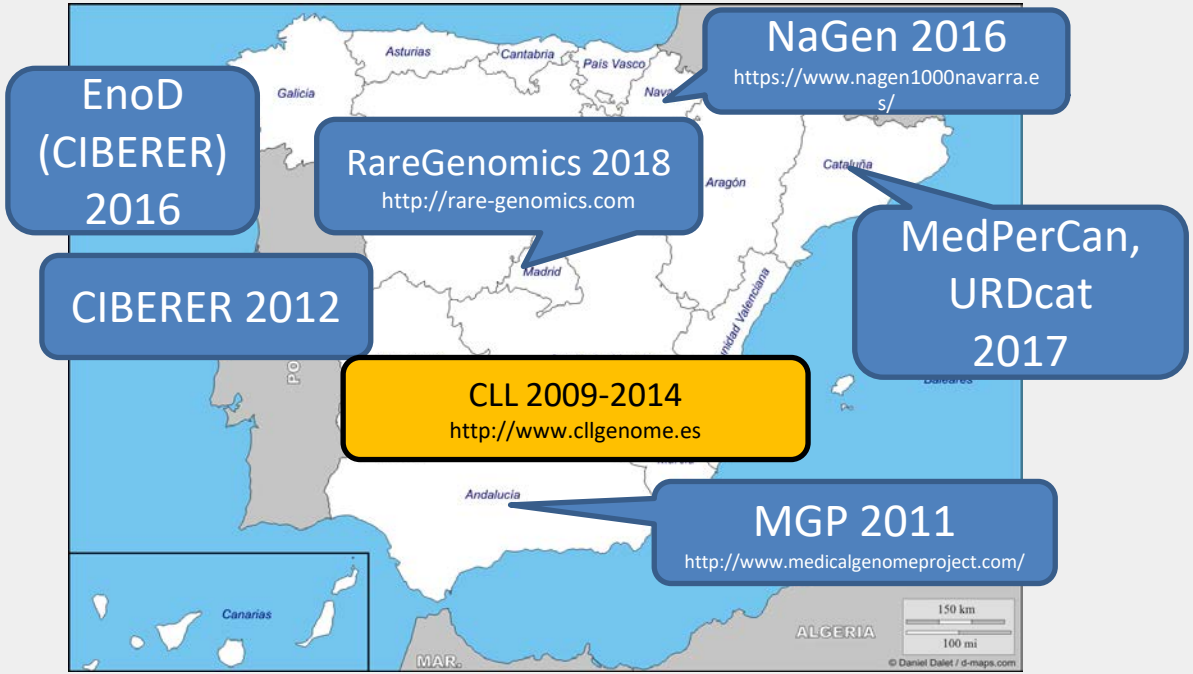
The Bioinformatics Area, created in June 2016 in the Fundación Progreso y Salud, has as main goal supporting the Program of Personalized Medicine of the Andalusian Community by facilitating the use of genomic data for precision diagnostic and treatment recommendation, implementing a prospective health care functionality in the public health system .

Personalized health care and the transition to precision medicine

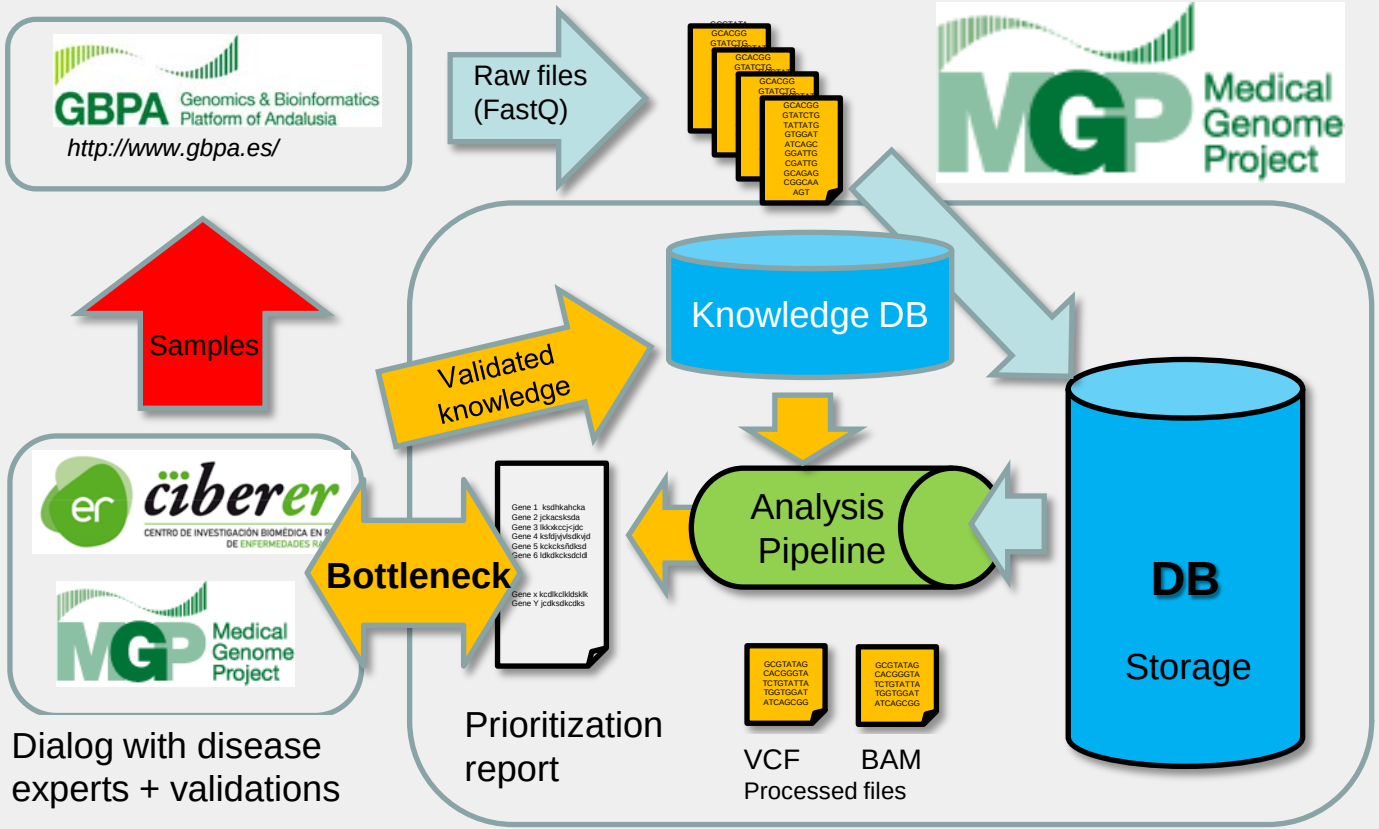


An historical perspective on data generation:

The role of International projects (ICGC) and the local genomic initiatives in Spain



Back to 2011: the Medical Genome Project



Solutions for managing the genomic data of the patient

Bioinformatician and biostatistician teams

- No scalability
- Expensive
- Lack of experts
- Inequity

Commercial software

- Expensive (pay per use)
- GDPR non compliant
- Inequity

Our solution: corporative software

- **Equity**
- **Scalability**
- **Affordable**
- **End user: clinician**
- **GDPR compliant**

Use of genomic data in the public health system requires sustainability

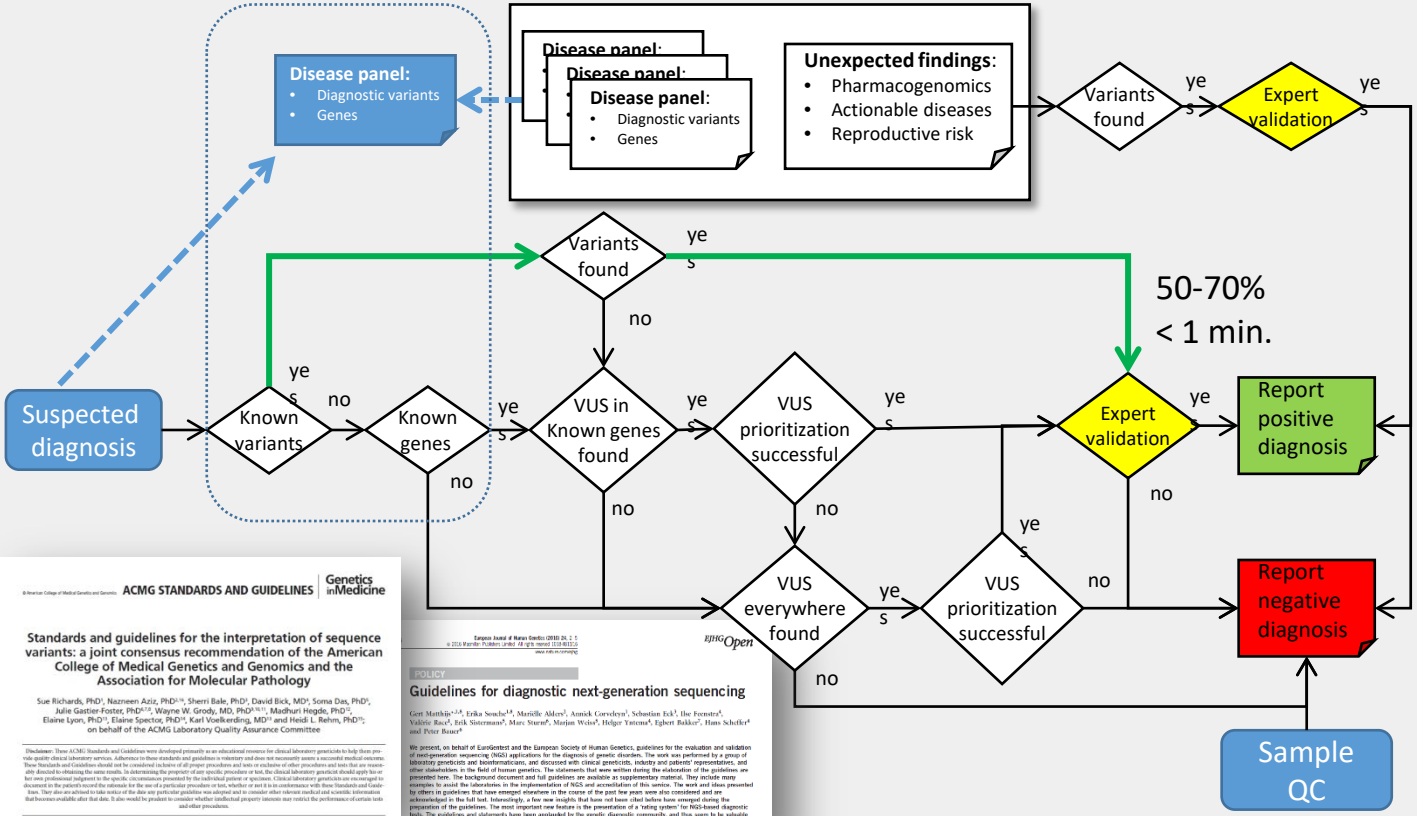
User: **clinician** (**not** bioinformatician)

- A sustainable solution for the management of genomic data requires tools for end users (the **complexity** of the analysis must be **hidden** to the clinician)
- It also must be **integrated** within the corporative systems like any other clinical tests offered by the health system.

Data: **internal** to the health system

- **Genomic** data must be **stored** in the system, **linked** to **clinical** data the same way that other data are for further potential prospective clinical studies
- **GDPR compliance**

Complexity of the general diagnosis protocol (rare diseases)



ACMG STANDARDS AND GUIDELINES | Genetics in Medicine

Standards and guidelines for the interpretation of sequence variants: a joint consensus recommendation of the American College of Medical Genetics and Genomics and the Association for Molecular Pathology

Sue Richards, PhD[1], Nazneen Aziz, PhD[2,3], Sherri Bale, PhD[4], David Bick, MD[5], Soma Das, PhD[6], Julie Gastier-Foster, PhD[4,7], Wayne W. Grody, MD, PhD[8,9,11], Madhuri Hegde, PhD[10], Elaine Lyon, PhD[11], Elaine Spector, PhD[12], Karl Voelkerding, MD[13] and Heidi L. Rehm, PhD[14]; on behalf of the ACMG Laboratory Quality Assurance Committee

European Journal of Human Genetics (2018) 26, 2–5

EJHG Open

POLICY

Guidelines for diagnostic next-generation sequencing

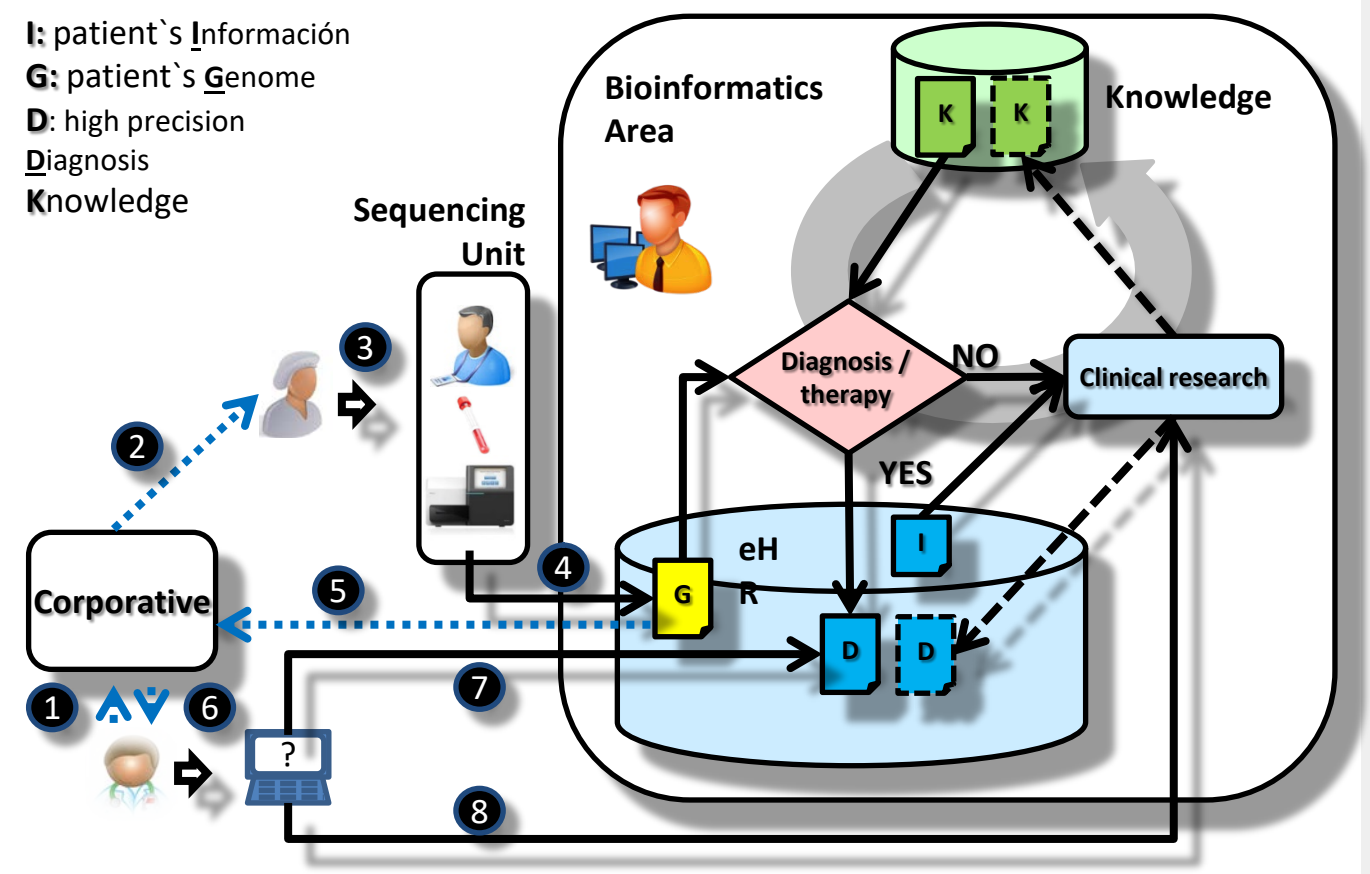
Gert Matthijs[1,2,3], Erika Souche[3,4], Marielle Alders[5], Annick Corveleyn[1], Sebastian Eck[1], Ilse Feenstra[6], Valerie Race[3], Erik Sistermans[6], Marc Sturm[6], Marjan Weiss[6], Helger Yntema[6], Egbert Bakker[7], Hans Scheffer[6] and Peter Bauer[8]

We present, on behalf of EuroGentest and the European Society of Human Genetics, guidelines for the evaluation and validation of next-generation sequencing (NGS) applications for the diagnosis of genetic disorders. The work was performed by a group of laboratory geneticists and bioinformaticians, and discussed with clinical geneticists, industry and patients' representatives, and other stakeholders in the field of human genetics. The statements that were written during the elaboration of the guidelines are presented here. The background document and full guidelines are available as supplementary material. They include many examples to assist the laboratories in the implementation of NGS and accreditation of this service. The work and ideas presented by others in guidelines that have emerged elsewhere in the course of the past few years were also considered and are acknowledged in the full text. Interestingly, a few new insights that have not been cited before have emerged during the preparation of the guidelines. The most important new feature is the presentation of a 'rating system' for NGS-based diagnostic tests. The guidelines and statements have been applauded by the genetic diagnostic community, and thus seem to be valuable for the harmonization and quality assurance of NGS diagnostics in Europe.

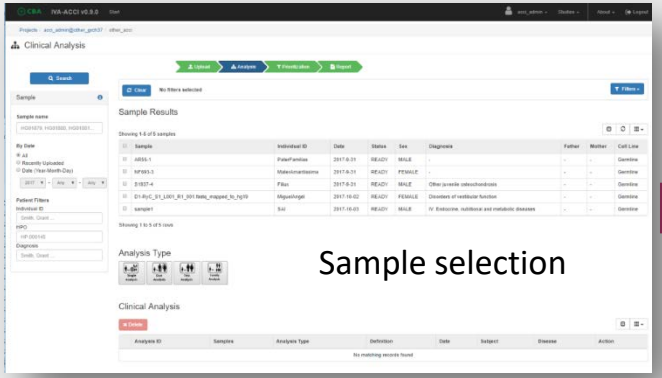
European Journal of Human Genetics (2018) 26, 5–15; doi:10.1038/ejhg.2015.226; published online 28 October 2015

Our approach: hiding the complexity

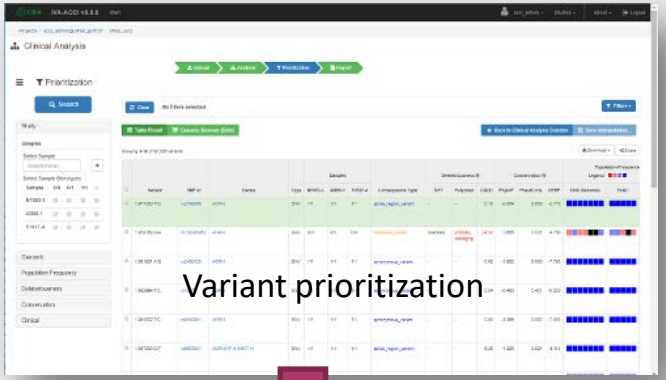
Decision support systems democratize the use of complex (genomic) data



Front end: Personalized Medicine Module (MMP)

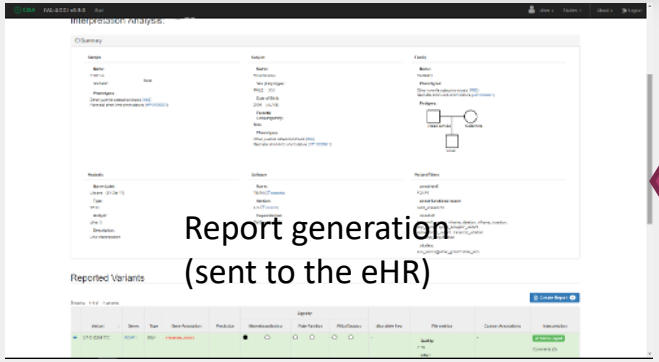


Sample selection



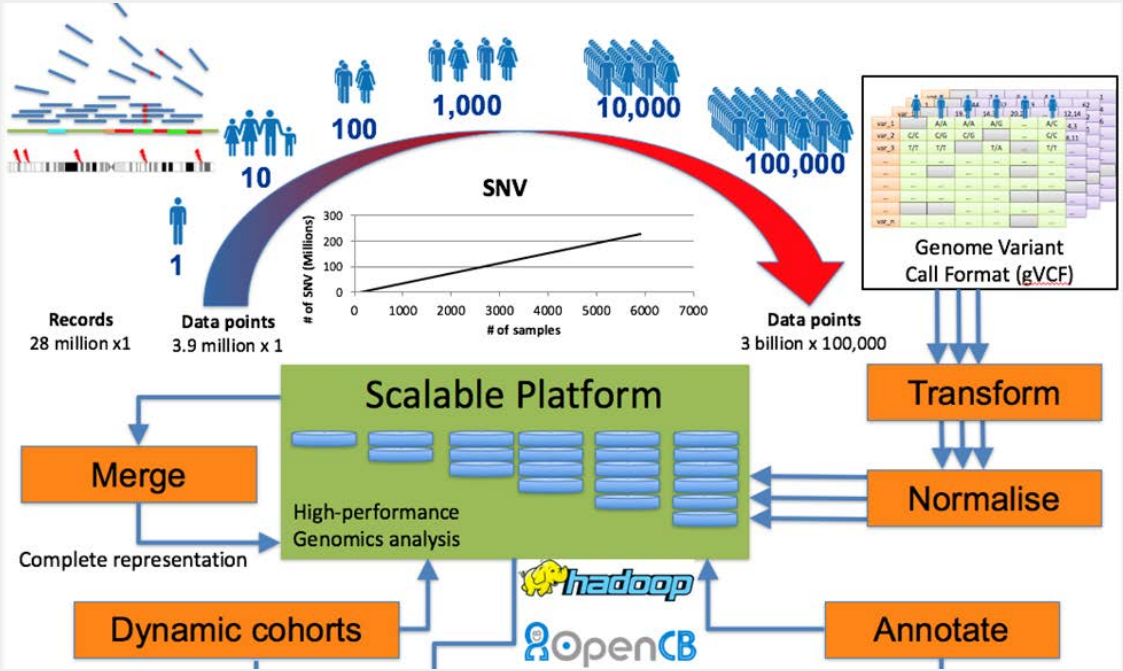
Variant prioritization

Selection of variants for the report



Report generation (sent to the eHR)

Backend: OpenCGA, a scalable storage and genomic data management platform



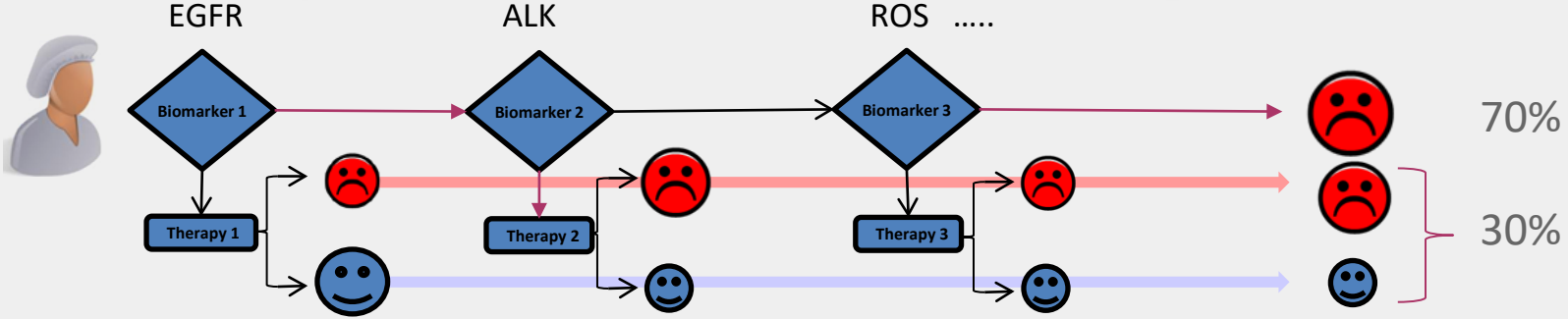
In collaboration with

Genomics england

Currently, the fastest and more powerful genomic database engine in the world.
Used in the GEL for genomic data management
Adopted by the French genomic initiaive

Pilot project of cancer treatment recommendation

Sequential biomarker testing circuit



Article

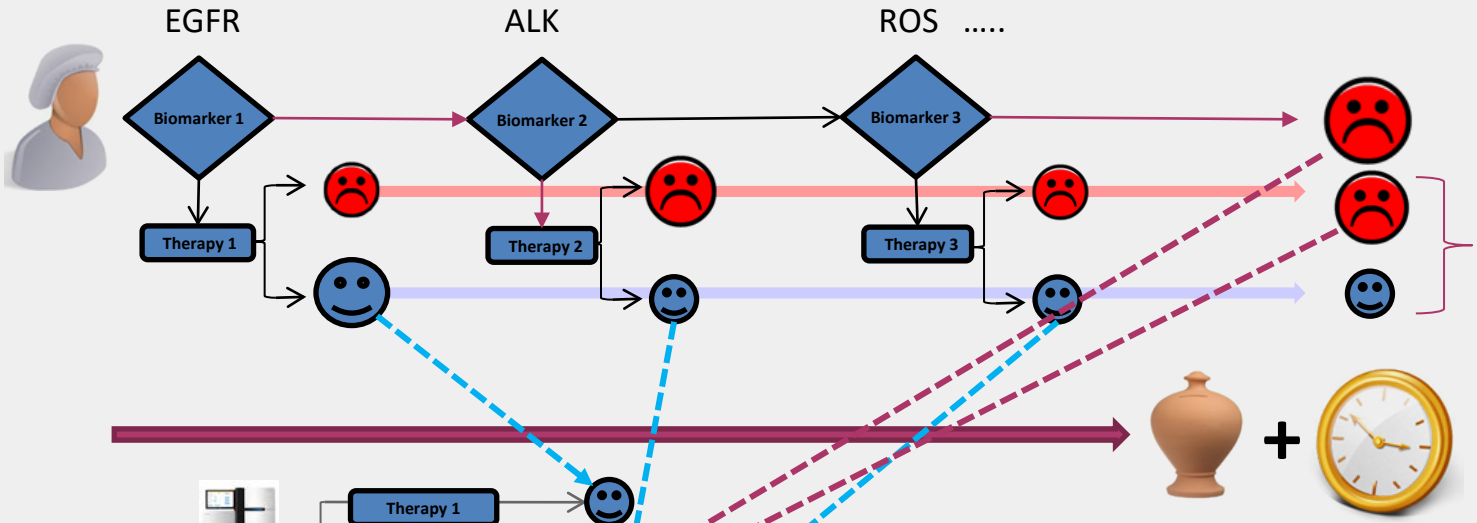
Cell

Oncogenic Signaling Pathways in The Cancer Genome Atlas

rence and mutual exclusivity. Eighty-nine percent of tumors had at least one driver alteration in these pathways, and 57% percent of tumors had at least one alteration potentially targetable by currently available drugs. Thirty percent of tumors had multiple targetable alterations, indicating opportunities for combination therapy.

We are missing many therapeutic opportunities in many patients

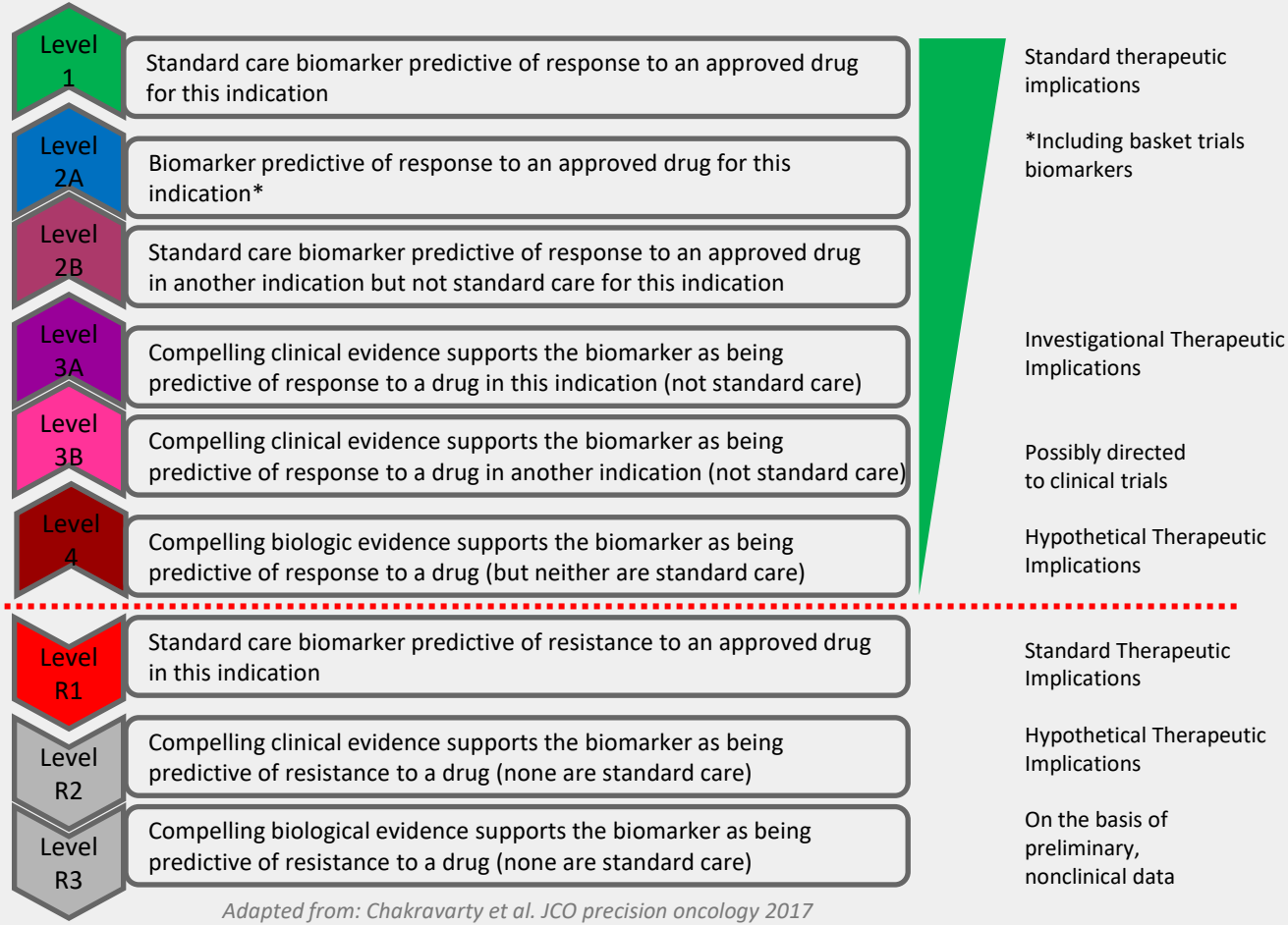
Personalized Medicine in cancer



Enhanced use of biomarkers

Patient genomic data analysis allows one-step association of biomarkers with therapies and enables the detection of new actionable biomarkers, or clinical trials compatible with patients saving time and cost and increasing treatment success

Levels of evidence for cancer treatment recommendation



Adapted from: Chakravarty et al. JCO precision oncology 2017

However, precision diagnosis or treatment recommendation is only the first step to implement personalized medicine in the health system

- Precision diagnosis using genomic data can be carried out everywhere (only a sequencer and the appropriate software is required)

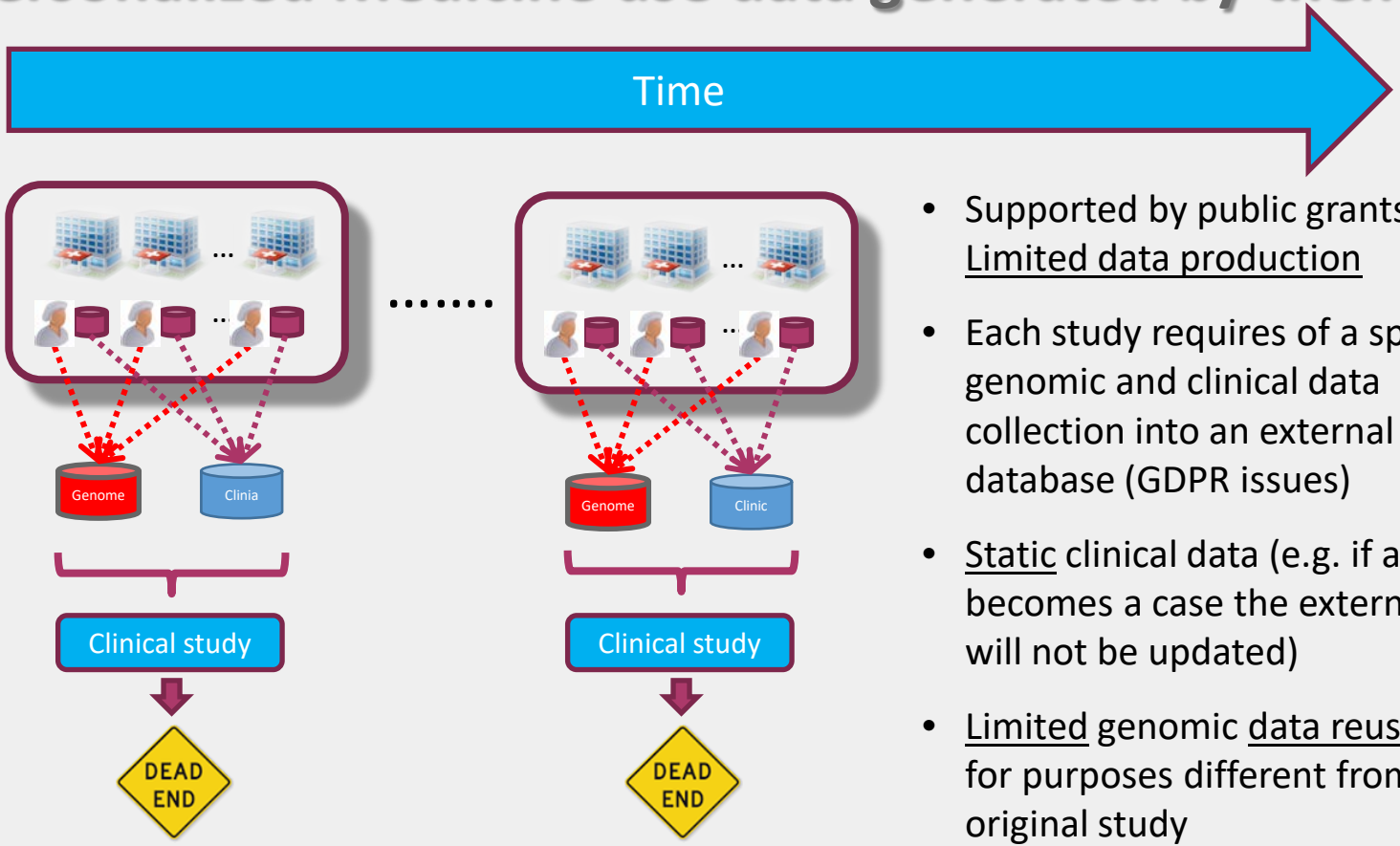
DISCONNECTED HEALTH SYSTEM

- Genomic data generation in a disconnected health system generates **silos** of data at different hospitals or even departments, which limits sample size for clinical studies and data reusability

HEALTH SYSTEM WITH UNIVERSAL EHR

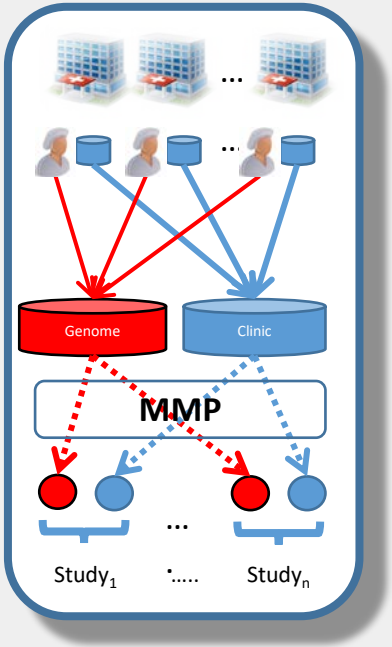
- Genomic data dynamically linked to patient clinical information foster data **reusability** in a **FAIR** (findable, accessible, interoperable and reusable) context

Genomic initiatives are clinical studies. Personalized Medicine use data generated by them



- Supported by public grants. Limited data production
- Each study requires of a specific genomic and clinical data collection into an external database (GDPR issues)
- Static clinical data (e.g. if a control becomes a case the external DB will not be updated)
- Limited genomic data reusability for purposes different from the original study

The real implementation of Personalized Medicine is facilitated by a model that integrates genomic data and universal EHR

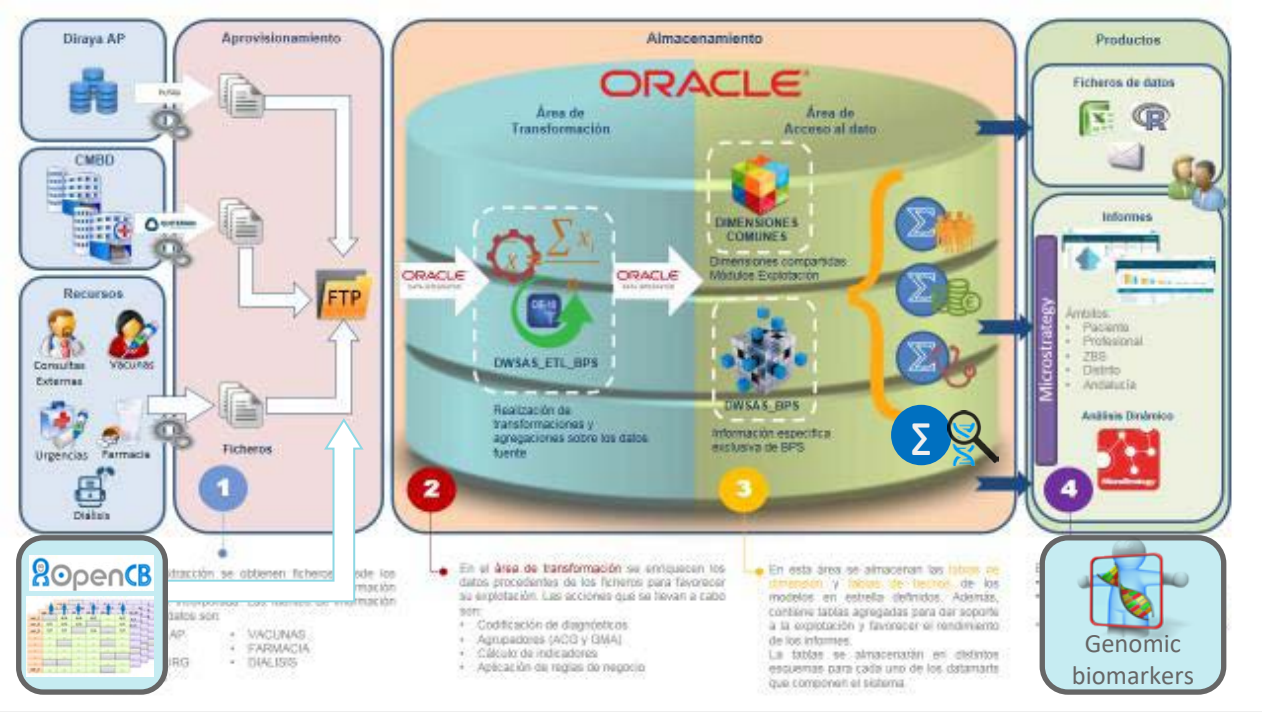


- Data generated by the health system, which increasingly uses genomic data for different purposes, major source of genomic data in the near future
- Genomic data dynamically linked to clinic information
- Possibility of many clinical studies by reanalyzing genomic data under diverse perspectives (with no extra investment)
- The whole health system becomes a enormous potential prospective clinical study

The population health database

BPS

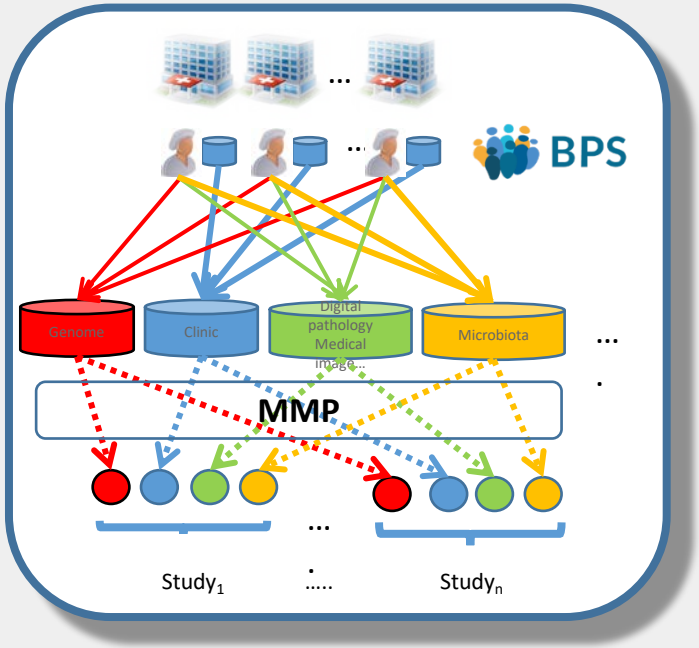
Possibly the largest database ever created with detailed clinical data, storing information on 12.083.681 patients since 2001



Soon, the genomic data collected by the SAS will be included in the BPS and queries that combine genomic and clinic data will be possible

Future vision involves *big data* integration:

Genomic data are especially relevant for discovering the genetic determinants of diseases, but not the only useful *big data*



- Other *big data* are being collected (medical image, digital pathology, wearable devices, etc.)
- Microbiota in the future (CR cancer screening)
- Clinical data In the BPS will be dynamically associated to different *big data*
- The whole health system becomes a enormous potential prospective clinical study
- Immense possibility for data reusability
- Growing genomic DB with increasing study possibilities

Fundación Progreso y Salud
CONSEJERÍA DE SALUD Y FAMILIAS

Clinical Bioinformatics Area
Fundación Progreso y Salud, Sevilla, Spain, and...

...the INB-ELIXIR-ES, National Institute of Bioinformatics and the BiER (CIBERER Network of Centers for Research in Rare Diseases)

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GDPR compliance

The system has been designed in a way that is compliant with EU and Spanish General Data Protection Regulation

- Clinicians requesting for a genomic diagnostic have access to eHR and only get the result of the test.
- Geneticists have access to eHR and can query the genomic data (but never extract them)
- IT have access to anonymized genomic data but not to eHR.