

From reads to disease variants

Introduction to openCGA and IVA for variant prioritization

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<http://www.clinbioinfospa.es>

Clinical Bioinformatics Area

Fundación Progreso y Salud / Servicio Andaluz de Salud
Seville



Fundación Progreso y Salud
CONSEJERÍA DE SALUD



Overview

- Introduction
- *Big Data* in Genomics
- OpenCB: Open source initiative for Computational Biology
- A case study: Personalized Medicine Module (MMP)

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- **Introduction**
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Introduction

About the Clinical Bioinformatics Area

Clinical Bioinformatics Area The Area Tools Publications Courses News

Welcome

The Clinical Bioinformatics Area has opened a position for a Web Programmer.
Submitted by jdopazo on Tue, 03/20/2018 - 09:54

Fundación Progreso y Salud
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Tools:

Other tools

Tweets by @ClinicalBioInfo

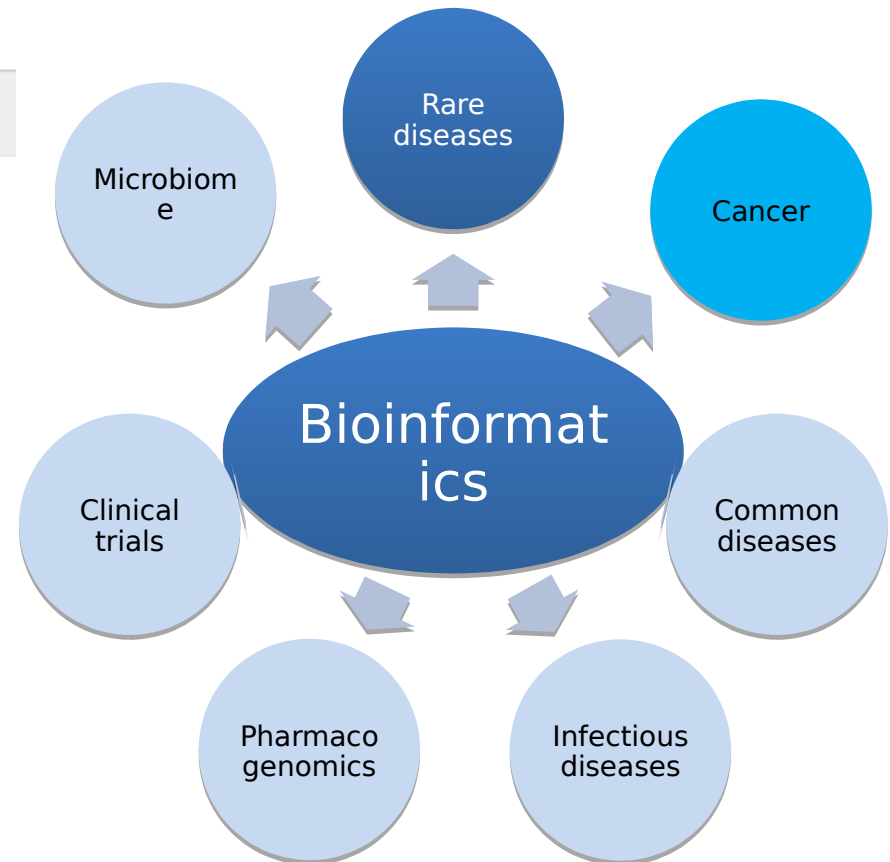
Clinical BioInfo Retweeted

Joaquín Dopazo @xdopazo
clinbioinfospa.es/content/beca-r...

Beca remunerada para...
Formación práctica y teo...
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Apr 30, 2018

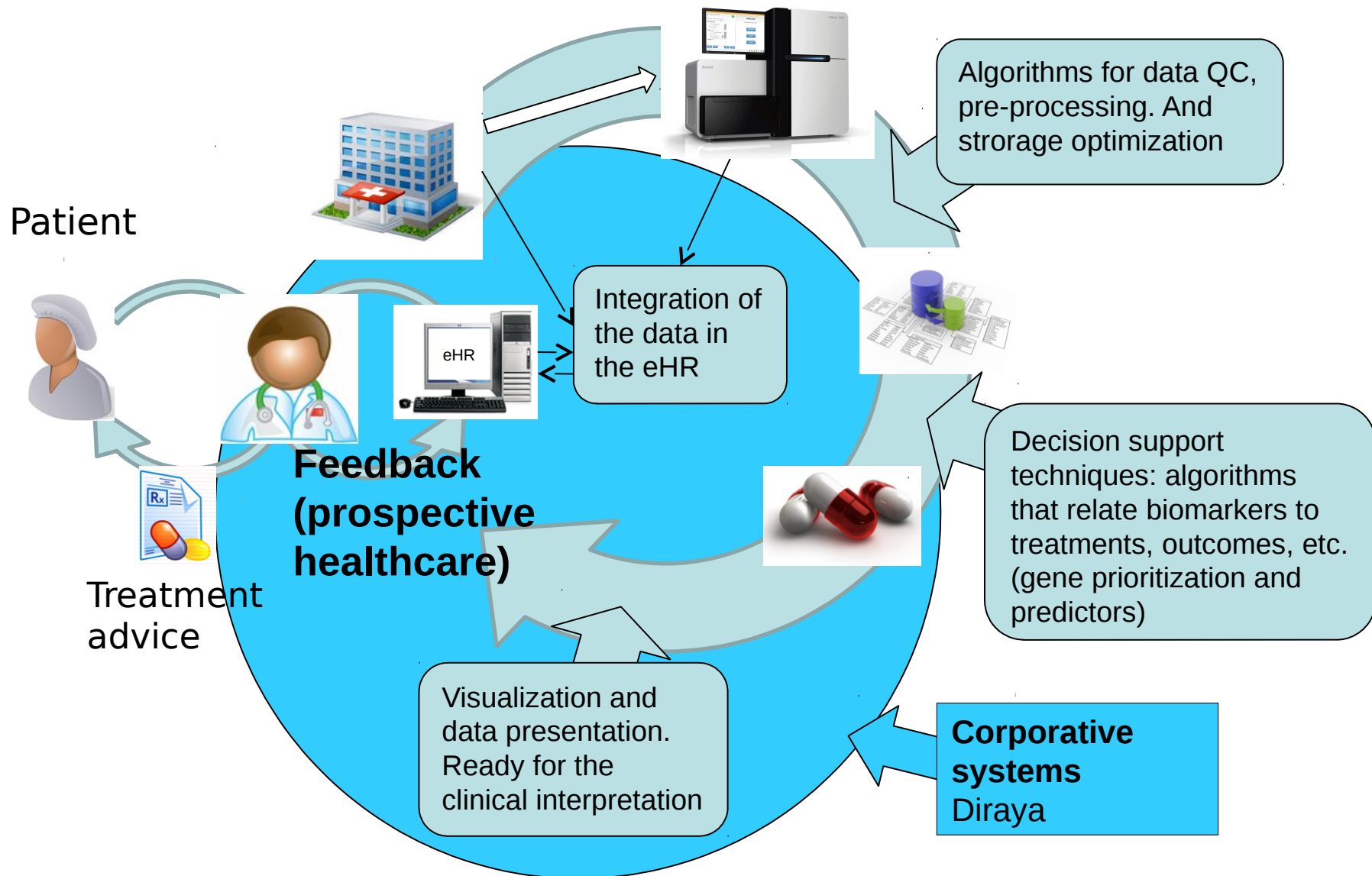
<http://www.clinbioinfospa.es/>



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 4 public health system.

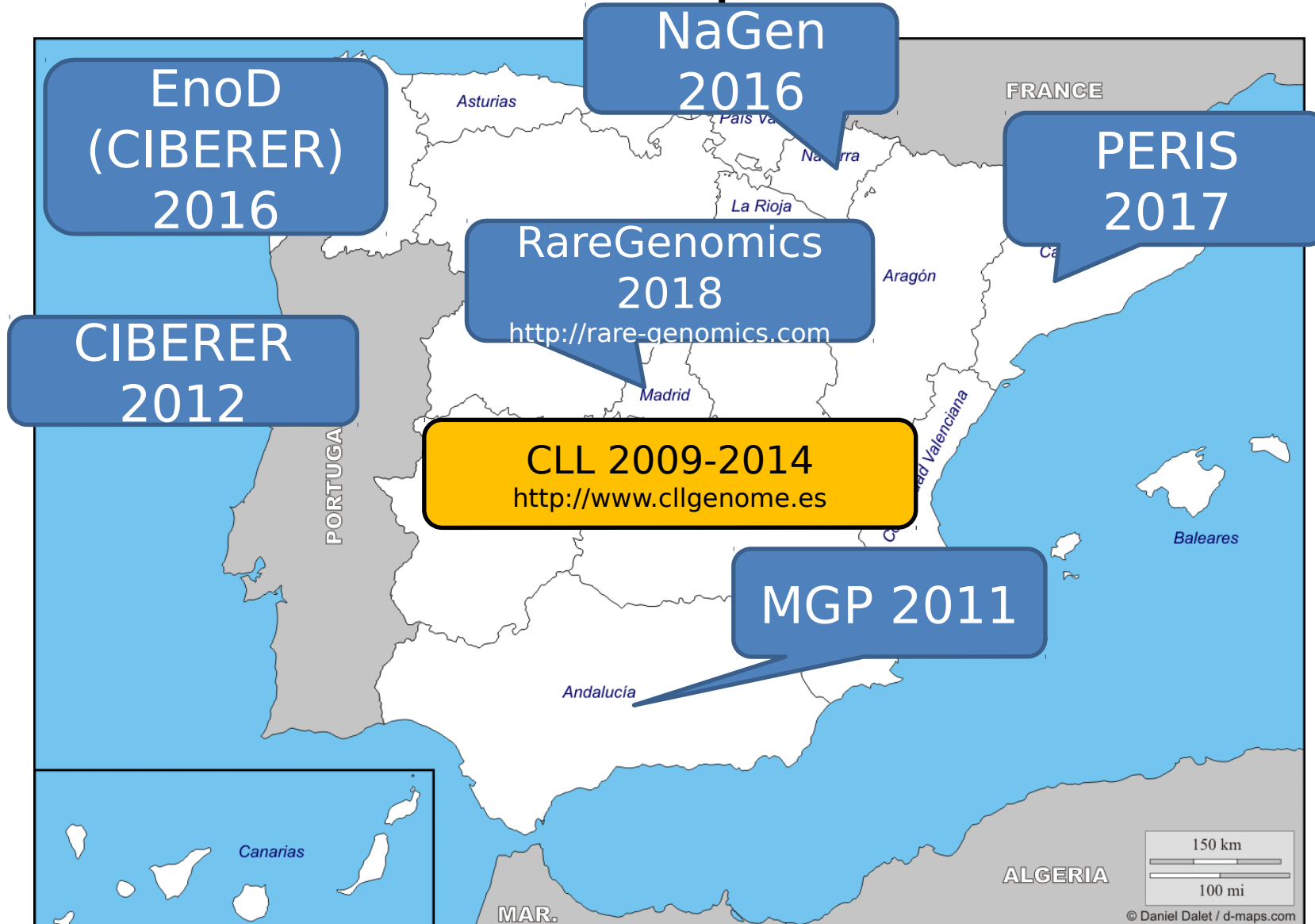
Introduction

Bioinformatics for personalized medicine within the Andalusian health system



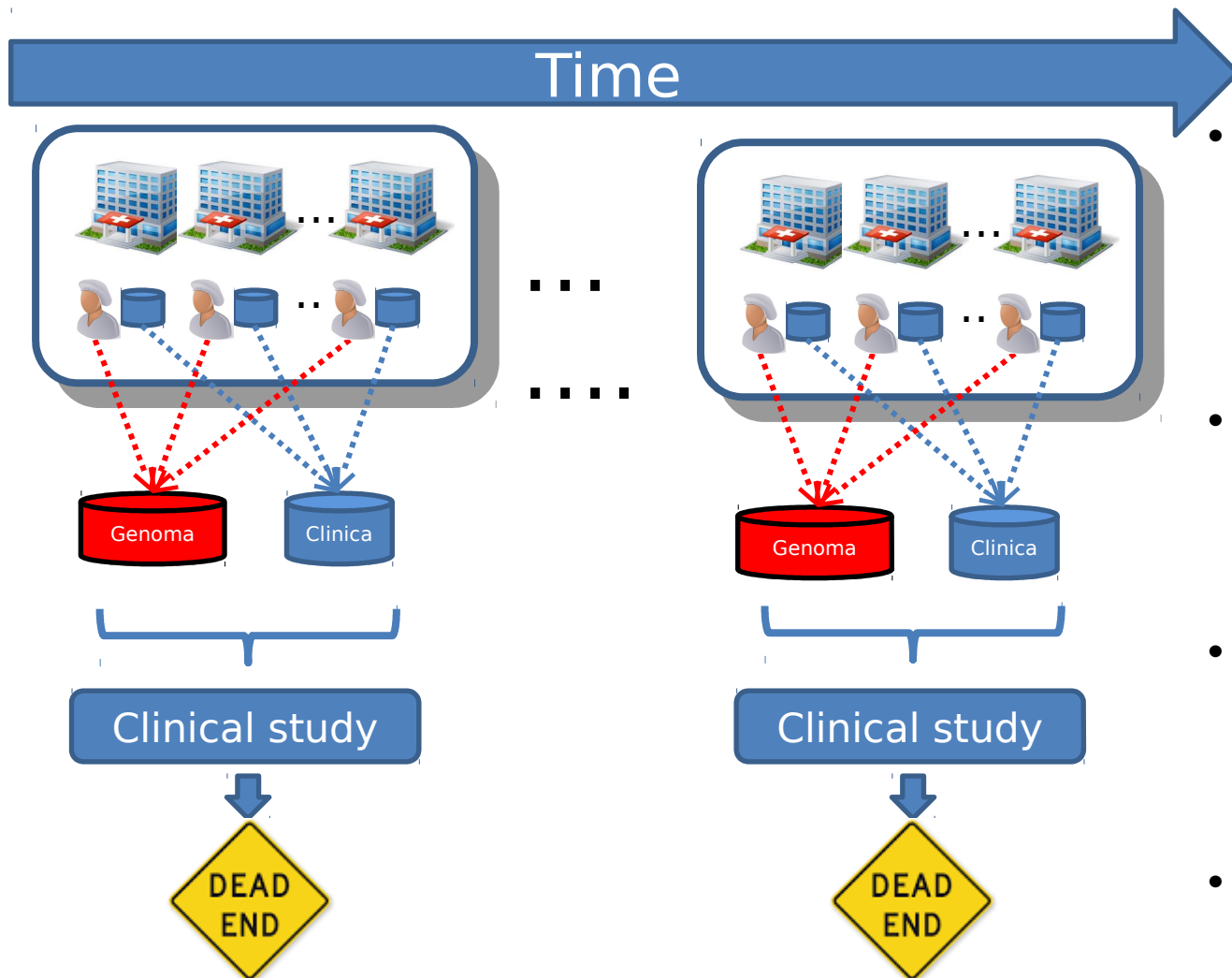
Introduction

Genomic initiatives in Spain



Introduction

Genomic initiatives without universal eHR are just clinical studies but not Personalized Medicine



- Each study requires of a specific genomic and clinical data collection into an external database
- Static clinical data (e.g. if a control becomes a case the external DB will not be updated)
- Limited genomic data reuse for purposes different from the original study
- Model of GEL (100,000 genomes) and other initiatives.

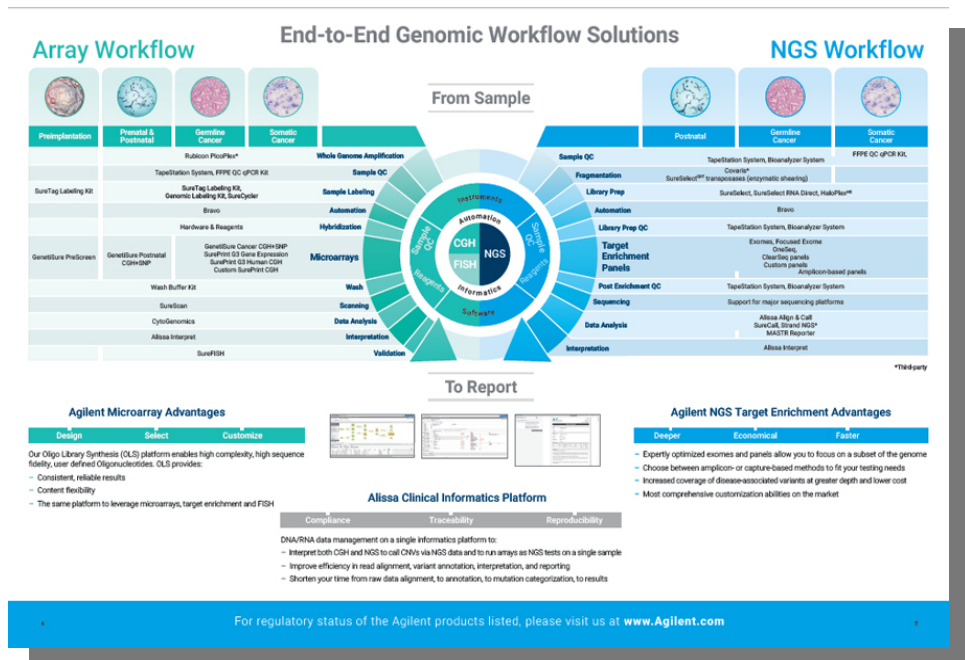
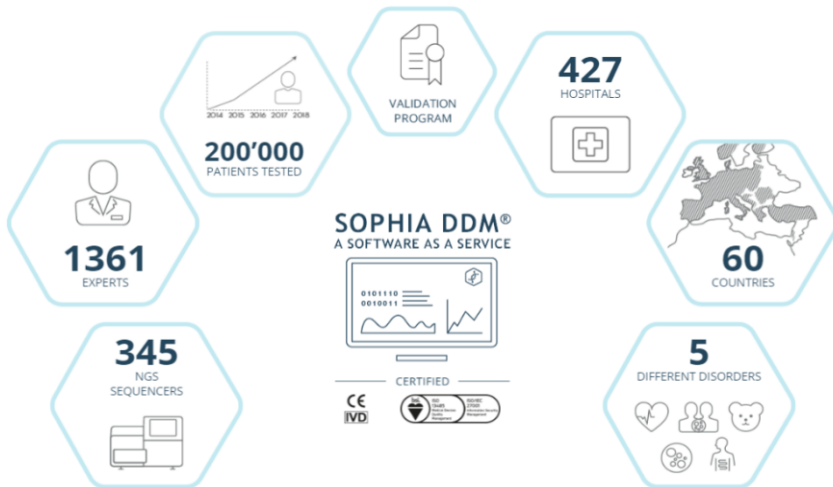
Introduction

The value of genomic data for the health system

SOPHIA GENETICS*

ACCESS TO SOPHIA GENETICS' COMMUNITY

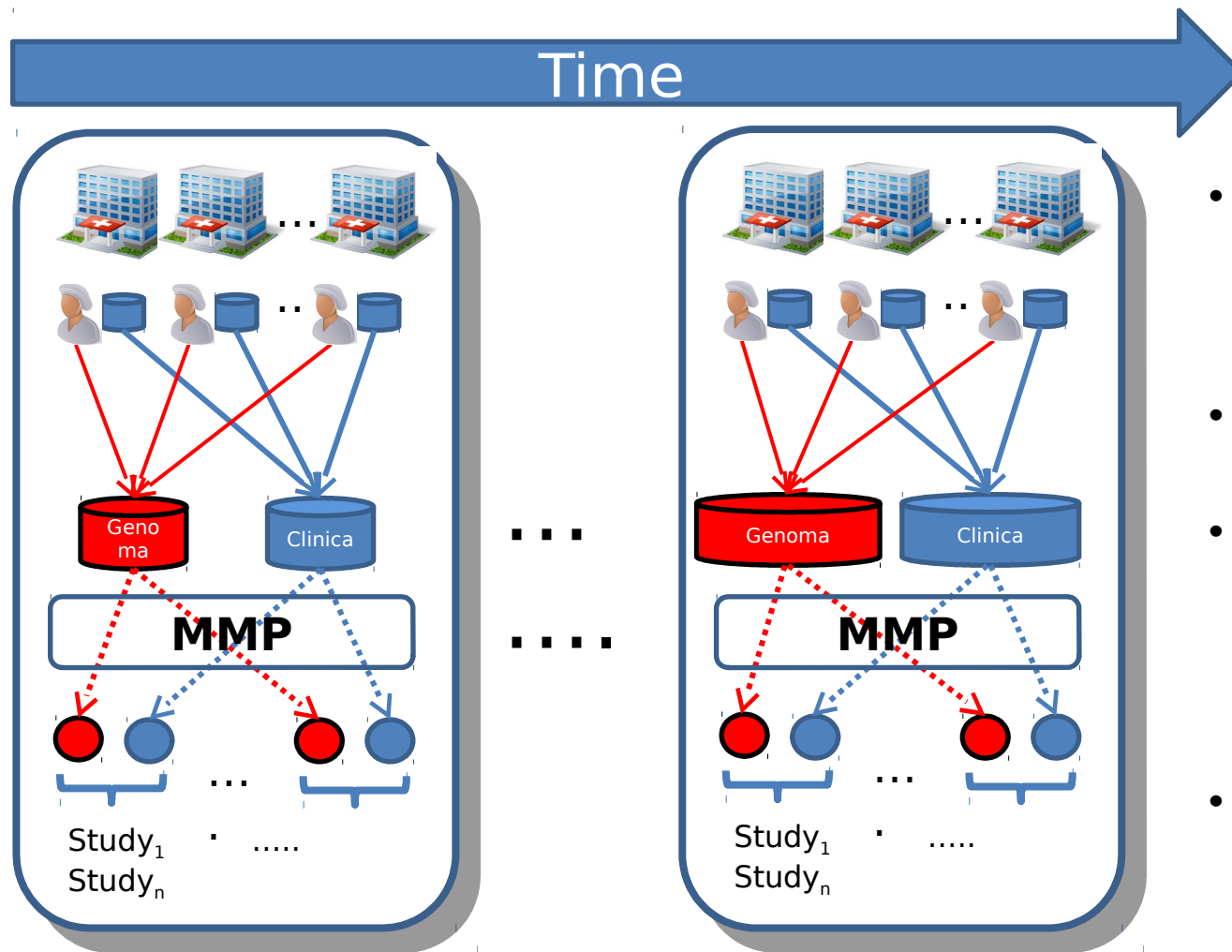
SOPHIA GENETICS has gathered hundreds of healthcare institutions participating in the democratization of Data-Driven Medicine. Through SOPHIA DDM, experts from hundreds of institutions can easily interpret the variants and flag them with the appropriate level of pathogenicity. This highly valuable information feeds the variant knowledge base and is anonymously and safely shared among the members of the community. Thus enabling clinicians around the world to collaborate, and find better treatment options for their patients.



Currently, because of the lack of adequate resources, genomic data analysis is externalized to companies or private software. We lose the control on the data externalized and actually work for external companies for free

Introduction

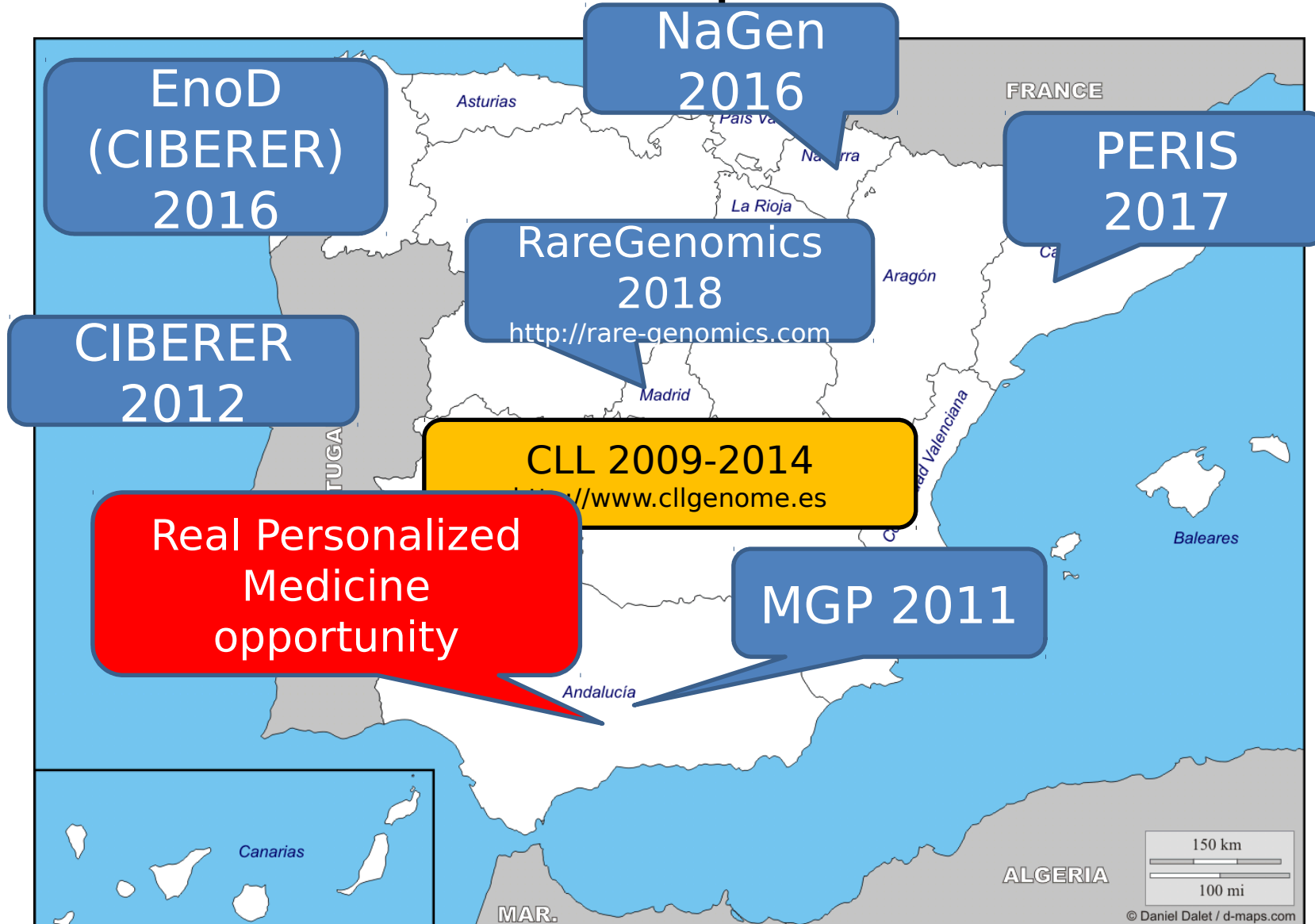
Personalized medicine requires a model that integrates genomic data and universal eHR



- The whole health system becomes a enormous potential prospective study
- Clinical data dynamically associated to patients
- Possibility of many clinical studies by reanalyzing genomic data under diverse perspectives (with no extra investment)
- Growing genomic DB with increasing study possibilities

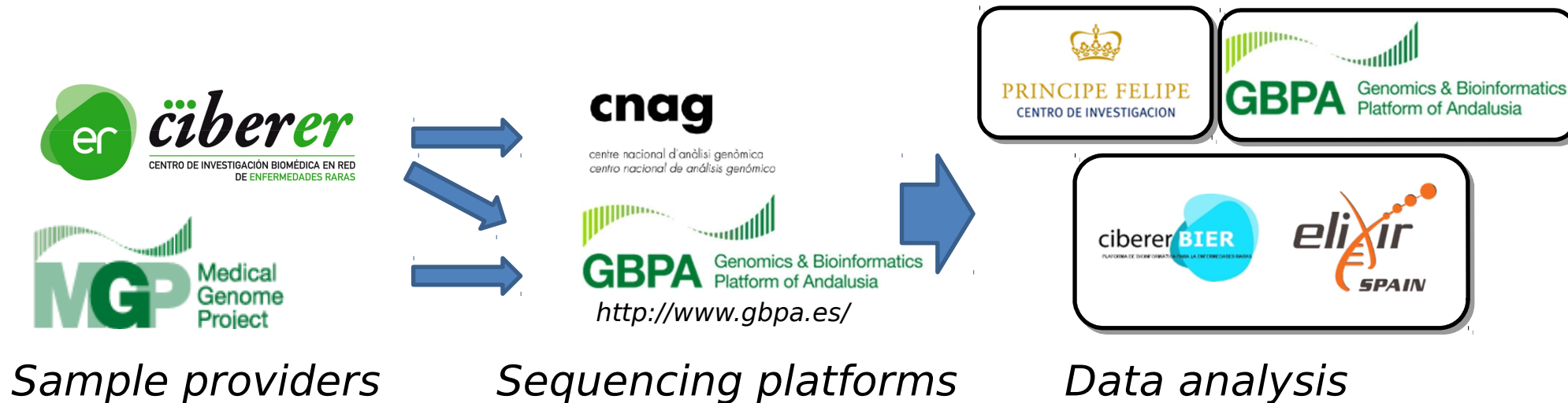
Introduction

Genomic initiatives in Spain



Introduction

Previous initiatives: MGP and CIBERER initiatives to sequence rare disease patient exomes



Diseases with

- Unknown causal genes
- No mutations in known genes

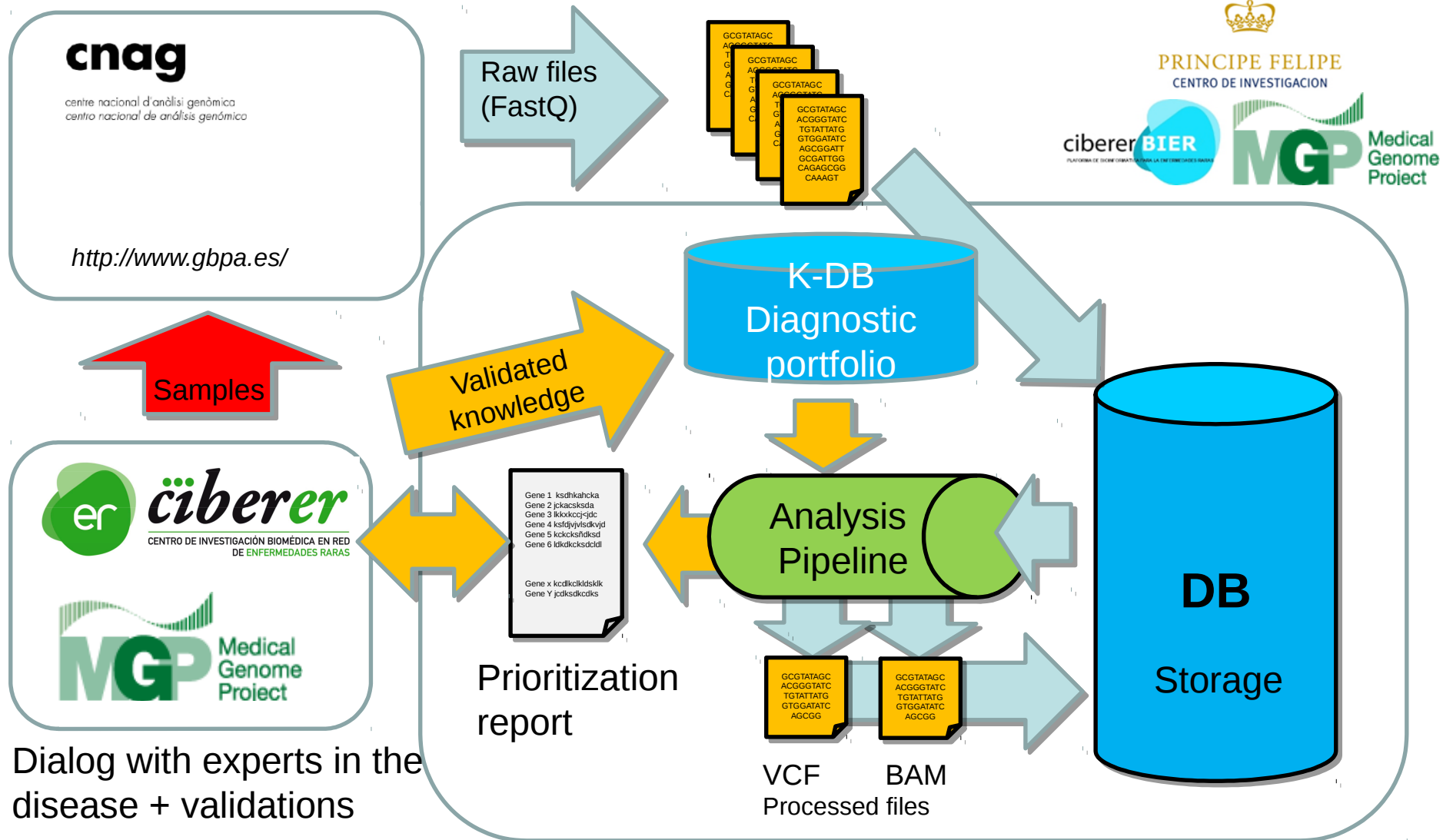
Search for:

- New disease genes
- Susceptibility genes

A total of 1044 exomes of 300 healthy controls and patients of more than 30 diseases were sequenced between 2012 and 2013.

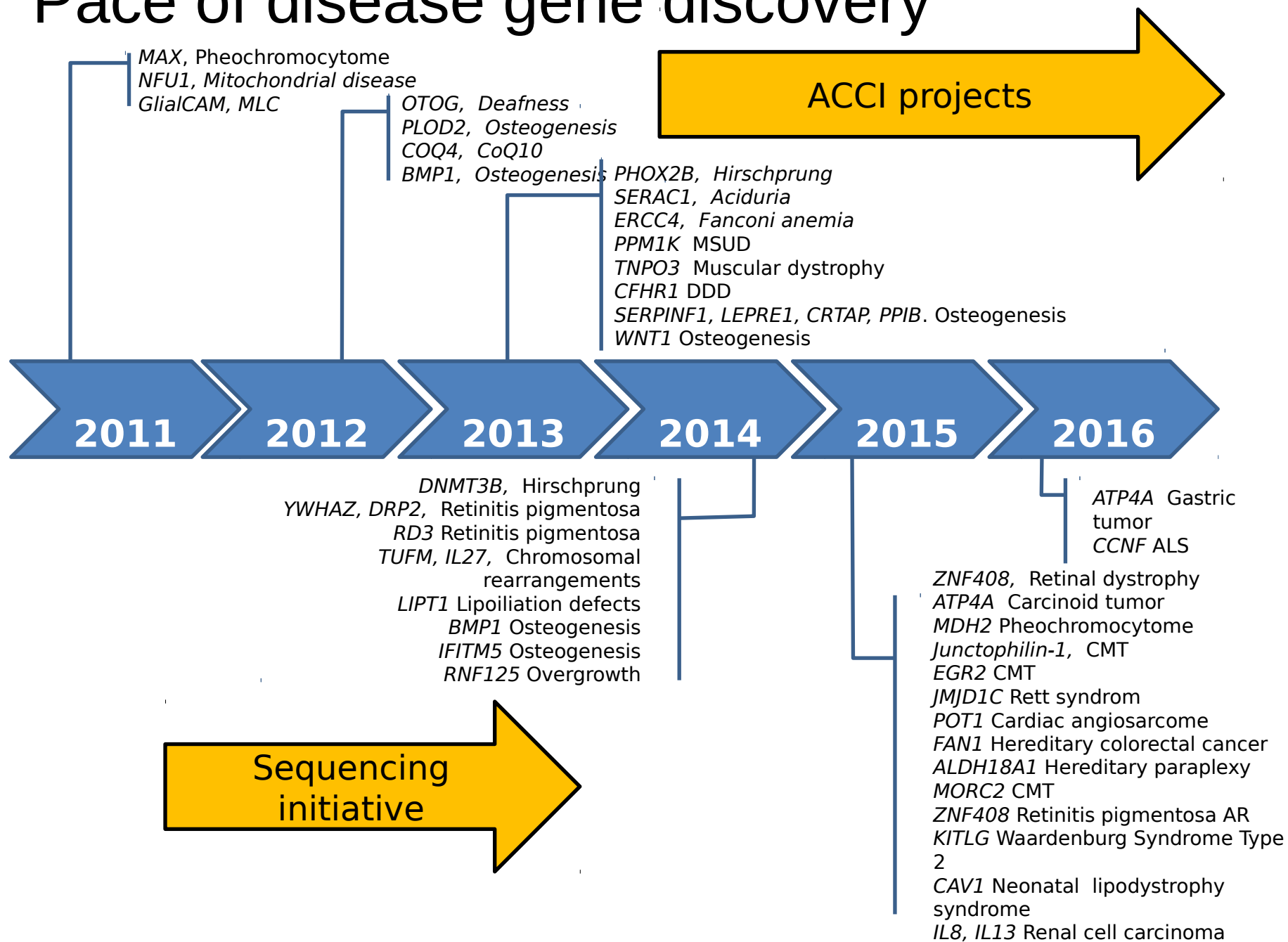
Introduction

Data analysis and the cycle of knowledge generation



Introduction

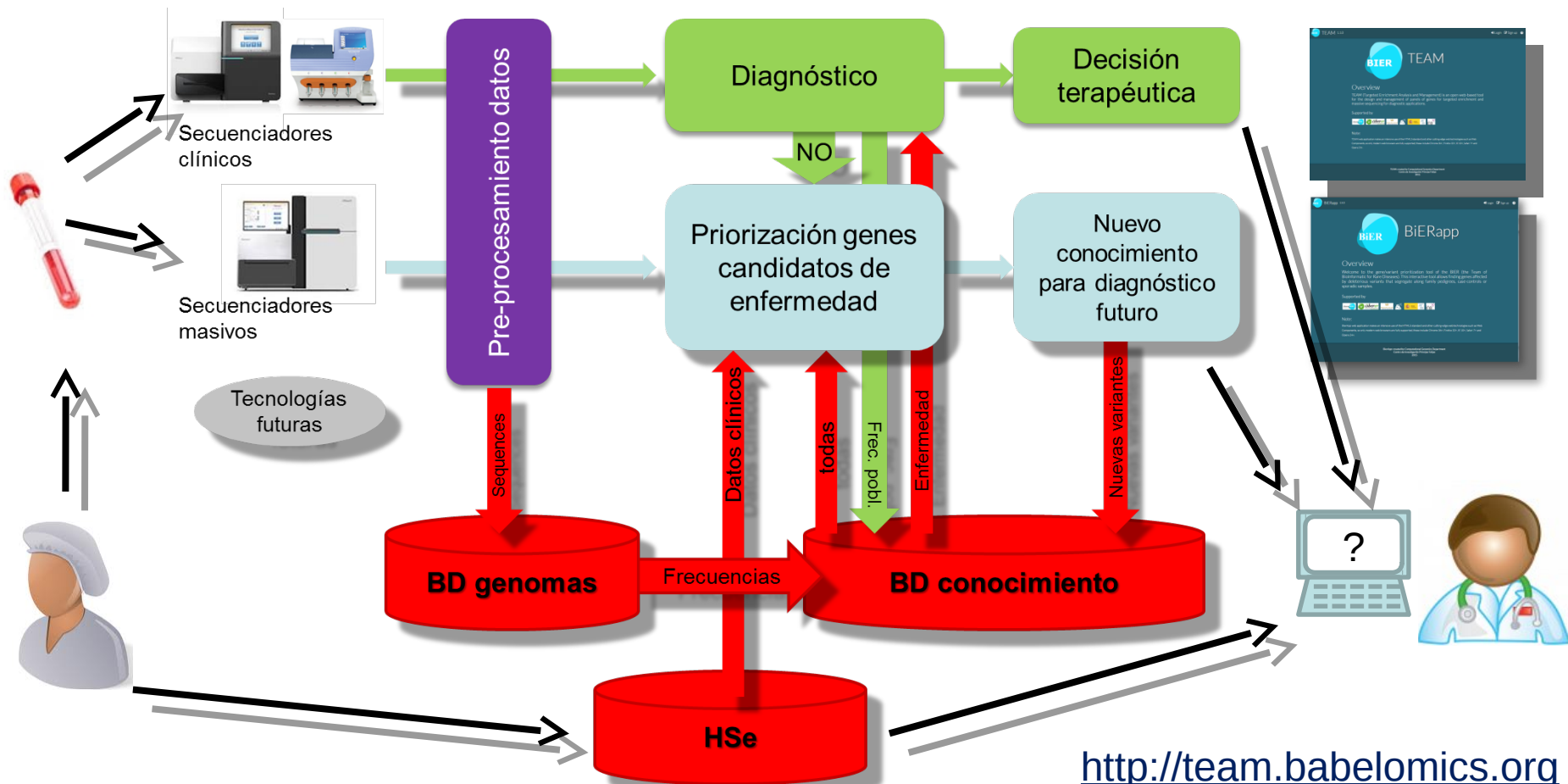
Pace of disease gene discovery



Introduction

CIBERER initiative for diagnosis and biomarker discovery using massive sequencing

Ongoing (second phase) Project with the collaboration of seven hospitals: La Paz, FJD, Ramón y Cajal, CBM (Madrid), Virgen del Rocío (Sevilla), Hospital del Mar (Barcelona), HU La Fe (Valencia)., within the context of CIBERER



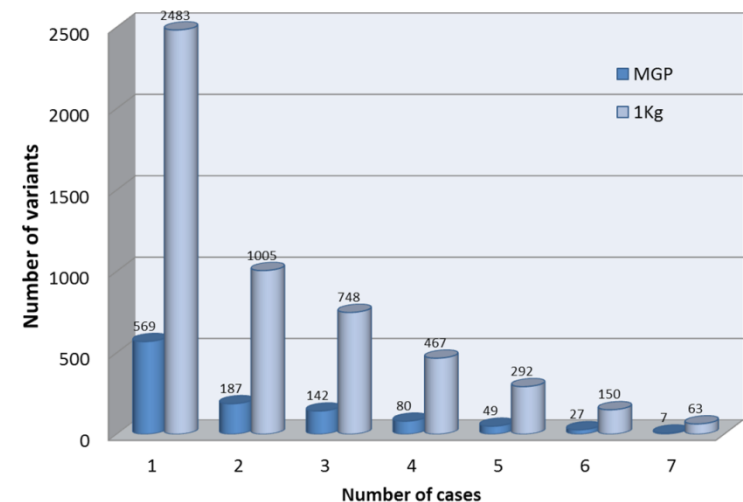
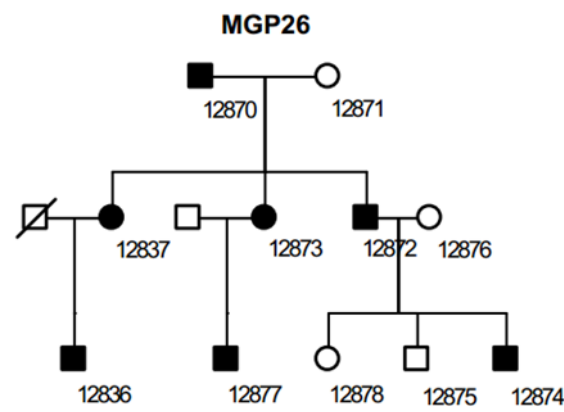
<http://team.babelomics.org>
<http://BiERapp.babelomics.org>

Introduction

Lessons learned: the importance of local variability in the prioritization process

The screenshot shows the Oxford Journals website for the article "267 Spanish Exomes Reveal Population-Specific Differences in Disease-Related Genetic Variation". The article is published in *Molecular Biology and Evolution*, Volume 33, Issue 5, pages 1205-1218. The authors listed are Joaquín Dopazo, Alicia Amadoz, Marta Bleda, Luz García-Alonso, Alejandro Alemán, Francisco García-García, Juan A. Rodríguez, Josephine T. Daub, Gerard Muntané, Antonio Rueda, Alicia Vela-Boza, Francisco J. López-Domingo, Javier P. Florido, Pablo Arce, Macarena Ruiz-Ferrer, Cristina Méndez-Vidal, Todd E. Arnold, Olivia Spleiss, Miguel Alvarez-Tejado, Arcadi Navarro, Shomi S. Bhattacharya, Salud Borrego, Javier Santoyo-López, and Guillermo Antñolo. The article is Open Access, with the abstract, full text (HTML), full text (PDF), and supplementary data all available for free. The current issue is November 2016, Volume 33, Issue 11.

We discovered some 12,000 “spanish” polymorphisms not present in other databases. The filtering efficiency enormously increases using local population data



Introduction

The CSVS is a crowdsourcing project

Collaborative Spanish Variant Server Search Stats Saturation

BIER CSVS

Start

Overview

Welcome to the Collaborative Spanish Variant Server. CSVS was created to provide information about the variability of the Spanish population to the scientific/medical community. It is useful for filtering polymorphisms and local variations in the process of prioritizing candidate disease genes. CSVS currently stores information on 1582 unrelated Spanish individuals. We accept submissions from WES or WGS. See the protocol for sending samples.

Supported by

Note:

CSVS web application makes an intensive use of the HTML5 standard and other cutting-edge web technologies such as Web Components, so only modern web browsers are fully supported, these include Chrome 36+, Firefox 32+, IE 10+, Safari 7+ and Opera 24+.

CSVS created by Clinical Bioinformatics Area
Fundación Program y Salud
2012-2017

Chromosomal Location	Gene	Variant	Type	RefSeq	rsID	1000G MAF (phase 2)																
						ALL	AME	South ASI	East ASI	AFR	EUR	FIN	IND	JPT	CHB							
10:43572511	G>A	RET			rs10902207	0.75	2	1	0	0.997	0.003	0.003	0.350	0.400	0.270	0.330	0.400	0.285	0.263	0.248	0.300	0.482
10:43572832	G>A	RET			rs12267460	0.08	52	18	0	0.924	0.076	0.076	0.350	0.400	0.270	0.330	0.400	0.410	0.438	0.410	0.305	
10:43595808	C>G	RET				0.575	3	0	0	0.997	0.003	0.003						0.365	0.418	0.410	0.305	
10:43595818	C>T	RET				0.575	3	0	0	0.997	0.003	0.003										
10:43595837	T>T	RET				0.474	71	33	0	0.881	0.119	0.119										
10:43595837	T>	RET				0.474	71	33	0	0.881	0.119	0.119										
10:43595968	A>G	RET			rs1800858	0.348	74	156	0	0.466	0.334	0.334	0.280	0.220	0.470	0.090	0.300	0.246	0.251	0.306	0.473	
10:43596003	G>A	RET				0.577	1	0	0	0.999	0.001	0.001										
10:43596179	G>A	RET			rs12453351	0.280	155	36	7	0.801	0.199	0.199	0.180	0.260	0.100	0.070	0.260	0.185	0.280	0.208	0.116	

<http://csvs.babelomics.org/>

Allelic population frequencies obtained from 1,600 exomes are currently available in CSVS

- Nearly 2000 samples expected in October, 2018 (including WGS)

Scenario: Sequencing projects of healthy population are expensive and funding bodies are reluctant to fund them

CSVS Aim: To offer increasingly accurate information on variant frequencies characteristic of Spanish population.

CSVS Main use: Frequency-based filtering of candidate variants

Main data source: Sequencing projects of individual researchers (CIBERER and others)

Problem: Most of the contributions correspond to patient exomes

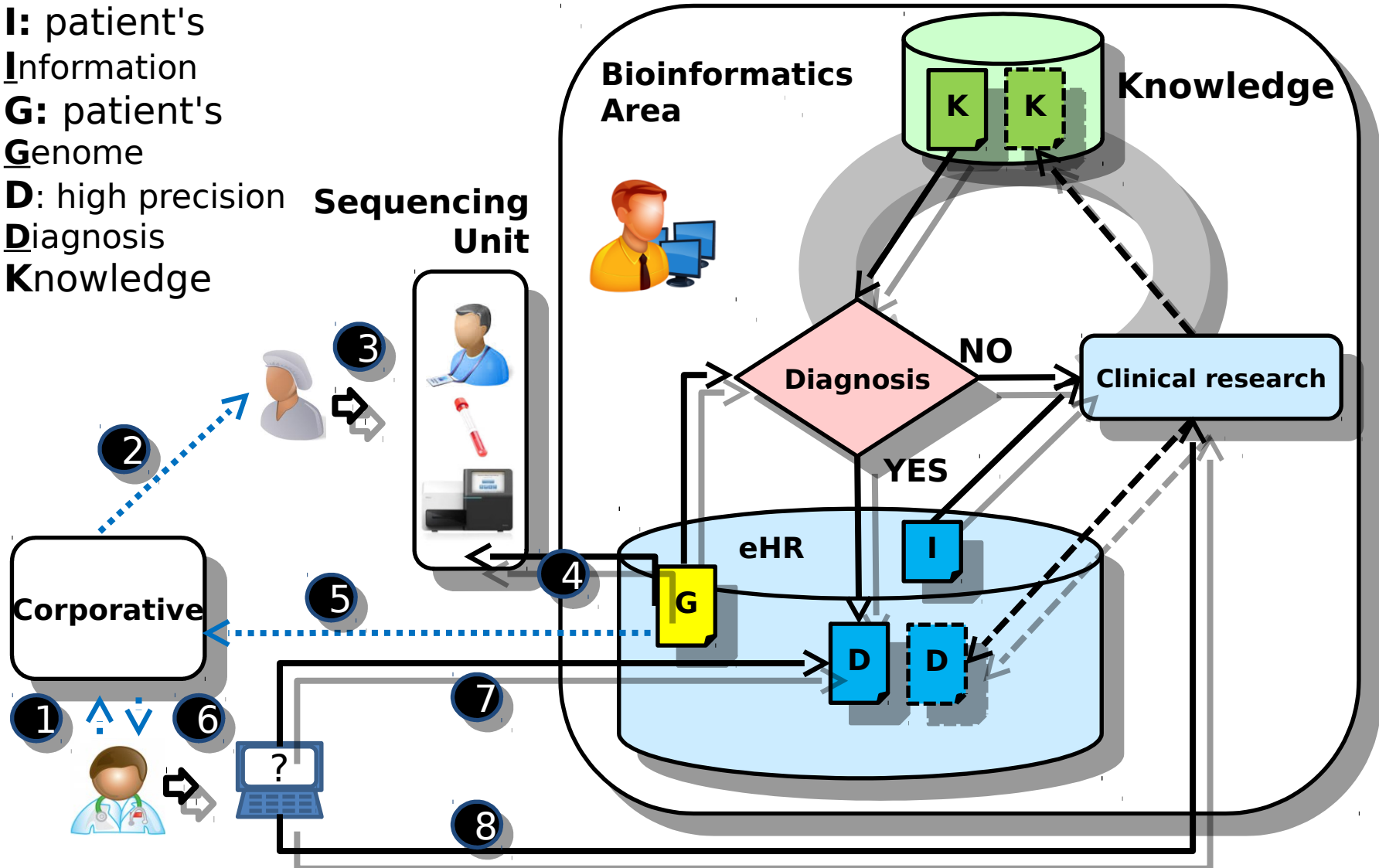
Idea: Patients of disease A can be considered healthy **pseudo-controls** for disease B (providing no common genetic background exist between A and B)

Beacon: CSVS has a Beacon server (Beacon network is search engine across beacons which enables global discovery of genetic mutations)

Introduction

MMP for diagnosis and clinical research within the Andalusian health system

I: patient's
Information
G: patient's
Genome
D: high precision
Diagnosis
Knowledge



Overview

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- ***Big Data* in Genomics**
- OpenCB: Open source initiative for Computational Biology
- A case study: Personalized Medicine Module (MMP)

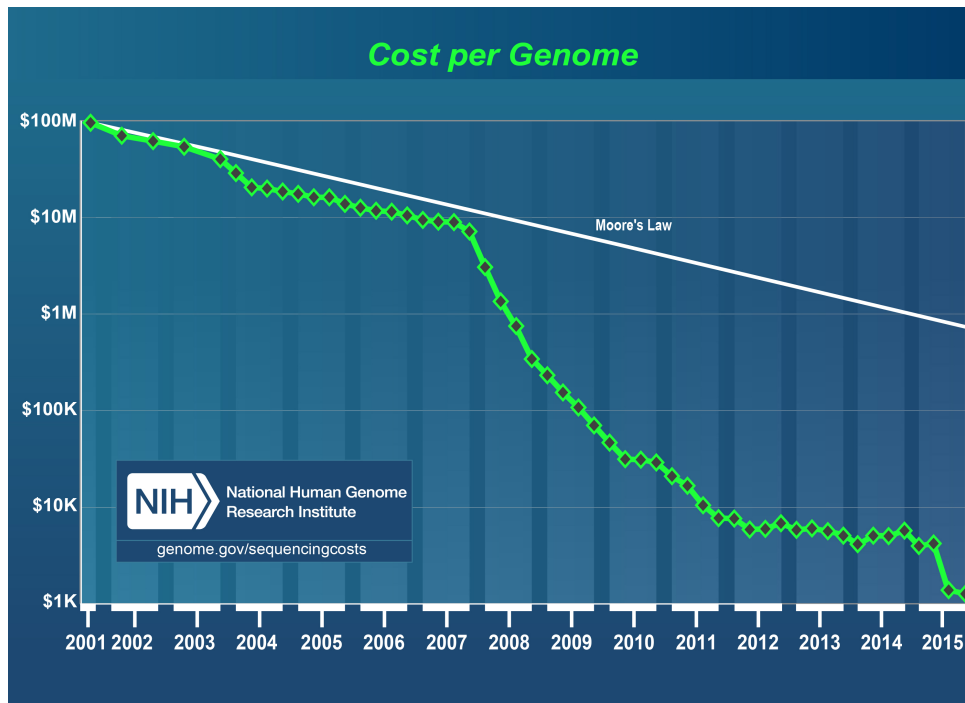
Big data in Genomics

A new scenario in biology

NGS experiments *have increased data size by more than 5000x* compared to microarrays.

Challenges:

- **Sequencing cost** keeps falling while throughput keeps increasing. Today a whole genome can be sequenced by less than **\$1000**
- **Variant analysis**: re-sequencing projects such as Whole Genome Sequencing (WGS) aims to find genomic variants and genes involved in phenotypes and diseases



A single HiSeq X Ten System can sequence ~20,000 human genomes a year

Human whole-genome sequencing power

Maximum throughput for population- and production-scale genomics.

HAVE QUESTIONS ABOUT THE HISEQ X SEQUENCING SYSTEMS? CONTACT A SALES REPRESENTATIVE >

The \$1000 Genome Is Here
Discover how HiSeq X Ten breaks the \$1000 genome barrier for human whole-genome sequencing.
[Learn more >](#)

New HiSeq X Five System Available
The HiSeq X Five is a set of five ultra-high-throughput sequencers for production-scale human whole-genome sequencing.
[Learn more >](#)

Big data in Genomics

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- Illumina NGS sequencer series:
 - **HiSeq 2500** provides high-quality 2x125bp: 50-1000Gb in 1-6 days, 90.2% bases above Q30. One human genome at ~60x coverage
 - **HiSeq 4000** provides high-quality 2x150bp: 125-1500Gb in 1-4 days, >75% bases above Q30. Up to 12 human genomes at ~40x coverage
- **Each sample** produces a **FASTQ** file ~**1TB** size containing ~**1-2B** reads
- **Illumina X Ten**: Consists of 10 ultra-high-throughput HiSeq X sequencers. First \$1000 human genome sequencer, it can sequence up to 20,000 genomes per year

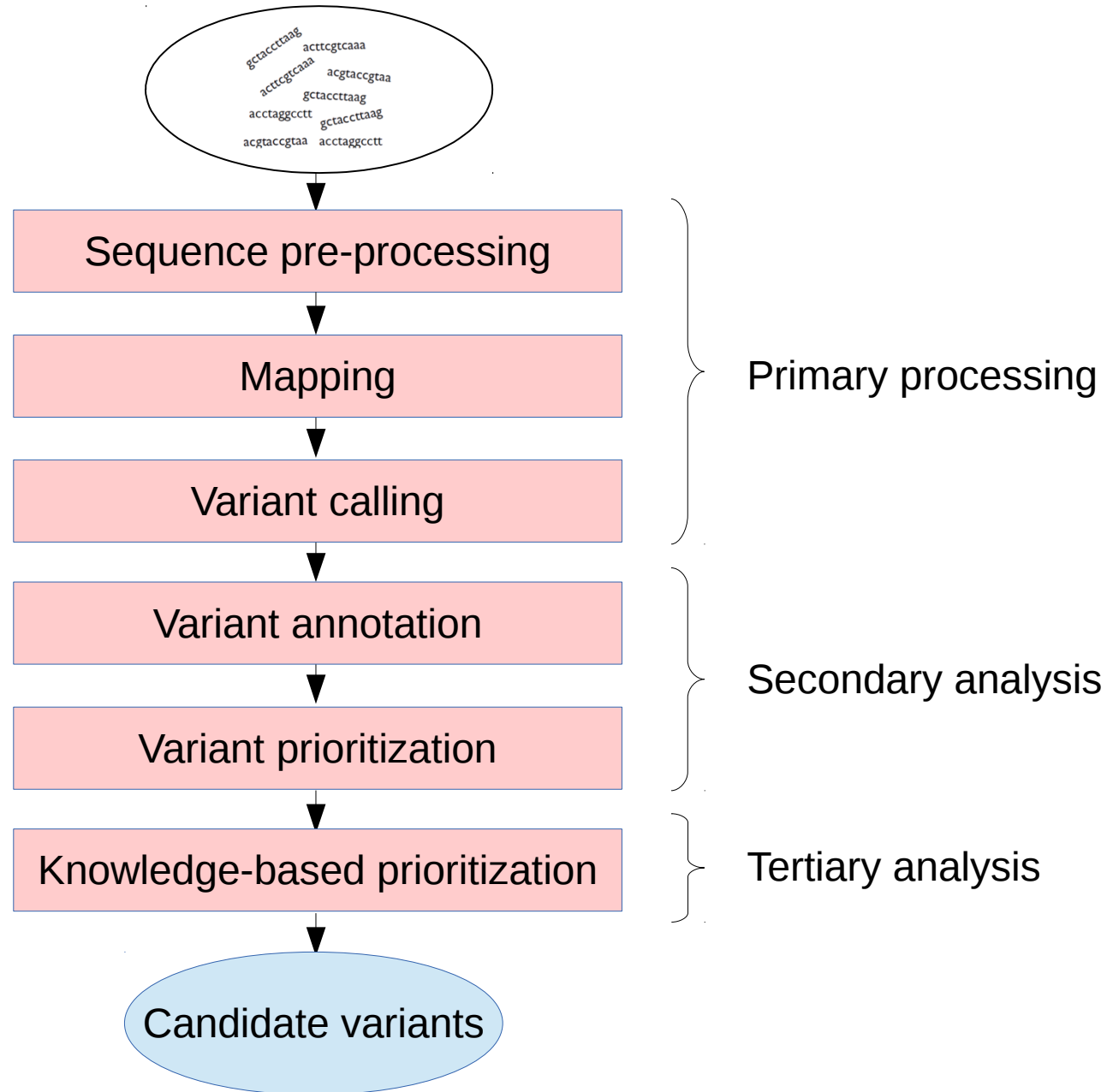


Real flexibility.
Real throughput.
Real data quality.

The HiSeq 2500 is ready for any application, any sample size—today.

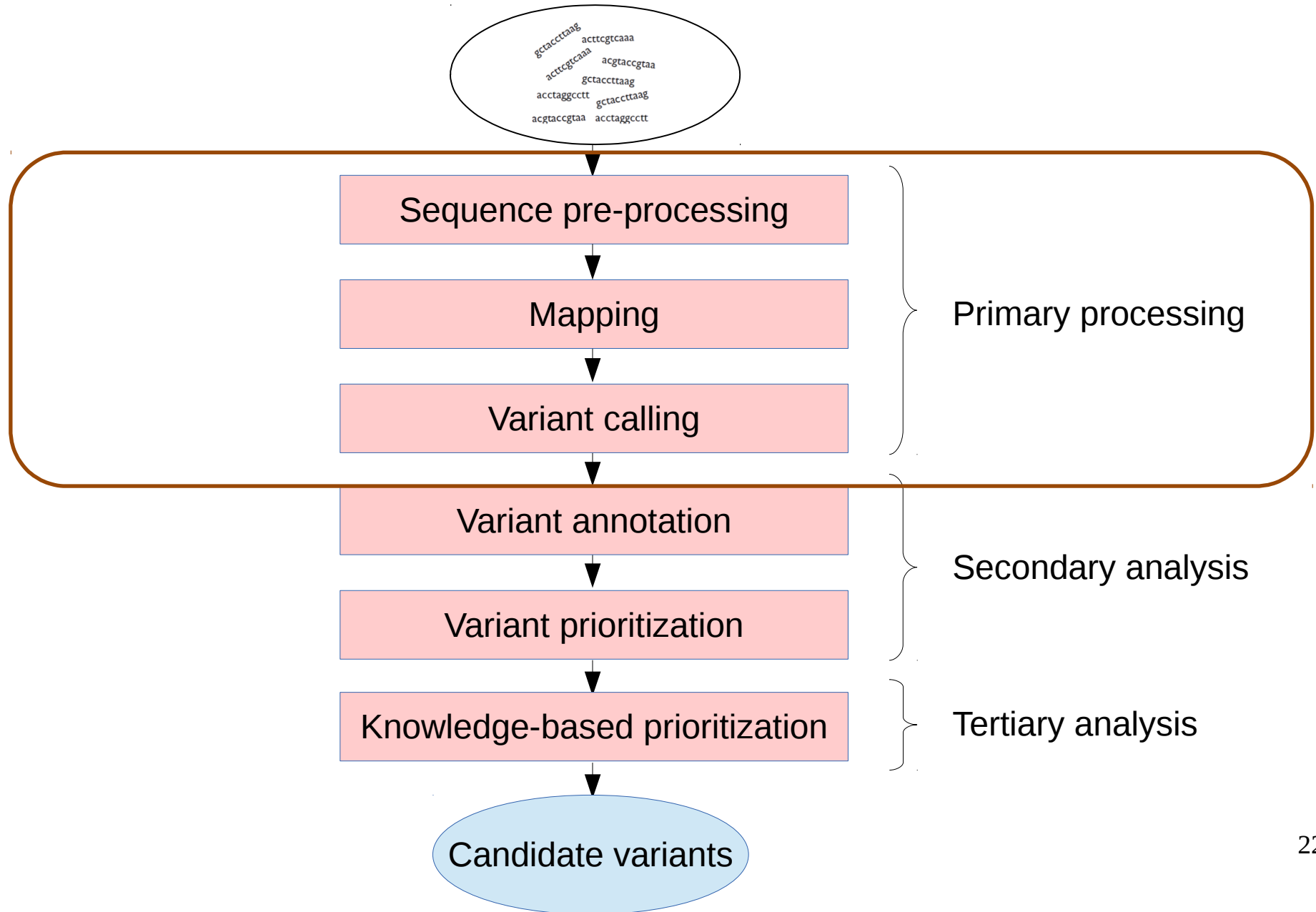
Big data in Genomics

Standard NGS variant data analysis



Big data in Genomics

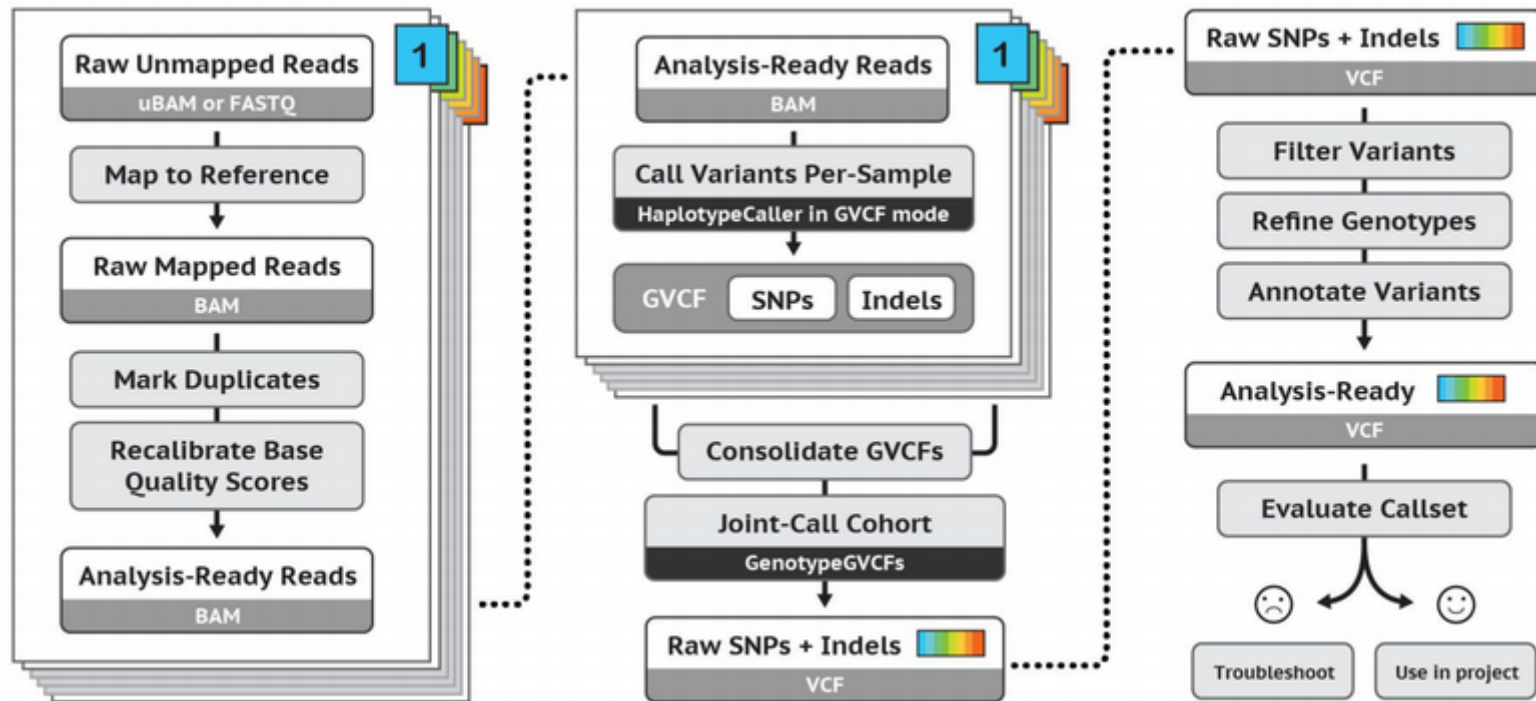
Standard NGS variant data analysis



Big data in Genomics

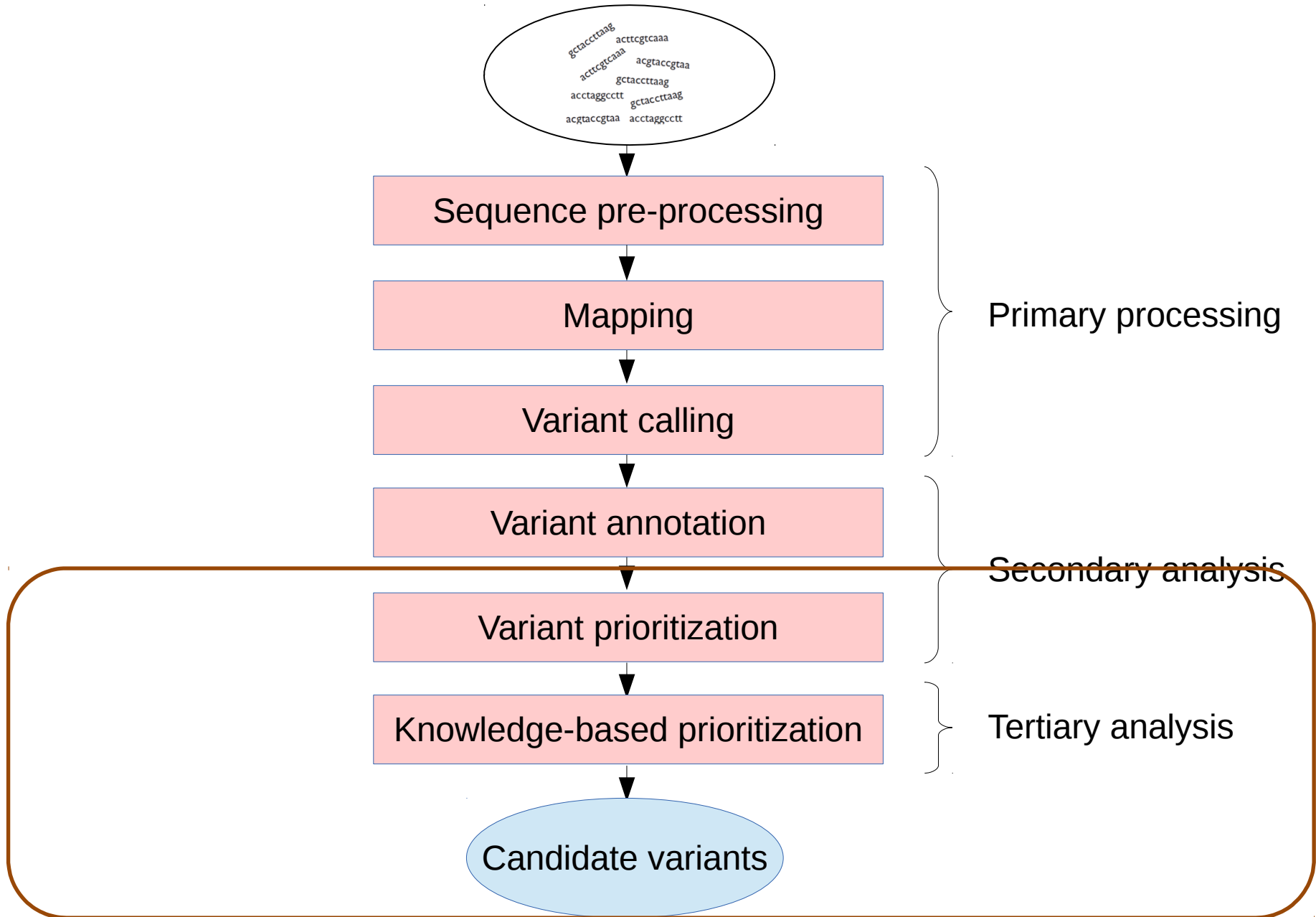
Standard NGS variant data analysis.

- Primary analysis based on GATK's Best Practices for Germline SNP & INDEL Discovery



Big data in Genomics

Standard NGS variant data analysis



Big data in Genomics

Standard NGS variant data analysis

CAUTION!

On average, each *normal* person is found to carry in the **exome**:

~11,000 **synonymous** variants

~11,000 **non-synonymous** variants

250 to 300 loss-of-function variants in annotated genes

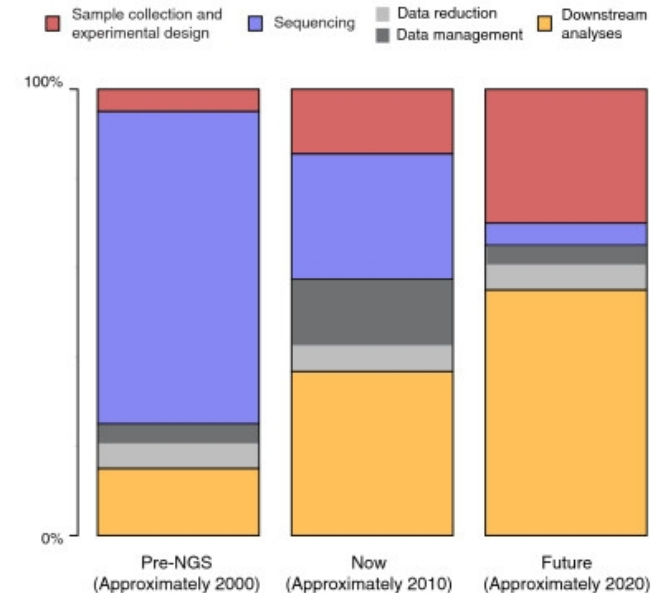
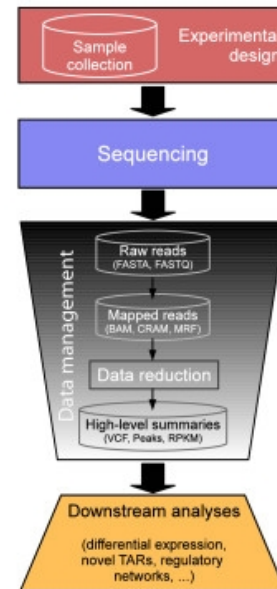
50 to 100 variants previously implicated in **inherited disorders**

1000 Genomes Project Consortium. *A map of human genome variation from population-scale sequencing.* **Nature.** 2010 Oct 28;467(7319):1061-73. PubMed PMID: 20981092



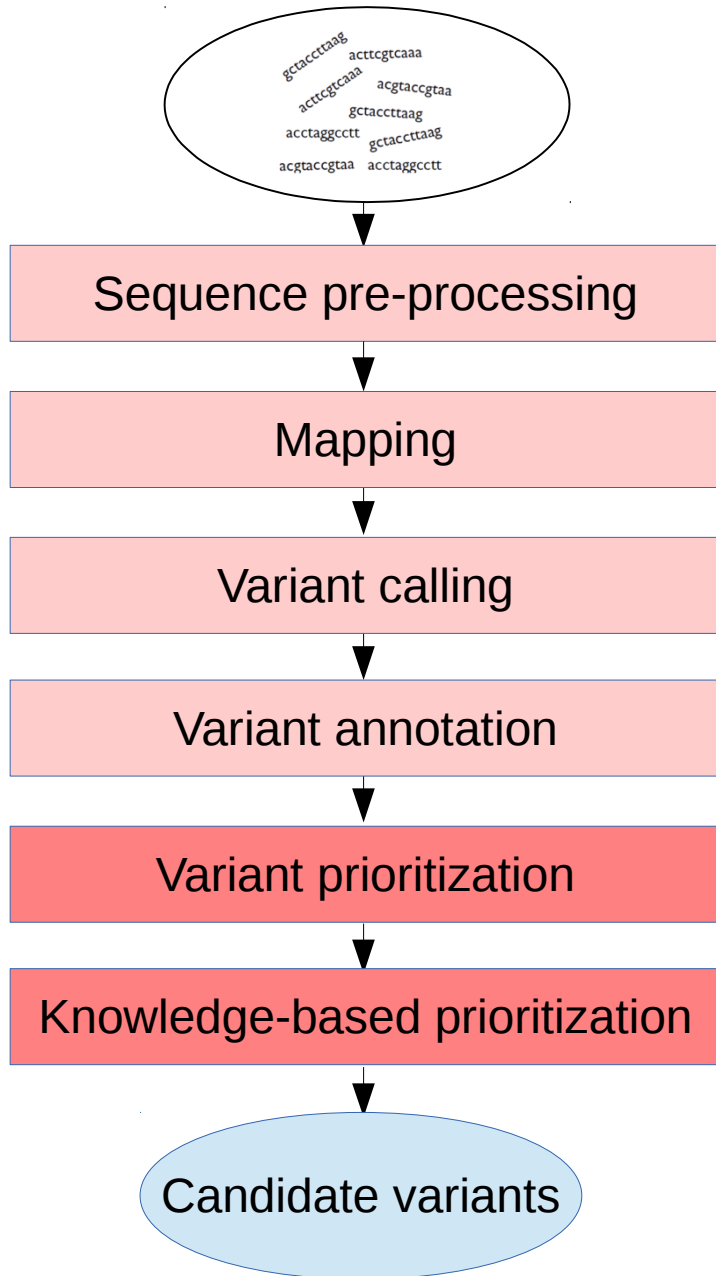
Still a challenge → **PRIORITIZATION**

- A **whole genome** can carry 3.5 million variants on average
- After annotating there will be **hundreds** of **deleterious** variants



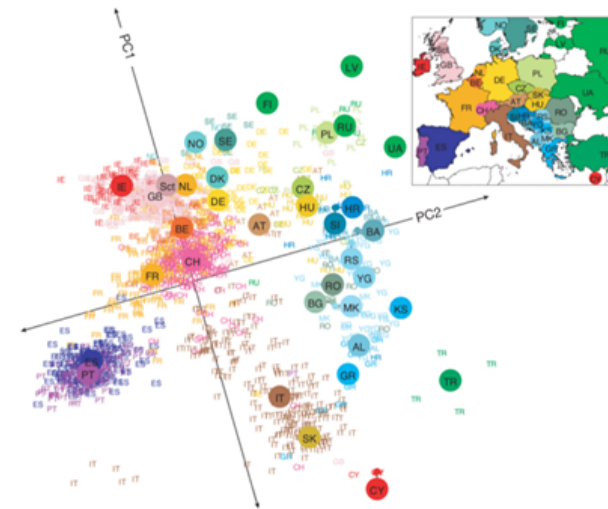
Big data in Genomics

Standard NGS variant data analysis



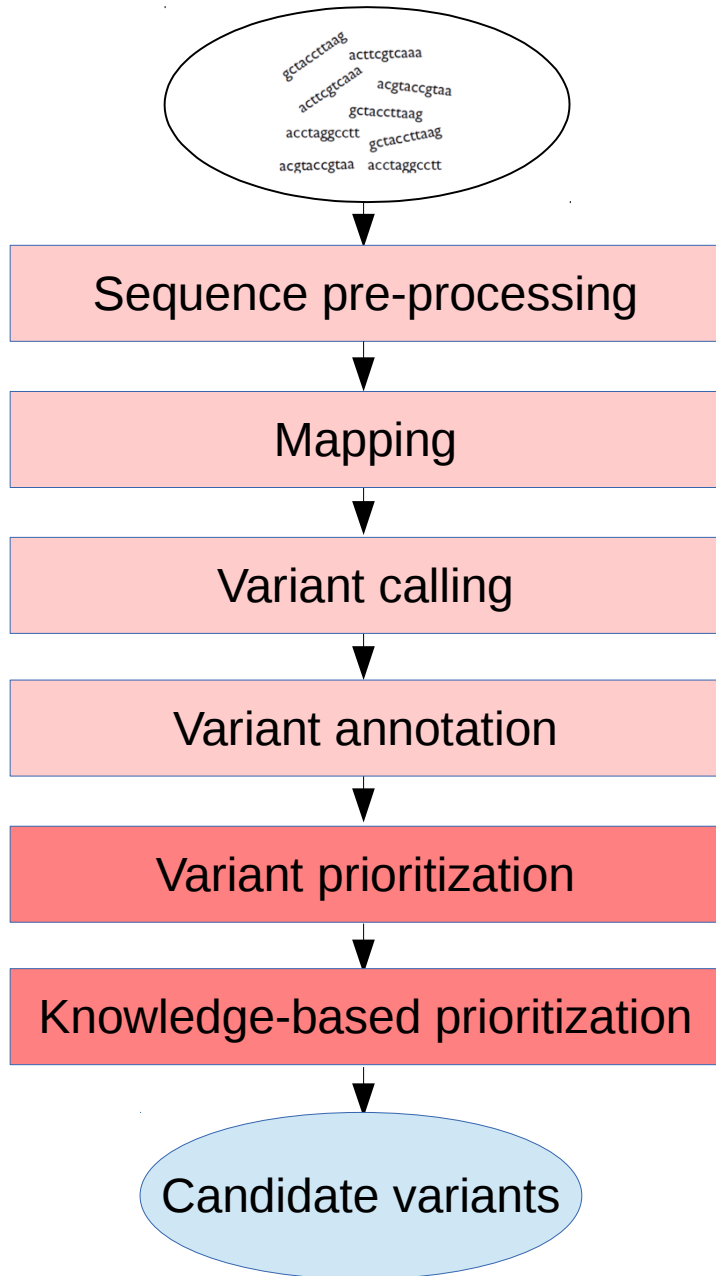
- **Variant level: population frequencies, conservation scores, protein substitution scores....**

The importance of local variability in the prioritization process. One of the most stringent filtering steps is the exclusion of known population polymorphisms. Public databases (1000 genomes, ESP, ExAC)

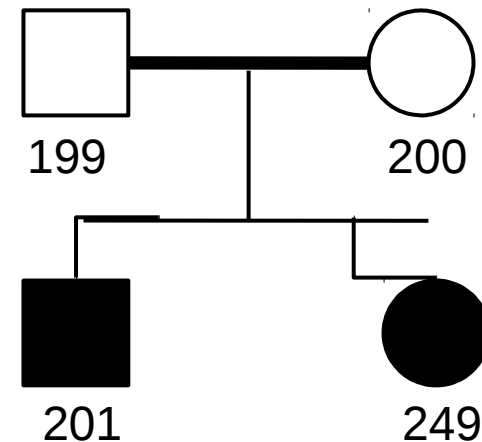


Big data in Genomics

Standard NGS variant data analysis

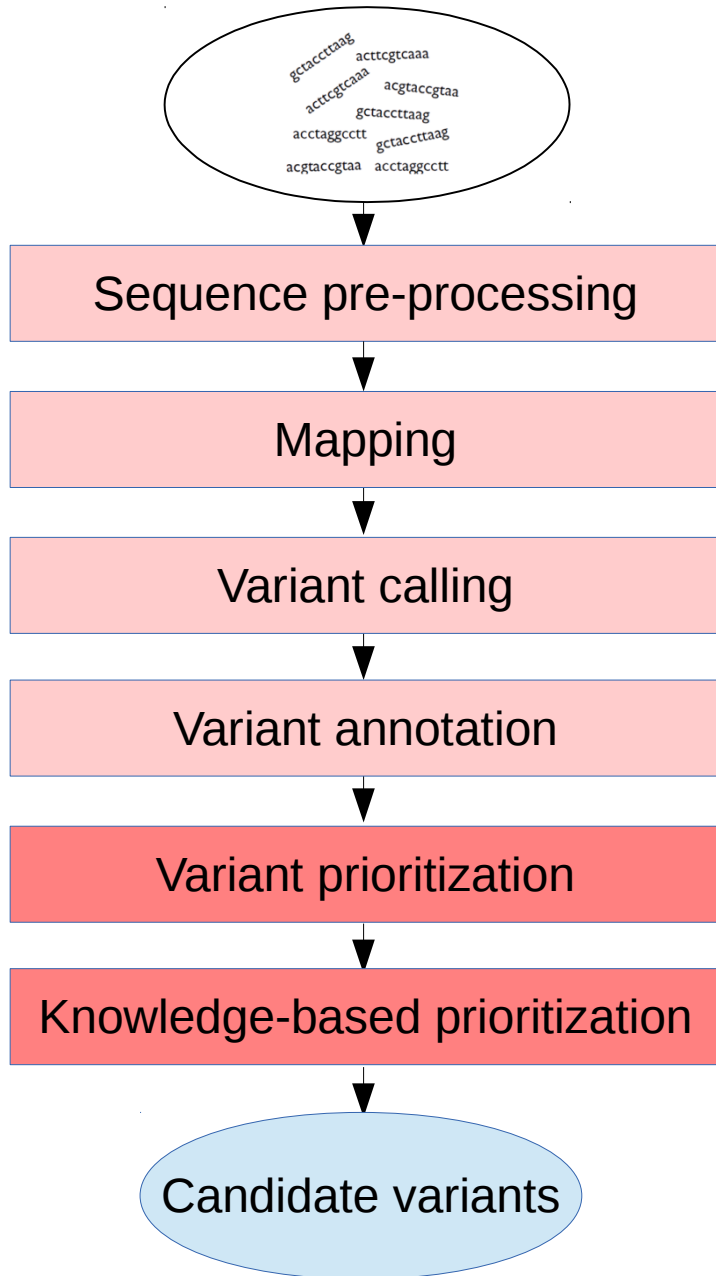


- Variant level: population frequencies, conservation scores, protein substitution scores....
- Experimental design level: case/control, Family, Trios, Disease Panels



Big data in Genomics

Standard NGS variant data analysis



- Variant level: population frequencies, conservation scores, protein substitution scores....
- Experimental design level: case/control, Family, Trios, Disease Panels

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Volume 33, Issue 5
May 2016

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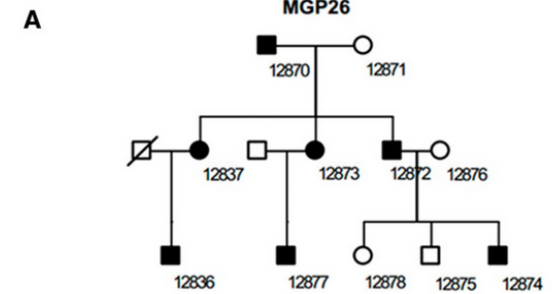
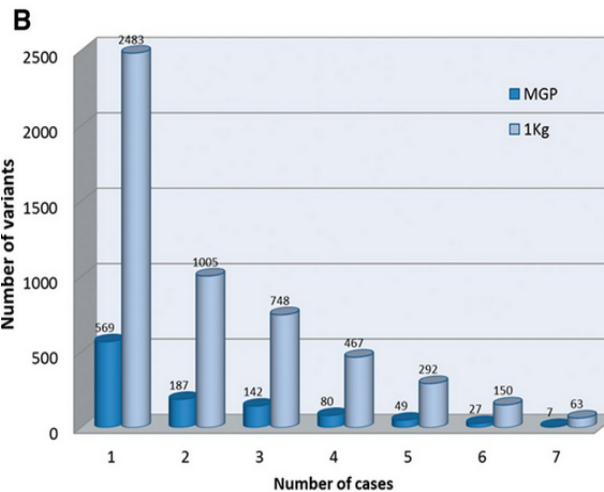
Abstract
Introduction
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267 Spanish Exomes Reveal Population-Specific Differences in Disease-Related Genetic Variation

Joaquín Dopazo, Alicia Amadoz, Marta Bleda, Luz García-Alonso, Alejandro Alemán, Francisco García-García, Juan A. Rodríguez, Josephine T. Daub, Gerard Muntané, Antonio Rueda Alicia Vela-Boza, Francisco J. López-Domingo, Javier P. Florido, Pablo Arce, Macarena Ruiz-Ferrer, Cristina Méndez-Vidal, Todd E. Arnold, Olivia Spleiss, Miguel Alvarez-Tejado, Arcadi Navarro, Shomi S. Bhattacharya, Salud Borrego, Javier Santoyo-López, Guillermo Antíñolo

Molecular Biology and Evolution, Volume 33, Issue 5, 1 May 2016, Pages 1205–1218,
<https://doi.org/10.1093/molbev/msw005>
Published: 13 January 2016

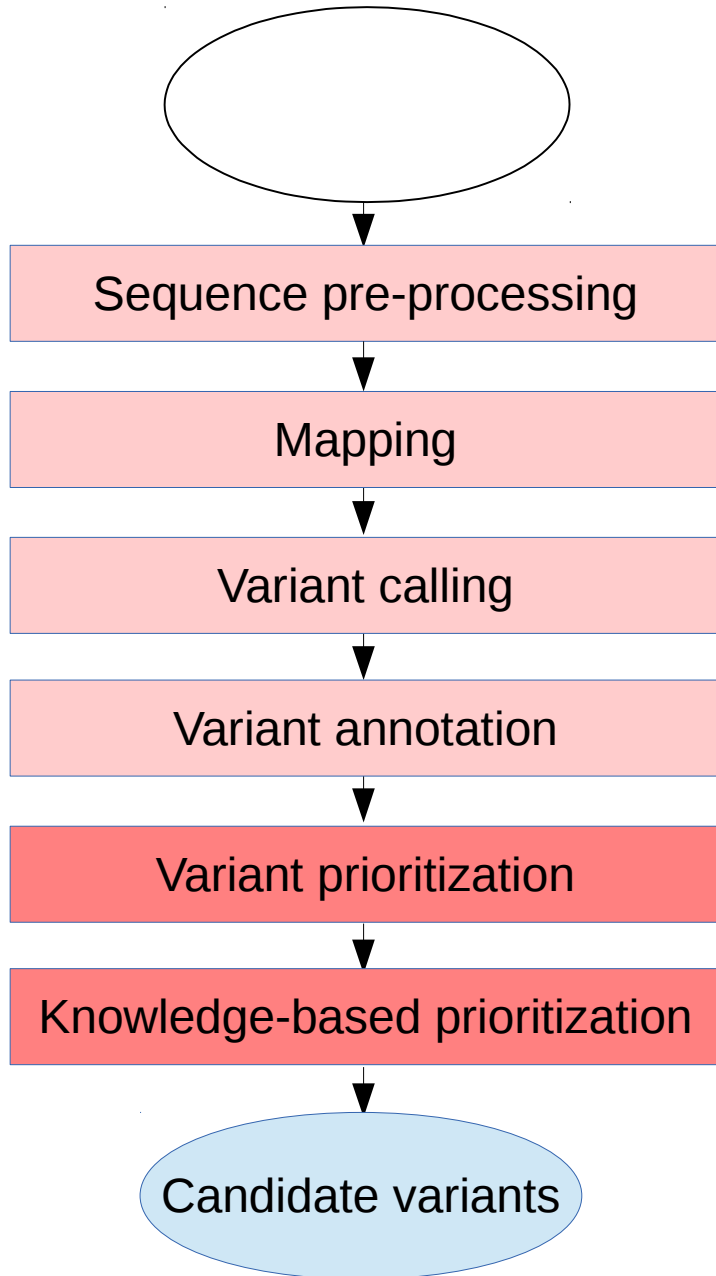
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The filtering efficiency of the local population can be between 5 and 10 times those of a general database, such as the 1000 genomes

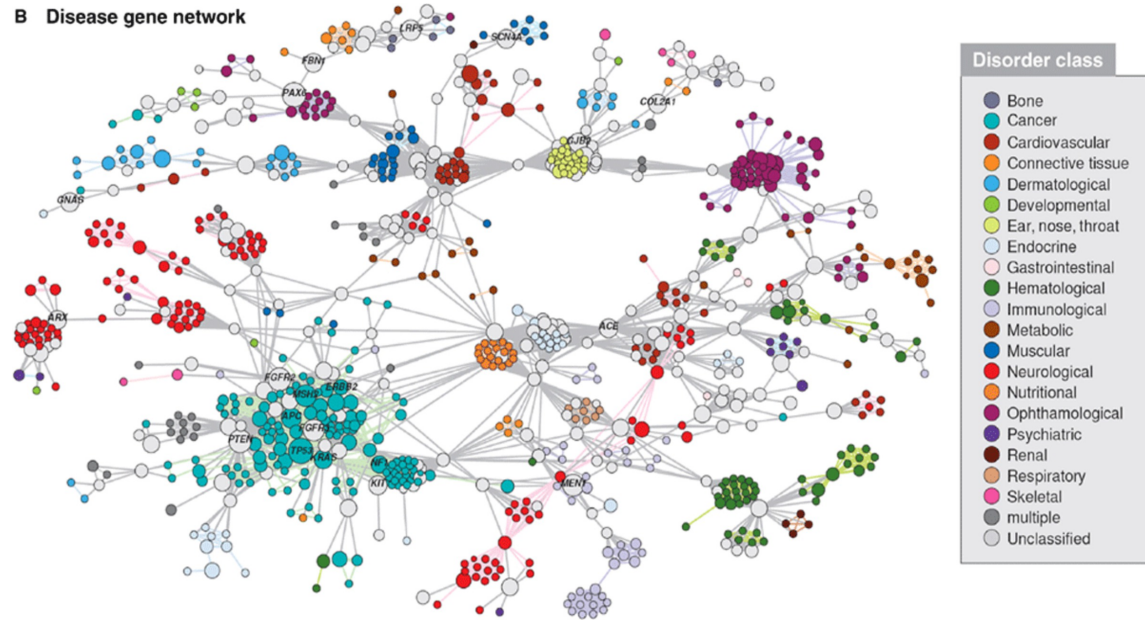
Big data in Genomics

Standard NGS variant data analysis



- **Functional (system) level: gene set, network analysis, pathway analysis, burden tests....**

B Disease gene network



Big data in Genomics

Genomic Variant Dataset, big and complex

Logical view of genomic variant dataset, data come from **different VCF files**.

Hundreds of millions of mutations, some meta data needed: **Variant annotation**

- Clinical info
- Consequence types
- Conservation scores
- Population frequencies
- ...

Genomic Variants

		Samples						
		var 1	28	32	29	28	35	32
		var 1	16,12	16,17	18,14	12,14	16,14	16,12
var_1	A/T	A/A	A/T	T/T	A/A	A/T		
var_2	C/C	C/G	C/C	C/G	C/C	G/G		
..		
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var_n		

Clinical data: Sample annotation

- Phenotype
- Family and population pedigree
- Clinical variables
- ...

Heterogeneous data analysis and algorithms, different technologies and solutions required:

- Search and filter using data and meta data
- Data mining, correlation
- Statistic tests
- Machine learning
- Interactive analysis
- Network-based analysis
- Visualization
- Encryption
- ...

Applications:

- Personalized medicine
- Clinical Genomics
- ...

Different layers of information:

- Genotype for samples
- Allele counts
- Quality scores
- Phase information
- ...

- Genomics England project:**
- **250M variants x 100K samples**, about **25 trillion** points
 - With different layers of data, about **100 trillion** points
 - A lot of meta data for variants and samples
 - About **400TB** to be indexed

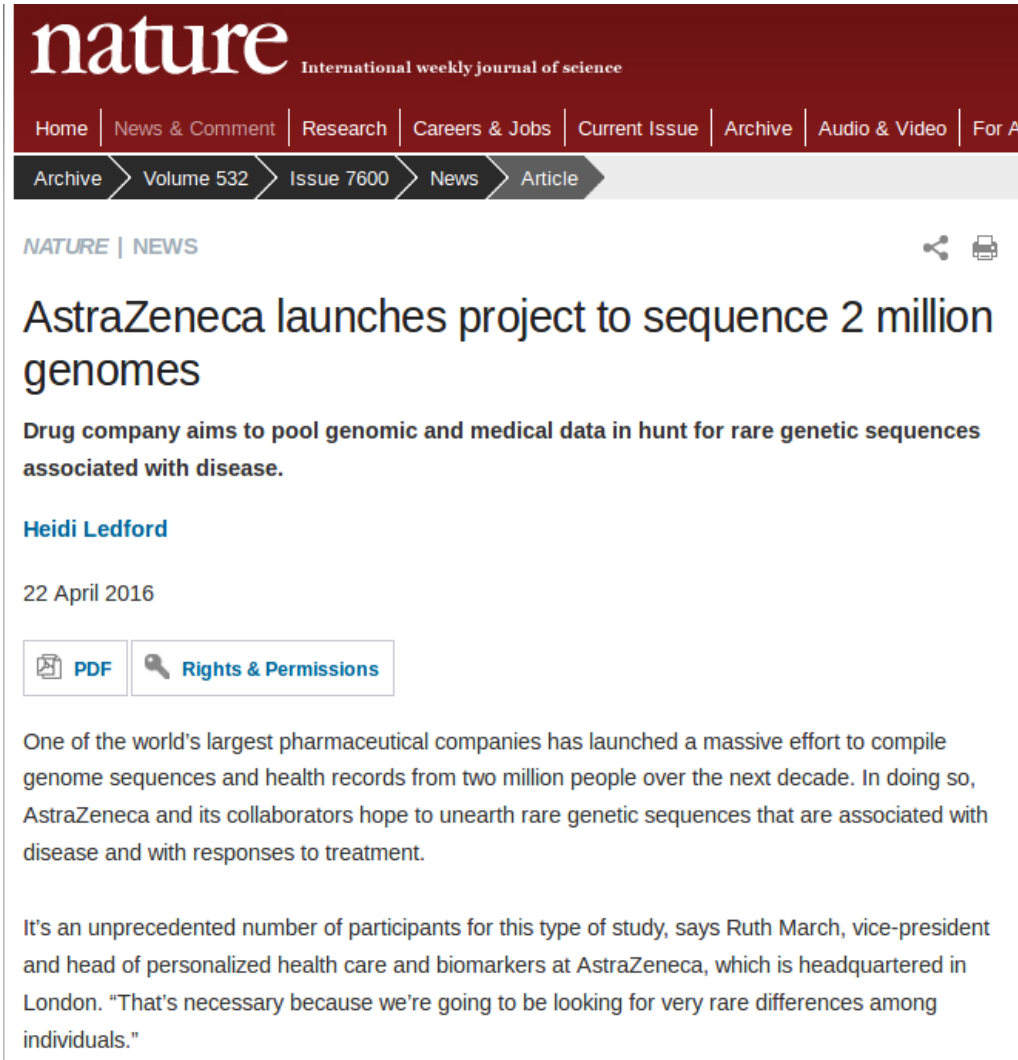
Big data in Genomics

Some *Big Data* current projects

- **NIHR BRIDGE**: 10,000 whole genomes from rare diseases, ~1-2PB of data expected
- **Genomics England (GEL)**: is sequencing **100,000** whole genomes from UK, several rare diseases and cancers being studied, data estimation: ~20PB of BAM and **~400TB of compressed VCF** data are expected! About 100 whole genomes/day, ~5-10TB/day
- **International Cancer Genome Consortium (ICGC)**: store more than 10,000 sequenced cancers, few PB of data
- **NAGEN**: 1000 whole genomes from rare diseases and cancer
- **France Médecine Génétique 2025**: 10.000 WGS correspondign to 20.000 patients with rare diseases and their families, and 50.000 patients with metastatic or refractory cancers
- **Genome of the Netherlands Consortium (GoNL)**: GoNL is interested in genetic variation in the Dutch Population.
- **Andalusian program for Personalized Medicine**: 4500 samples per year (targeted sequencing, rare diseases)
-
- Danish National Strategy of Personalized Medicine (2017-2020)
- Qatar Genome Programme (QGP)
-

Big data in Genomics

Some *Big Data* current projects





The screenshot shows the top portion of a news article on the Nature website. The header is dark red with the 'nature' logo in white. Below the logo is the tagline 'International weekly journal of science'. A navigation bar contains links for Home, News & Comment, Research, Careers & Jobs, Current Issue, Archive, Audio & Video, and For A. Below this is a secondary navigation bar with arrows pointing to Archive, Volume 532, Issue 7600, News, and Article. The article title is 'AstraZeneca launches project to sequence 2 million genomes'. The sub-headline reads 'Drug company aims to pool genomic and medical data in hunt for rare genetic sequences associated with disease.' The author is Heidi Ledford, and the date is 22 April 2016. There are buttons for PDF and Rights & Permissions. The main text begins with 'One of the world's largest pharmaceutical companies has launched a massive effort to compile genome sequences and health records from two million people over the next decade. In doing so, AstraZeneca and its collaborators hope to unearth rare genetic sequences that are associated with disease and with responses to treatment.' A quote from Ruth March, vice-president and head of personalized health care and biomarkers at AstraZeneca, follows: 'It's an unprecedented number of participants for this type of study, says Ruth March, vice-president and head of personalized health care and biomarkers at AstraZeneca, which is headquartered in London. "That's necessary because we're going to be looking for very rare differences among individuals."

nature International weekly journal of science

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Archive > Volume 532 > Issue 7600 > News > Article



NATURE | NEWS  

AstraZeneca launches project to sequence 2 million genomes

Drug company aims to pool genomic and medical data in hunt for rare genetic sequences associated with disease.

Heidi Ledford

22 April 2016

 PDF  Rights & Permissions

One of the world's largest pharmaceutical companies has launched a massive effort to compile genome sequences and health records from two million people over the next decade. In doing so, AstraZeneca and its collaborators hope to unearth rare genetic sequences that are associated with disease and with responses to treatment.

It's an unprecedented number of participants for this type of study, says Ruth March, vice-president and head of personalized health care and biomarkers at AstraZeneca, which is headquartered in London. "That's necessary because we're going to be looking for very rare differences among individuals."

Big data in Genomics

Big data analysis challenges

- **Data Analysis and visualization:** Real-time and Interactive graphical data analysis and visualization is needed.
- **Data mining:** Complex queries, aggregations, correlations, ...
- **Security:** sometimes data access require authentication, authorization, *encryption*, ...
- **Performance and scalability:** software must be high-performance and scalable
- **Data Integration:** different types of data such as variation, expression, ChIP, ...
- **Share and collaboration:** data models to ease the collaboration among different groups. Avoid moving data.
- **Knowledge base and sample annotations:** many of the visual analytic tools need genome and sample annotations



Do current bioinformatic tools solve these problems?

Big data in Genomics

Current status of *big data* tools in bioinformatics

- Many bioinformatic tools are great but, in general, not designed and implemented for processing and analyzing *big data*.
- Tools usually don't exploit the parallelism of modern hardware and current high-performance and scalable technologies. Poor performance and scalability.
- We need to develop new generation of software and methodologies to:
 - Improve performance and scalability of analysis
 - Store data efficiently and secured to be queried and visualized
- **Bioinformaticians have new challenges and requirements, given the volume, complexity, heterogeneity and nature of data.**



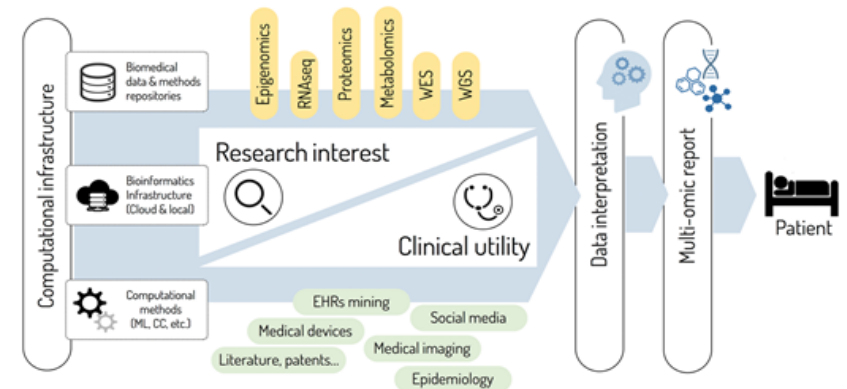
Briefings in Bioinformatics, 2017, 1–15

doi: 10.1093/bib/bbx144
Paper

Precision medicine needs pioneering clinical bioinformaticians

Gonzalo Gómez-López, Joaquín Dopazo, Juan C. Cigudosa, Alfonso Valencia and Fátima Al-Shahrour

Corresponding author: Fátima Al-Shahrour, Bioinformatics Unit, Spanish National Cancer Research Centre (CNIO), C/Melchor Fernández Almagro, 3. ES-28029 Madrid, Spain. Tel: +34 91 732 80 00; E-mail: falshahrour@cnio.es



Overview

- Introduction
- Big Data in Genomics
- **OpenCB: Open source initiative for Computational Biology**
- A case study: Personalized Medicine Module (MMP)

OpenCB

Open source initiative for Computational Biology

- OpenCB is a collaborative project that **aims** to design and develop high-performance and scalable solutions for genomic big data analysis using **most modern computing technologies**.
- OpenCB is a collaborative project with more than 15 active developers and data analysts and more than 12 repositories (<http://www.opencb.org>)
- No one computing programming language oriented: BioPerl, BioPython, Bioconductor, ... Good software solutions may use different languages and technologies to solve different problems and use cases
- So far, is where all the software we develop is being released. About 15 active committers. Available as open-source at GitHub <https://github.com/opencb>

Open source for Computational Biology

Cambridge, UK <http://www.opencb.org> lgmecas@gmail.com

Repositories 19 People 24 Projects 0

Grow your team on GitHub

GitHub is home to over 28 million developers working together. Join them to grow your own development teams, manage permissions, and collaborate on projects.

Sign up

Dismiss

Search repositories... Type: All Language: All

opencga
An Open Computational Genomics Analysis platform for big data processing and analysis in genomics
Java ★ 71 47 Apache-2.0 Updated 4 hours ago

biodata
Java library that models biological entities and their equivalents in different file formats typically used in bioinformatics
Java ★ 15 25 Apache-2.0 Updated 15 hours ago

iva
Generic Interactive Variant Analysis browser
HTML ★ 12 9 Apache-2.0 Updated 6 days ago

Top languages
Java HTML C JavaScript CSS

People 24 >

OpenCB

Some relevant projects

- **biodata** (<https://github.com/opencb/biodata>) and **ga4gh** (<https://github.com/opencb/ga4gh>)
 - Contain all data models (Variant, Alignment...) parsers and converters (*avro*, *protobuf*) for all OpenCB projects
- **CellBase** (<https://github.com/opencb/cellbase>)
 - A NoSQL database the integrates the most relevant biological information about genomic features and proteins, gene expression regulation, etc. **The biological knowledge-base for OpenCB project** . A **Variant Annotation** tool implemented.
 - A high-performance NoSQL implementation, a CLI and web services implemented
- **HPG BigData** (<https://github.com/opencb/hpg-bigdata>)
 - Hadoop-based implementation of data converters (*avro*, *parquet*) and bioinformatic tools (ie. *samtools*)
 - Simple indexing for HBase, Hive and Impala developed
 - C code embedded using JNI to speed-up processing
- **OpenCGA** (<https://github.com/opencb/opencga>)
 - Integrates most of the OpenCB projects to provide a scalable and high-performance platform for the analysis of HT genomic data
 - **OpenCGA Catalog** provides an authenticated environment, files and sample annotations, system audit, ...
 - **OpenCGA Storage** is a plugin-oriented framework that allows to index hundreds of millions of variants for thousands of samples in different storage engines. Stats and annotation implemented..
- **Interactive Variant analysis (IVA)**
 - Web-based variant analysis tool
- **Genome Maps** (<https://github.com/opencb/genome-maps>)
 - A web-based NGS and genome browser: <http://genomemaps.org/>
- Many other related projects for big data analysis and visualization, check <https://github.com/opencb>

OpenCB: CellBase

An integrative database and RESTful Web Service API

- **CellBase** is a comprehensive integrative NoSQL database and a *RESTful Web Service API*, designed to provide a **high-performance and scalable** solution.
- It integrates the most relevant biological information about genomic features and proteins, gene expression regulation, functional annotation, genomic variation...Currently contains more than 2TB of data
- Used by EMBL-EBI, ICGC, GEL, MMP among others

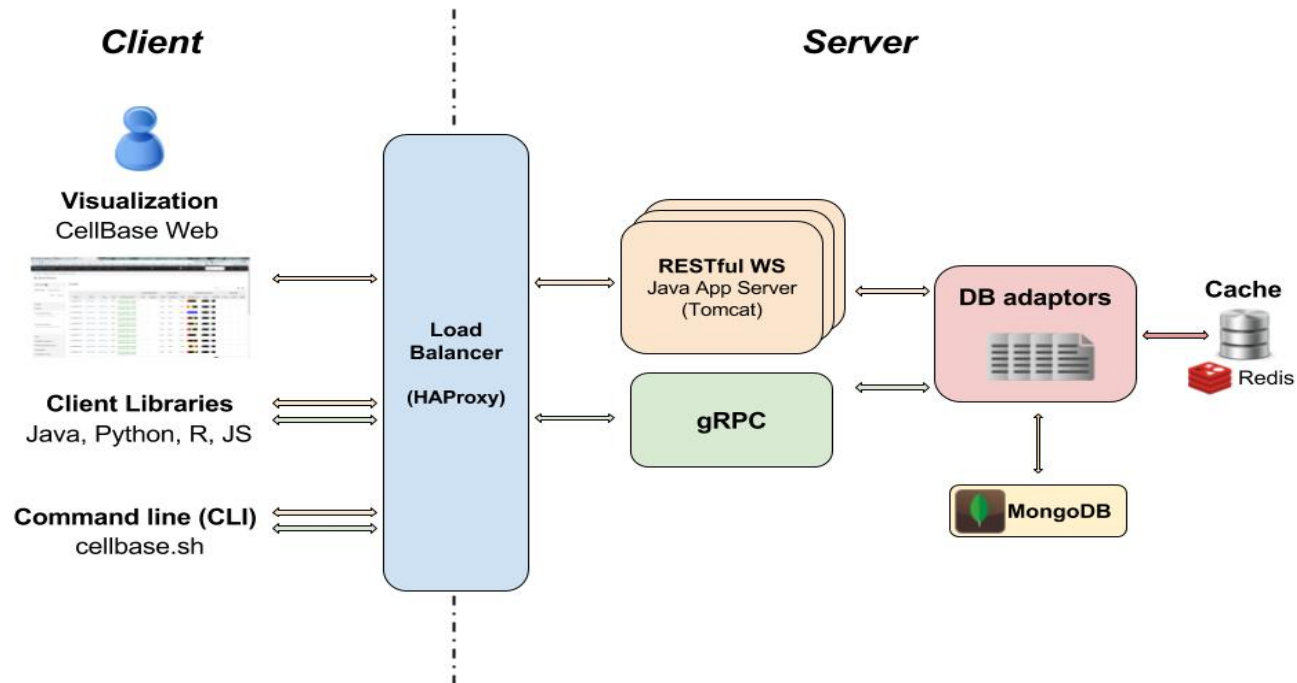
Category	Data source	Version/Date	
		CellBase v3 (March 2015)	CellBase v4 (June 2016)
Core	Ensembl Core	v79	v82
Protein	UniProt	March 2015	Release 2015_10
	InterPro	v50	v54
	Polyphen2/Sift	Ensembl 79	Ensembl v82
Variation	Ensembl Variation	v79	v82
	1000 genomes project		Phase 3 2016-05
	ExAC		0.3.1
	GoNL		Release 5
	UK10K		2016-05
	ESP		2016-05
Regulatory	Ensembl Regulatory	v79	v82
Conservation	PhastCons		June 2016
	PhyloP		June 2016
	GERP++		June 2016

Clinical	ClinVar	March 2015	2016-12
	COSMIC	v71	v79
	HPO		2015-11
	DisGeNET		Version 3.0
Biological Networks	Reactome	v51	June 2016
	IntAct	March 2015	June 2016
Others	DGIdb		2.0
	Gene Expression Atlas		June 2016
	CADD		v1.3

- **Official Domain and swagger:** <http://bioinfo.hpc.cam.ac.uk/cellbase/webservices/>
- **Current version:** v4.6.1
- **Data sources for homo sapiens:**
<http://bioinfo.hpc.cam.ac.uk/cellbase/webservices/rest/v4/meta/hsapiens/versions?assembly=grch37&limit=-1&skip=-1&skipCount=false&count=false&Output%20format=json>
- **Project:** <https://github.com/opencb/cellbase> **Wiki:** <http://docs.opencb.org/display/cellbase/>

OpenCB: CellBase

Architecture



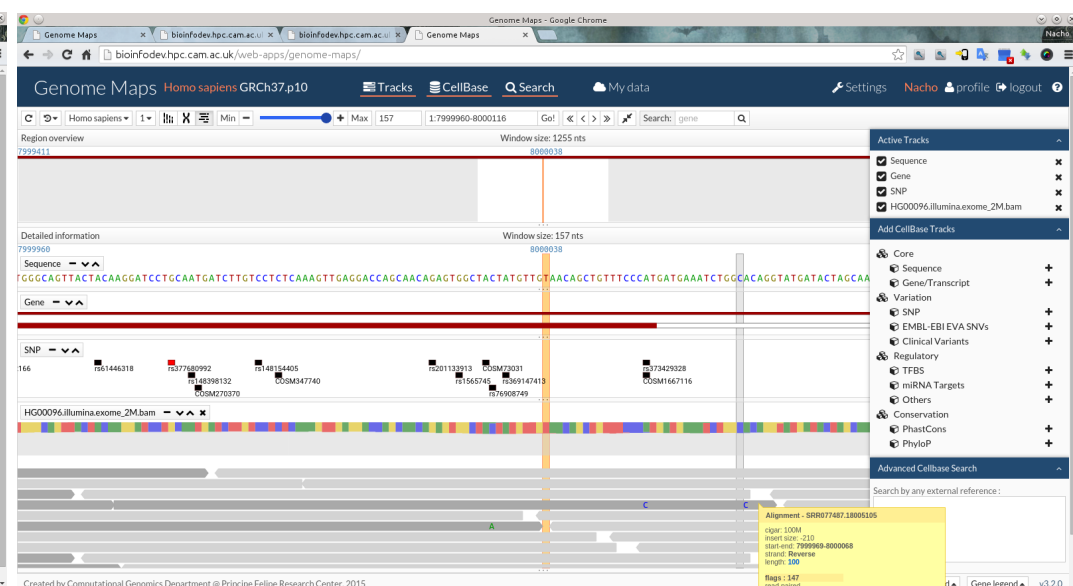
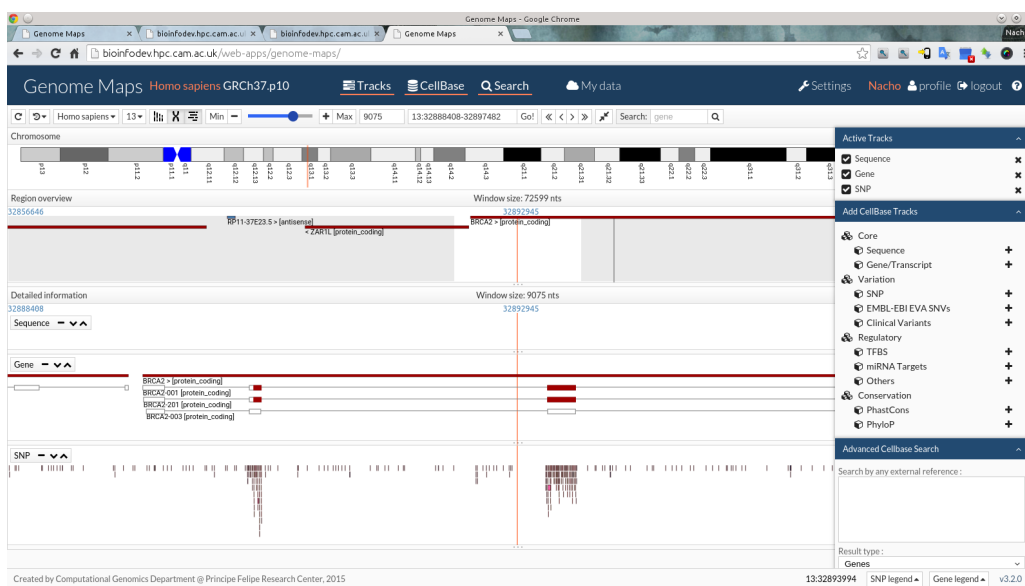
- **Example of variant annotation:**

- <http://bioinfo.hpc.cam.ac.uk/cellbase/webservices/rest/v4/hsapiens/genomic/variant/19:45411941:T:C/annotation>

OpenCB: Genome Maps

A big data HTML5+SVG genome browser

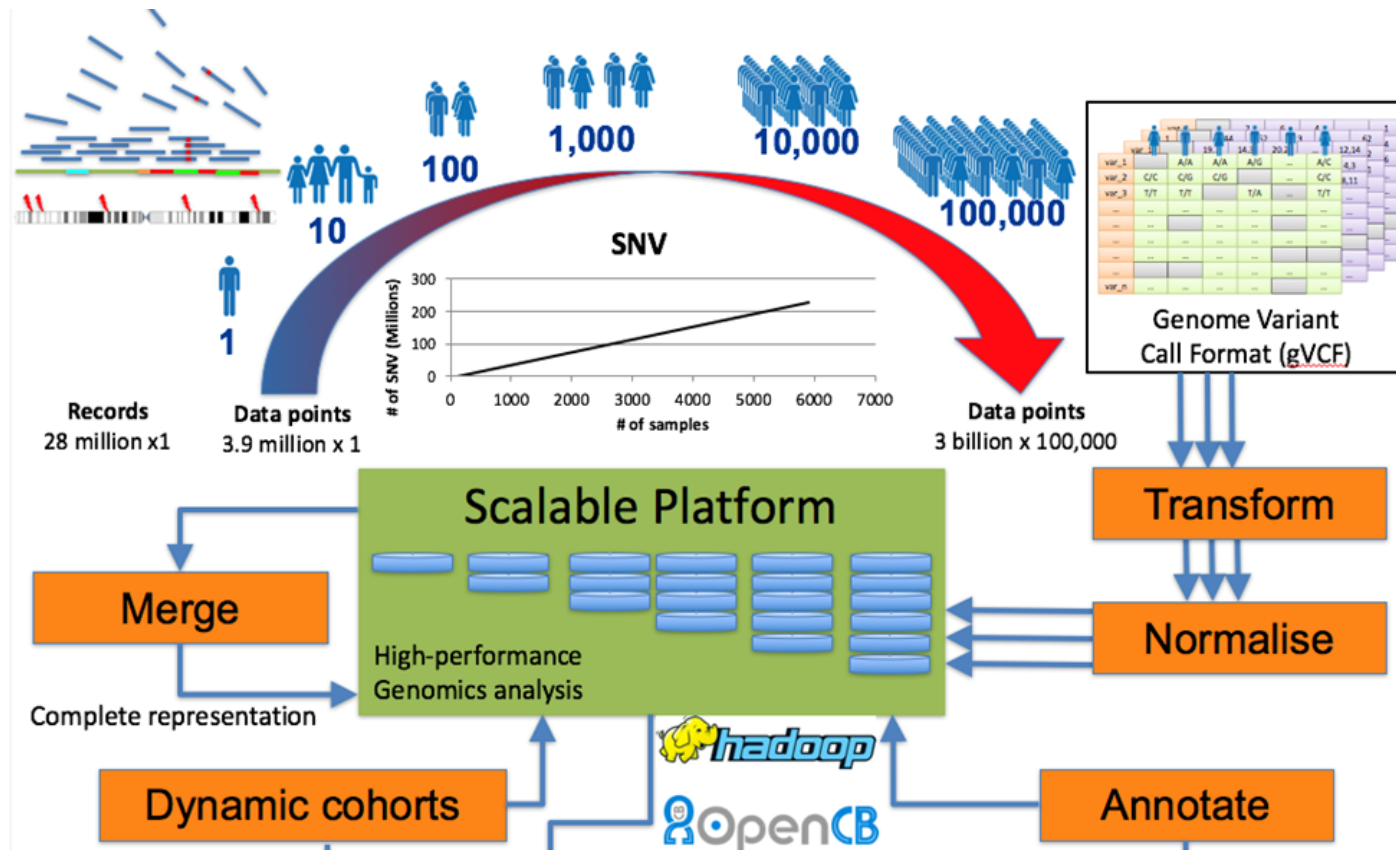
- Genome scale data **visualization** is an important part of the data analysis
- Main features of **Genome Maps** (www.genomemaps.org, published at NAR 2013)
 - 100% HTML5 web based: **HTML5+SVG, and other JavaScript libraries**. Always updated, **no browser plugins needed**
 - Genome data is mainly consumed from **CellBase and OpenCGA** database through **RESTful web services**. **JSON** data is parsed and SVG is rendered, making server lighter and improve network transfers
 - Other features: NGS data viewer, Multi species, Feature caches, API oriented, embeddable, key navigation, ...



OpenCB: OpenCGA

Overview and goals

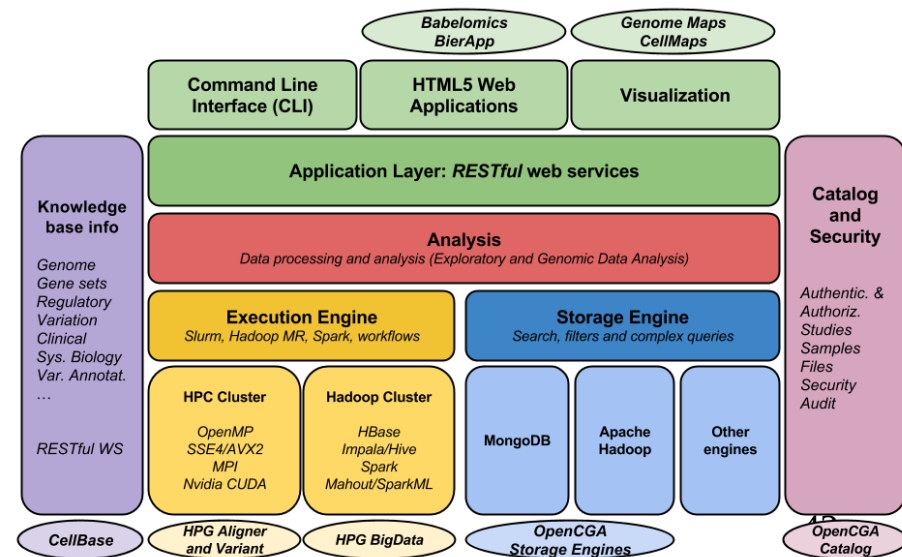
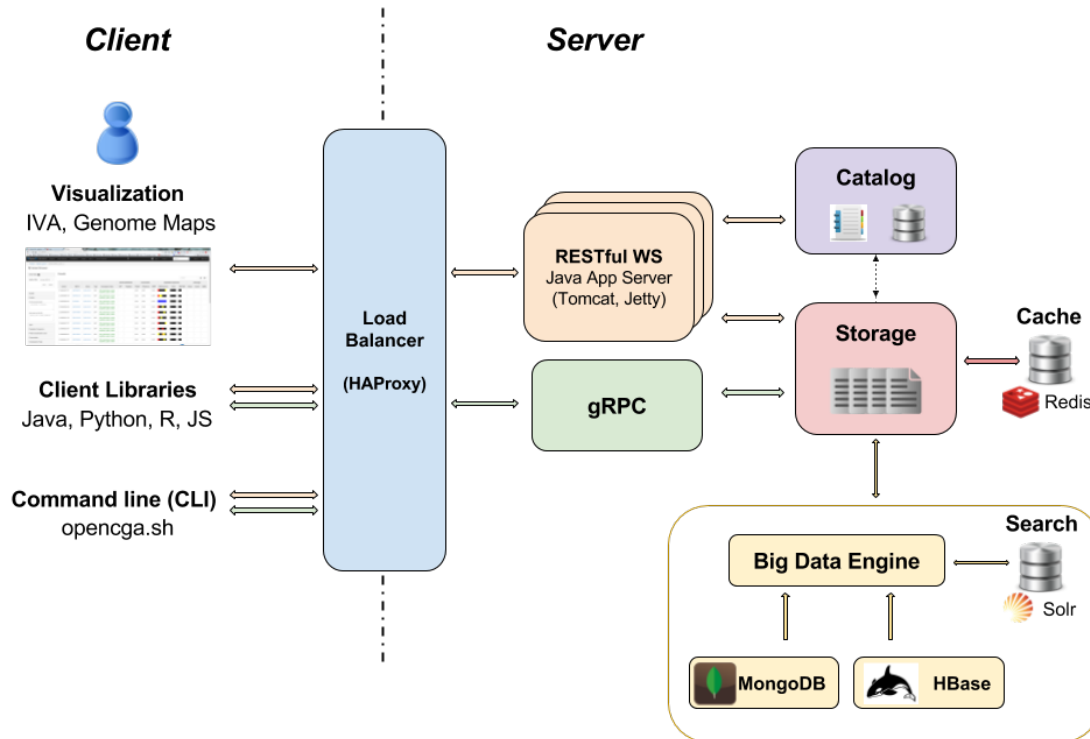
- Open-source Computational Genomics Analysis (**OpenCGA**) aims to provide to researchers and clinicians a **high performance and scalable solution** for genomic big data processing and analysis
- **OpenCGA** is built on OpenCB
- Project: <https://github.com/opencb/opencga> ; Doc: <http://docs.opencb.org/display/opencga>
- Currently, the fastest and more powerful genomic engine in the world. Used in Genomics England (GEL) and MMP



OpenCB: OpenCGA

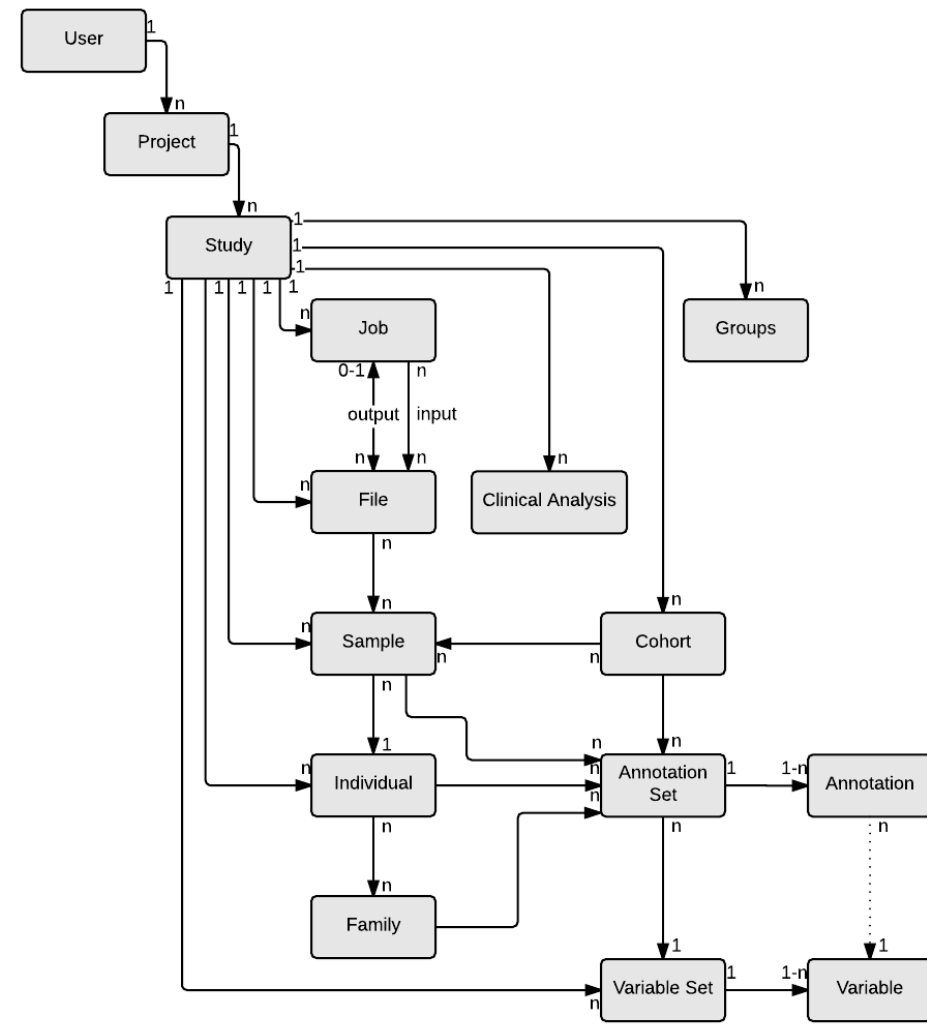
Overview and goals

- Main features:
 - High-performance and scalable variant storage and index that allow to load and merge VCF/gVCF files
 - Annotate and calculate statistics for all the variants
 - Client libraries developed in Java, Python, R and Javascript
 - Clinical interpretation analysis of samples and families
 - Integrated Catalog keeps track of users, files, jobs, clinical data...
 - Interactive web-based data mining tool based on IVA



OpenCB: OpenCGA Catalog, a *metadata* database

- **OpenCGA Catalog** provides a user authentication and authorization environment, implements *sample annotation* database, tracks all files and job, audit, ...
- **Authentication & authorization**: *roles* definition, detailed ACL system implemented to share sample, file, jobs, ...
- **File and jobs**: file and jobs are tracked, stats calculated
- **Sample annotations** is one of the main features:
 - Allow complex queries and aggregations
 - Allow to detect bias and other problems with the data
 - Cohort definitions
- **Audit**: all actions (login, data indexing, ...) and queries are audited
- Allow to the different big data storage engines to perform optimizations
- Implements a job launcher and a execution monitor
- Data models at <https://github.com/opencb/opencga/tree/develop/opencga-catalog/src/main/java/org/opencb/opencga/catalog/models>

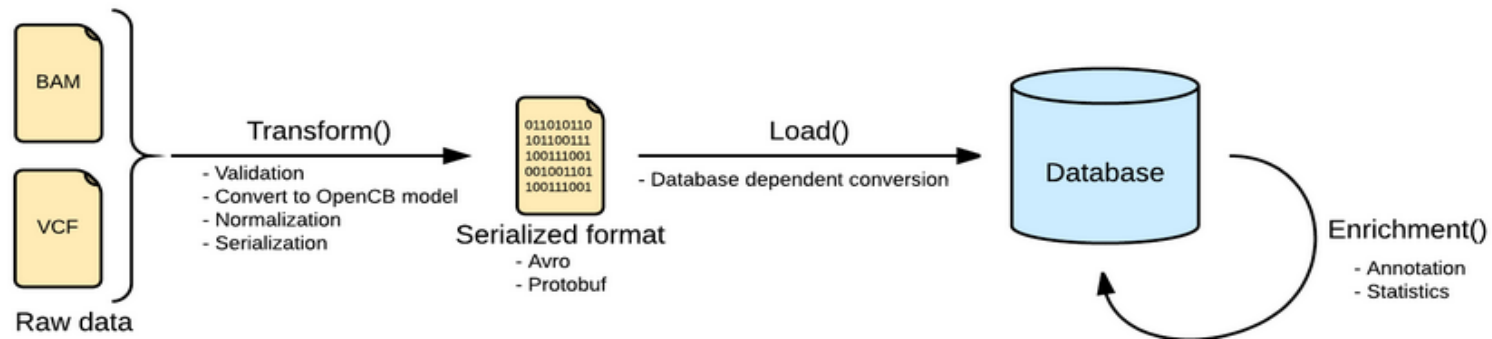


OpenCB: OpenCGA

Storage Engines

OpenCGA Storage provides a *pluggable* Java framework for storing and querying alignment and variant data

- Two default implementations: **MongoDB** and **Hadoop** for huge performance and scalability ~ hundreds of thousands of samples



Variant Index Pipeline

1. Transform

- Validation: VCF files are read using the library HTSJDK → validation
- Files are converted to Biodata models. The metadata is stored into a file serializing in json a single instance of the biodata model “VariantSource” (header and some general stats). The real variants data is serialized in file (avro) with a set of variant records described as the biodata model “Variant”
- Normalization → unify the variants representation, since the VCF specification allows multiple ways of referring to a variant and some ambiguities.

2. Load

- Variants are loaded into the database and merged with the existent ones.

3. Enrichment

- Variant annotation (from Cellbase or read from local files provided by the user)
- Stats calculation useful for filtering variants

OpenCB: OpenCGA

User interfaces: REST, command lines and client libs

- **RESTful API:**
 - more than 160 web services developed for **Catalog** (e.g. search *samples* or *files*) and **Analysis** (e.g. query *variants* or fetch *alignment reads*)
 - Other features: authentication and authorization, Swagger documentation (<http://bioinfo.hpc.cam.ac.uk/hgva/webservices/>), ...
- ***opencga.sh*** command line: you can query remote REST or gRPC services after authentication
- **Client libs:** allow to easily query REST web services. At the moment Java, Python, R and Javascript are fully developed and with similar level of functionality (e.g. authentication, parallel fetches, error support, ...).
- **Current version:** v1.3.8
 - Roadmap: <http://docs.opencb.org/display/opencga/Roadmap>

OpenCB: Interactive Variant Analysis (IVA)

An interactive web-based variant analysis suite

- A collaborative project to implement a rich and interactive web-based variant analysis tool on top of **OpenCGA**, currently supports:
 - Variant Browser
 - Prioritization
 - Clinical Analysis
 - Panels
 - Tools
 - ...



The screenshot shows the OpenCB IVA v1.1.3 web application interface. The top navigation bar includes the OpenCB logo, the version number 'IVA v1.1.3', and several menu items: 'Variant Browser', 'Variant Interpretation', 'Clinical', 'Facets', 'Panels', 'Beacon', and 'Tools'. On the right side of the navigation bar, there are links for 'Studies', a search input field, 'About', and 'Login'. Below the navigation bar, the breadcrumb trail reads 'Projects / platinum / illumina_platinum'. The main content area features the title 'IVA v1.1.3' and a sub-section 'Overview'. The overview text states: 'Welcome to the IVA tool for whole genome variant analysis. This interactive tool allows finding genes affected by deleterious variants that segregate along family pedigrees, case-controls or sporadic samples.' A 'Note' section follows, stating: 'IVA web application makes an intensive use of the HTML5 standard and other cutting-edge web technologies such as Web Components, so only modern web browsers are fully supported, these include Chrome 49+, Firefox 45+, Microsoft Edge 14+, Safari 10+ and Opera 36+'. At the bottom of the page, there is the OpenCB logo and a link to 'Report an issue here'.

OpenCB: Interactive Variant Analysis (IVA)

An interactive web-based variant analysis suite

Projects / test@enod_solr / study_solr

Variant Interpreter

Search

Clear No filters selected

Filters

Study and Cohorts

Samples

Select Sample:

Search name...



Select Sample Genotypes:

No samples selected

Sample Genotypes Query Options

Approximate Count

Select all multi-allelic variants

Genomic

Population Frequency

Deleteriousness

Conservation

Consequence Type

Gene Ontology

Phenotype-Disease

VCF Metrics

Table Result Genome Browser (Beta)

Save Interpretation...

Download Share

Showing 1-10 of 139,840 variants

	Variant	SNP Id	Genes	Type	Consequence Type	Deleteriousness			Conservation			Population Frequencies			Phenotype	
						SIFT	Polyphen	CADD	PhyloP	PhastCons	GERP	1000 Genomes	gnomAD Genomes	ESP6500	Clinvar	Cosmic
<input type="checkbox"/>	2:179575511 C/T	rs72648998	TTN,TTN-AS1	SNV	missense_variant	-	-	23.50	0.655	0.925	5.300				Cardiovascular phenotype	carcinoma
<input type="checkbox"/>	2:179576596 A/T	rs2742331	TTN,TTN-AS1	SNV	intron_variant regulatory_region_variant	-	-	0.44	-2.157	0.000	-3.230				-	-
<input type="checkbox"/>	2:179578109 -/ACAAA	rs71393436	TTN,TTN-AS1	INDEL	intron_variant regulatory_region_variant	-	-	-	0.528	0.093	1.260				-	-
<input type="checkbox"/>	2:179578730 G/A	rs2562839	TTN,TTN-AS1	SNV	synonymous_variant	-	-	15.67	-0.254	0.990	1.840				Cardiovascular phenotype	haematopoietic neoplas
<input type="checkbox"/>	2:179579093 T/C	rs12693164	TTN,TTN-AS1	SNV	missense_variant	-	-	0.06	-2.240	0.345	2.250				cardiovascular phenotype Cardiovascular phenotype	haematopoietic neoplas
<input type="checkbox"/>	2:179579212 T/C	rs2562838	TTN,TTN-AS1	SNV	synonymous_variant	-	-	2.39	-0.119	0.862	4.180				cardiovascular phenotype Cardiovascular phenotype	haematopoietic neoplas
<input type="checkbox"/>	2:179579822 T/A	rs2562836	TTN,TTN-AS1	SNV	synonymous_variant	-	-	12.76	-0.257	0.790	-4.710				Cardiovascular phenotype cardiovascular phenotype	haematopoietic neoplas
<input type="checkbox"/>	2:179580093 A/C	rs12622914	TTN,TTN-AS1	SNV	intron_variant 2KB_downstream_variant regulatory_region_variant	-	-	3.74	-0.213	0.121	-3.450				-	-
<input type="checkbox"/>	2:179580583 T/C	rs2562834	TTN,TTN-AS1	SNV	intron_variant 2KB_downstream_variant regulatory_region_variant	-	-	4.44	0.533	0.079	-0.892				-	-
<input type="checkbox"/>	2:179582162 C/T	rs62178977	TTN,TTN-AS1	SNV	intron_variant regulatory_region_variant	-	-	0.00	-0.302	0.001	-7.590				-	-

Showing 1 to 10 of 139840 rows 10 rows per page

1 2 3 4 5 ... 13984

Other OpenCB projects: HGVA

The Human Genomic Variation Archive

- Integrates variants from the main reference human projects
 - Adds valuable information such as variant annotation: consequence types, population frequencies, protein effect predictions, variant-associated phenotype, etc
- Main features:
 - Annotation performed using CellBase
 - Population frequencies calculated, including populations and super-populations
 - Data is indexed using OpenCGA
 - Rich interactive web-based data mining tool based on IVA

Current Projects and Studies

Reference Studies GRCh37

- 1000 Genomes Phase 3
- Exome Aggregation Consortium (ExAC)
- Exome Sequencing Project (ESP6500)
- Genome of the Netherlands (GoNL)
- UK10K project
- Spanish Medical Genome Project (MGP)

Reference Studies GRCh38

- 1000 Genomes Phase 3

Cancer GRCh37

- QIMR Berghofer Melanoma
- Chronic Myeloid Leukemia - Russian Academy of Medical Sciences

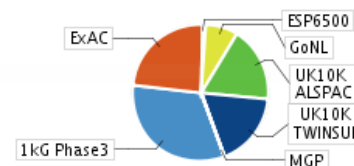
Platinum

- Illumina Platinum

Statistics

More than **250M** variants reported and about **120M** of unique variants

Variant Studies GRCh37



- 1kG Phase3 (85,170,328 - 32%)
- ExAC (63,000,000 - 24%)
- ESP6500 (1,997,952 - 1%)
- GoNL (20,708,427 - 8%)
- UK10K ALSPAC (46,618,311 - 18%)
- UK10K TWINSUK (46,618,311 - 18%)
- MGP (711,005 - 0%)

Other OpenCB projects: HGVA

The Human Genomic Variation Archive

OpenCB HGVA v2.0.0 Variant Browser Facets (New) Beacon Studies Search About

Projects / reference_grch37 / UK10K

Variant Browser

Search

Clear No filters selected Filters

Table Result Summary (Beta)

Showing 1-10 of 46,665,970 variants

Download Share

Variant	SNP Id	Genes	Type	Consequence Type	Deleteriousness			Conservation			Population Frequencies			Phenotype		
					SIFT	Polyphen	CADD	PhyloP	PhastCons	GERP	1000 Genomes	gnomAD Genomes	ESP6500	Clinvar	Co	
2:179588838 G/A	rs202089818	TTN,RP11-171I2.1,TTN-AS1	SNV	synonymous_variant	-	-	14.15	0.655	0.993	4.240	■■■■■■■■	■■■■■■■■	■■■	-	-	Dilated cardiomyopathy 1G limb-girdle muscular dystrophy, type 2j
2:179588874 T/C	rs375874660	TTN,RP11-171I2.1,TTN-AS1	SNV	splice_region_variant	-	-	9.43	0.533	0.721	-3.180	■■■■■■■■	■■■■■■■■	■■■	-	-	-
2:179588908 A/C	rs72648963	TTN,RP11-171I2.1,TTN-AS1	SNV	intron_variant non_coding_transcript_exon_variant regulatory_region_variant	-	-	7.36	-0.256	0.727	-1.160	■■■■■■■■	■■■■■■■■	■■■	-	-	-
2:179588996 C/T	rs72648962	TTN,RP11-171I2.1,TTN-AS1	SNV	missense_variant	-	-	20.80	0.655	0.477	6.020	■■■■■■■■	■■■■■■■■	■■■	-	-	dilated cardiomyopathy 1g Cardiovascular phenotype Limb-girdle muscular dystrophy, type 2J

Study

Studies Filter

In all (AND)

UK10K

1kG_phase3_chrMT

MGP

GONL

DISCOVERHR

EXAC

GNOMAD_GENOMES

GNOMAD_EXOMES

1kG_phase3_chrY

ESP6500

1kG_phase3

Genomic

Population Frequency

Deleteriousness

Conservation

- Published at NAR, 2017
- <http://hgva.opencb.org>

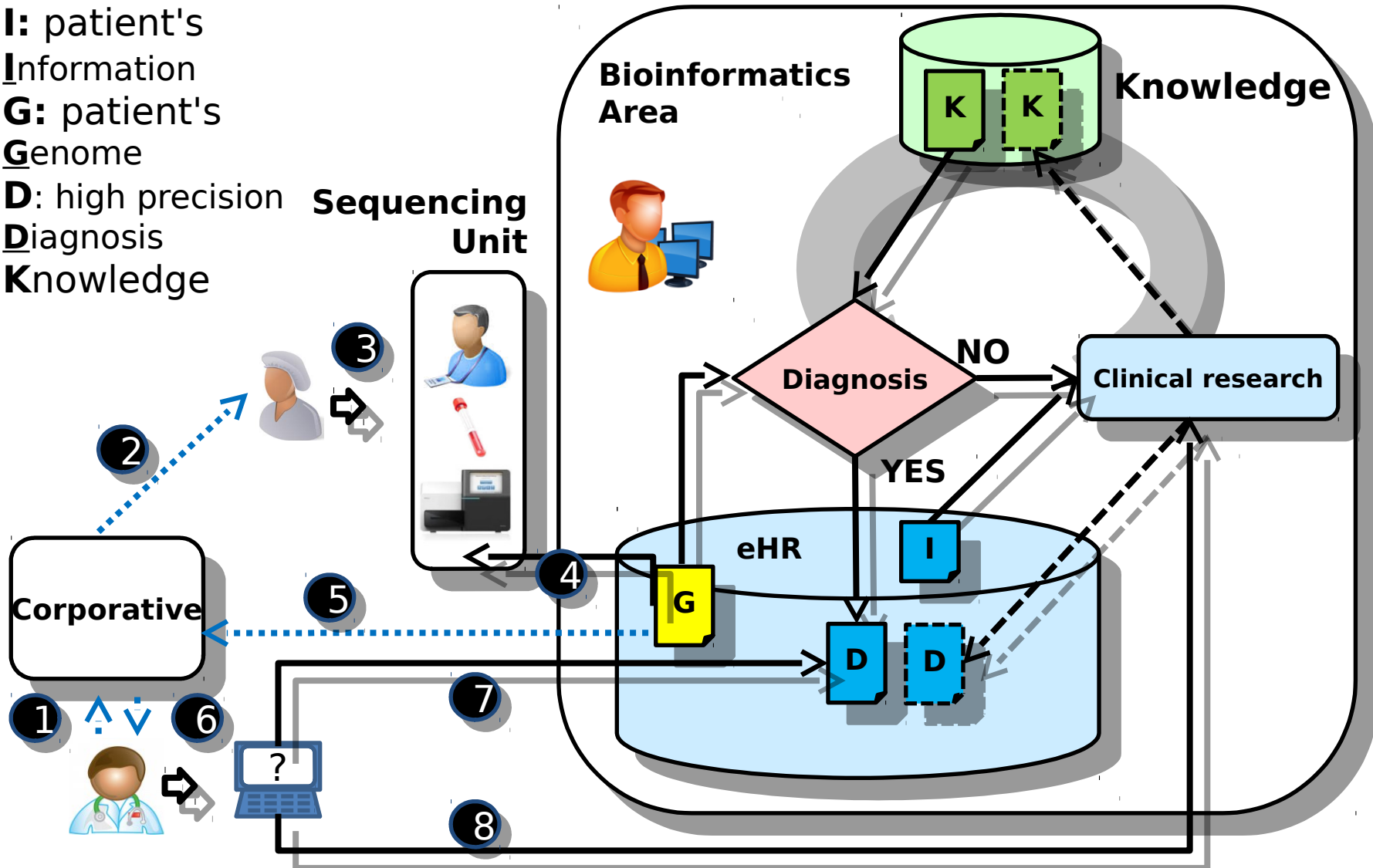
Overview

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- **A case study: Personalized Medicine Module (MMP)**

Big data in Genomics

MMP for diagnosis and clinical research within the Andalusian health system

I: patient's Information
G: patient's Genome
D: high precision Diagnosis
K: Knowledge

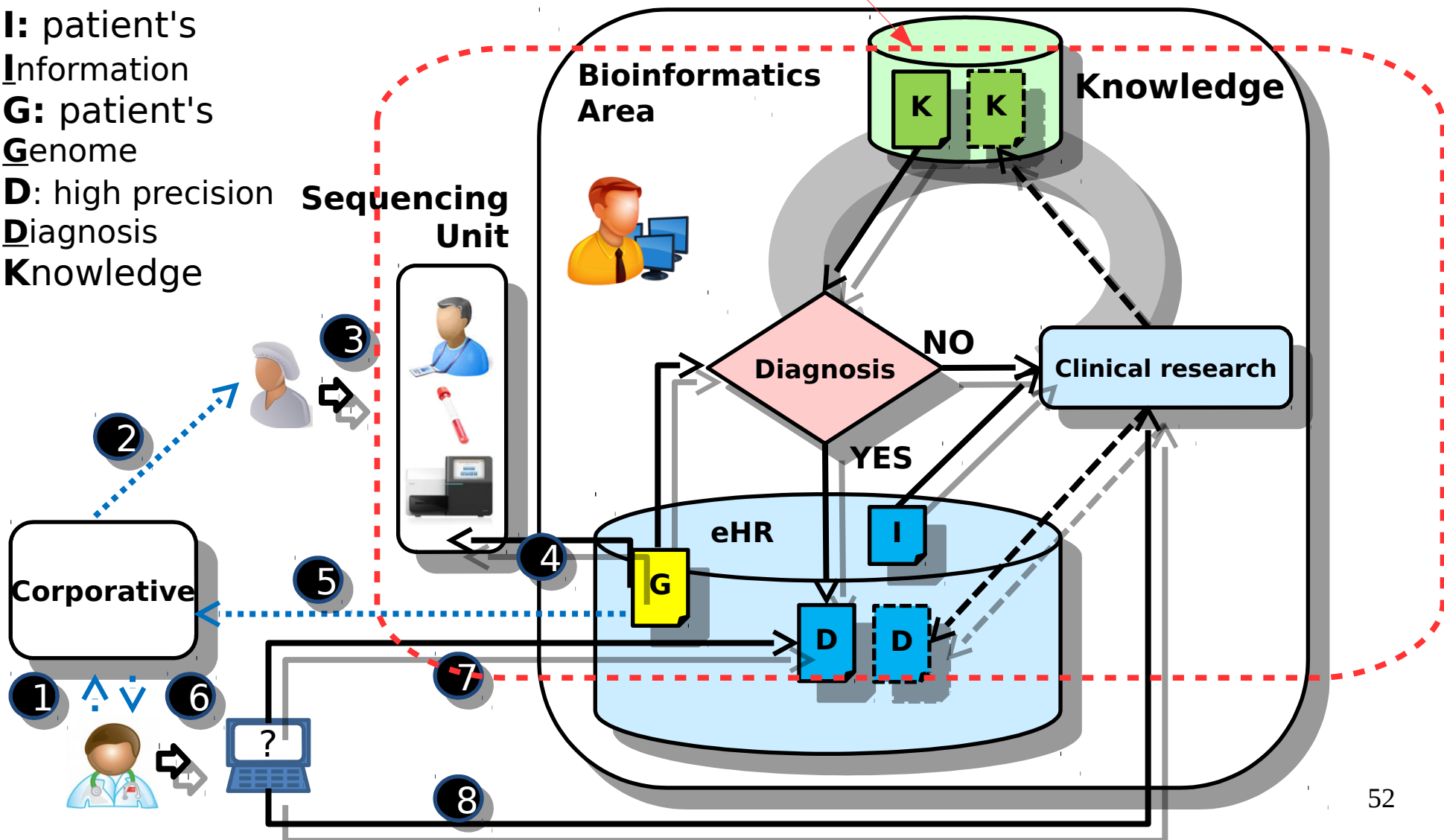


Big data in Genomics

MMP for diagnosis and clinical research within the Andalusian health system

Back-end: OpenCGA

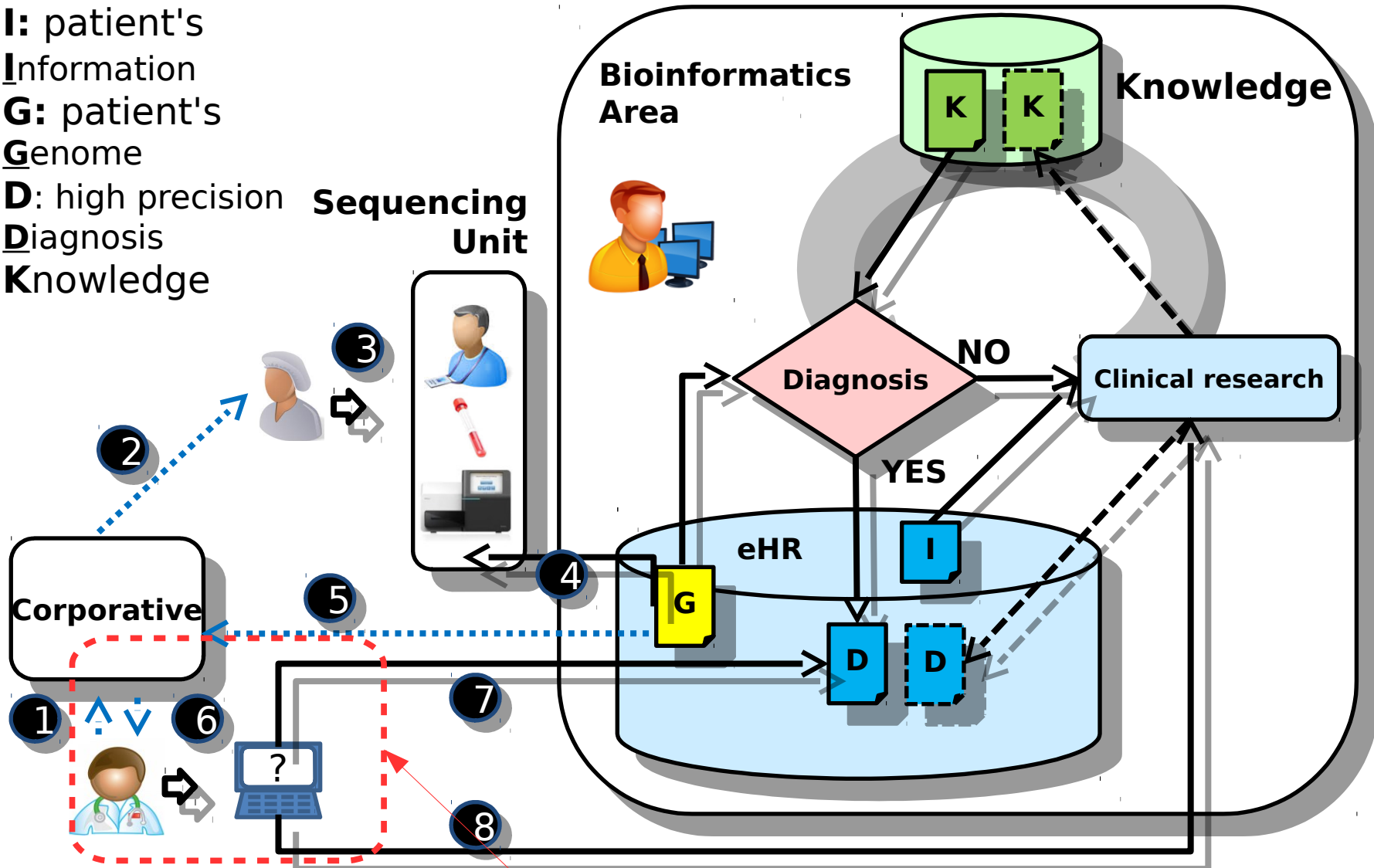
I: patient's Information
G: patient's Genome
D: high precision Diagnosis
K: Knowledge



Big data in Genomics

MMP for diagnosis and clinical research within the Andalusian health system

I: patient's Information
G: patient's Genome
D: high precision Diagnosis
K: Knowledge



Front-end: Customized IVA (MMP-SAS)

Front-end: MMP-SAS

IVA v1.1.9

Overview

Welcome to the MMP-SAS tool for whole genome variant analysis. This interactive tool allows finding genes affected by deleterious variants that segregate along family pedigrees, case-controls or sporadic samples.

Supported by:



Servicio Andaluz de Salud
CONSEJERÍA DE SALUD



Clinical Bioinformatics Area



Fundación Progreso y Salud
CONSEJERÍA DE SALUD



Note:

MMP-SAS web application makes an intensive use of the HTML5 standard and other cutting-edge web technologies such as Web Components, so only modern web browsers are fully supported, these include Chrome 49+, Firefox 45+, Microsoft Edge 14+, Safari 10+ and Opera 36+.

[Report an issue here](#)

Front-end: MMP-SAS

Name

 mmp_admin

Password



Sign In

Front-end: MMP-SAS

Clinical Analysis



Patient Information

Patient ID

Chromosomal Gender

Affectation Status

Life Status

Year of Birth

Year of Birth must be prior to year of Test

Birth Place

Ethnicity

Parental Consanguinity

- no
- yes

Front-end: MMP-SAS

Upload and check file

Type of sample

Cell line

- constitutive (germline)
- somatic

Hospital

Physician

Year of Test

Age of Test

NGS Platform

Technical data

VCF or gVCF file

Front-end: MMP-SAS

Clinical Analysis



Search

Clear No filters selected Filters

Sample

Sample name
HG01879, HG01880, HG01881...

By Date

- All
- Recently Uploaded
- Date (Year-Month-Day)

2018 - Any - Any

Patient Filters

Individual ID
Smith, Grant ...

HPO
HP:000145

Diagnosis
Smith, Grant ...

Sample Results

Showing 1-4 of 4 samples

<input type="checkbox"/>	Sample	Individual ID	Date	Status	Sex	Diagnosis	HPO	Father	Mother	Cell Line	QC
<input type="checkbox"/>	prueba	43-215	2018-0-08	READY	MALE	-	Vitreoretinal degeneration	-	-	Germline	Download
<input type="checkbox"/>	3_38	3_38	2018-3-13	READY	FEMALE	-	Subretinal deposits	-	-	Germline	Download
<input type="checkbox"/>	33_12550	Fake_patient	2018-4-02	READY	FEMALE	-	Breast carcinoma	-	-	Germline	Download
<input type="checkbox"/>	68_24021	fake_patient2	2018-4-02	READY	FEMALE	-	Mucinous gastric carcinoma	-	-	Germline	Download

Showing 1 to 4 of 4 rows

Analysis Type

Single Analysis
 Duo Analysis
 Trio Analysis
 Family Analysis

Clinical Analysis

Delete (J) []

Analysis ID	Description	Samples	Analysis Type	Definition	Date	Subject	Disease	Action
No matching records found								

Front-end: MMP-SAS

Projects / enod@enod_grch37 / agilent_sureselect_v3_p1_1

Clinical Analysis



Search

No filters selected

Sample

Sample name
HG01879, HG01880, HG01881...

By Date

- All
- Recently Uploaded
- Date (Year-Month-Day)

2018 - Any - Any

Patient Filters

Individual ID
Smith, Grant ...

HPO
HP:000145

Diagnosis
Smith, Grant ...

Sample Results

Showing 1-3 of 3 samples

<input checked="" type="checkbox"/>	Sample	Individual ID	Date	Status	Sex	Diagnosis	HPO	Father	Mother	Cell Line
<input checked="" type="checkbox"/>	0044-018-COHO_1	0044-018-COHO_1	2018-0-15	READY	MALE	Unspecified intellectual disabilities	Intellectual disability	-	-	Germline
<input checked="" type="checkbox"/>	0044-018-COHO_2	0044-018-COHO_2	2018-0-15	READY	MALE	-	-	-	-	Germline
<input checked="" type="checkbox"/>	0044-018-COHO_3	0044-018-COHO_3	2018-0-15	READY	FEMALE	-	-	-	-	Germline

Showing 1 to 3 of 3 rows

Analysis Type

Clinical Analysis

There are unsaved analyses!

	Analysis ID	Description	Samples	Analysis Type	Definition	Date	Subject	Disease	Action
<input type="checkbox"/>	AN-4163		0044-018-COHO_1,0044-018-COHO_2,0044-018-COHO_3	Trio	<input type="button" value="Edit"/>	7/05/2018	0044-018-COHO_1	F79	<input type="button" value="Save"/>

Front-end: MMP-SAS

Family Editor



Name

FA-6031

Description

|

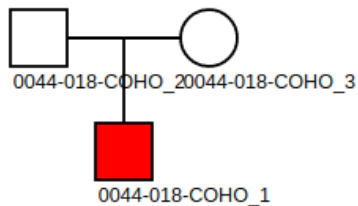
Diseases

⊞ Add custom disease

Unspecified intellectual disabilities(F79)

Intellectual disability(HP:0001249)

Sample ID	Father	Mother	Phenotypes	Deceased	Parental Consanguinity	Sex
0044-018-COHO_1 (0044-018-COHO_1)	0044-018-COHO_2	0044-018-COHO_3	<input type="checkbox"/> F79 <input checked="" type="checkbox"/> HP:0001249	<input type="checkbox"/>	<input type="checkbox"/>	MALE
0044-018-COHO_2 (0044-018-COHO_2)	Select a sample...	Select a sample...	<input type="checkbox"/> F79 <input type="checkbox"/> HP:0001249	<input type="checkbox"/>	<input type="checkbox"/>	MALE
0044-018-COHO_3 (0044-018-COHO_3)	Select a sample...	Select a sample...	<input type="checkbox"/> F79 <input type="checkbox"/> HP:0001249	<input type="checkbox"/>	<input type="checkbox"/>	FEMALE



Cancel

OK

Front-end: MMP-SAS

Projects / enod@enod_grch37 / agilent_sureselect_v3_p1_1

Clinical Analysis



Clinical Analysis AN-3622

Select Recent Analysis:

AN-3622

Select analysis: [Browse...](#)

AN-3622 Clinical Analysis Summary

Clinical Analysis

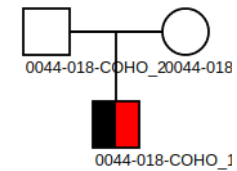
Name: AN-3622
Disease: Unspecified intellectual disabilities (F79)
Type: TRIO
Date: 15 Jan 18

Sample

Name: 0044-018-COHO_1
Somatic: false
Phenotypes: Unspecified intellectual disabilities (F79)
Intellectual disability (HP:0001249)

Subject

Name: 0044-018-COHO_1
Sex (karyotype): MALE (XY)
Date of Birth: 1920 (UNKNOWN)
Pedigree:



Phenotypes: Unspecified intellectual disabilities (F79)
Intellectual disability (HP:0001249)

Interpretation Algorithms

Several prioritization and interpretation algorithms are available, you can choose an **interactive** tool:

Interactive Prioritization (based on [TEAM](#) paper)

[OK](#)

Front-end: MMP-SAS

Projects / enod@enod_grch37 / agilent_sureselect_v3_p1_1

Clinical Analysis



☰ Prioritization

🔍 Search

🔄 Clear genotype

🔽 Filters

📄 Table Result **🗺️ Genome Browser (Beta)**

🔙 Back to Clinical Analysis Selector **📄 Save Interpretation...**

Study and Cohorts

Samples

Select Sample Genotypes:

Inheritance Mode:
Autosomal Dominant

Sample	0/0	0/1	1/1	.I.
0044-018-COHO_1	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
0044-018-COHO_2	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
0044-018-COHO_3	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Any allele in multi-allelic variants

Cohort Stats (MAF)

Project not found

Studies Filter

In (AND)

agilent_sureselect_v3_p1_1

Showing 1-10 of 1,810 variants

📄 Download **↔️ Share**

	Variant	SNP Id	Genes	Type	Samples			Consequence Type	Deleteriousness			Conservation			Population Frequencies		
					0044-018-COHO_1	0044-018-COHO_2	0044-018-COHO_3		SIFT	Polyphen	CADD	PhyloP	PhastCons	GERP	1000 Genomes	gnomAD Genomes	ESP650
<input type="checkbox"/>	1:1509825 A/G	rs6666293	SSU72,AL645728.1	SNV	A / G	A / A	A / A	intron_variant 2KB_upstream_variant regulatory_region_variant TF_binding_site_variant	-	-	5.09	-2.220	0.049	-4.570			
<input type="checkbox"/>	1:5940092 CA/-	rs140612295	NPHP4	INDEL	CA / -	CA / CA	CA / CA	intron_variant NMD_transcript_variant regulatory_region_variant	-	-	-	0.113	0.005	-0.338			
<input type="checkbox"/>	1:11156046 T/-	rs374028571	EXOSC10,RP4-635E18.6	INDEL	T / -	T / T	T / T	intron_variant NMD_transcript_variant regulatory_region_variant	-	-	-	-1.193	0.108	1.070			
<input type="checkbox"/>	1:17570466 T/C	rs2293921	PADI1	SNV	T / C	T / T	T / T	intron_variant regulatory_region_variant	-	-	3.54	-0.282	0.003	-0.769			
<input type="checkbox"/>	1:16974869 G/C	rs4570422	CROCCP2,MST1P2	SNV	G / C	G / G	G / G	non_coding_transcript_exon_variant regulatory_region_variant	-	-	6.23	0.000	0.000	0.000			
<input type="checkbox"/>	1:19611487 A/T	rs59348345	AKR7A3	SNV	A / T	A / A	A / A	intron_variant	-	-	0.39	-1.496	0.017	-1.350			
<input type="checkbox"/>	1:19612477 C/T	rs2231198	AKR7A3	SNV	C / T	C / C	C / C	missense_variant	tolerated	benign	18.62	0.194	0.263	3.040			
<input type="checkbox"/>	1:25256444 G/A	rs71514255	RUNX3	SNV	G / A	G / G	G / G	intron_variant 2KB_upstream_variant regulatory_region_variant	-	-	12.75	0.186	0.370	2.020			
<input type="checkbox"/>	1:29037241 -/T	rs11415888	GMEB1	INDEL	- / T	- / -	- / -	intron_variant regulatory_region_variant	-	-	-	0.650	0.067	0.875			
<input type="checkbox"/>	1:36884530 G/A	rs72663495	OSCP1,SNORA63	SNV	G / A	G / G	G / G	intron_variant 2KB_downstream_variant 2KB_upstream_variant	-	-	4.83	-0.965	0.086	0.613			

Showing 1 to 10 of 1810 rows **10** rows per page

1 2 3 4 5 ... 181

- Genomic
- Population Frequency
- Deleteriousness
- Conservation
- Consequence Type

Front-end: MMP-SAS

0044-018-COHO_2

0044-018-COHO_3

Any allele in multi-allelic variants

Cohort Stats (MAF) ⓘ

Project not found

Studies Filter ⓘ

In (AND) ▾

agilent_sureselect_v3_p1_1

Genomic

Population Frequency

Deleteriousness

Conservation

Consequence Type

Gene Ontology

Phenotype-Disease

VCF Metrics

<input type="checkbox"/>	1:5940092 CA/-	rs140612295	NPHP4	INDEL	CA / -	CA / CA	CA / CA	regulatory_region_variant TF_binding_site_variant															
<input type="checkbox"/>	1:11156046 T/-	rs374028571	EXOSC10,RP4-635E18.6	INDEL	T / -	T / T	T / T	intron_variant NMD_transcript_variant regulatory_region_variant	-	-	-	0.113	0.005	-0.338	■■■■■■■	■■■■■■■	■■■						
<input type="checkbox"/>	1:17570466 T/C	rs2293921	PADI1	SNV	T / C	T / T	T / T	intron_variant regulatory_region_variant	-	-	3.54	-0.282	0.003	-0.769	■■■■■■■	■■■■■■■	■■■						
<input type="checkbox"/>	1:16974869 G/C	rs4570422	CROCCP2,MST1P2	SNV	G / C	G / G	G / G	non_coding_transcript_exon_variant regulatory_region_variant	-	-	6.23	0.000	0.000	0.000	■■■■■■■	■■■■■■■	■■■						
<input type="checkbox"/>	1:19611487 A/T	rs59348345	AKR7A3	SNV	A / T	A / A	A / A	intron_variant	-	-	0.39	-1.496	0.017	-1.350	■■■■■■■	■■■■■■■	■■■						
<input type="checkbox"/>	1:19612477 C/T	rs2231198	AKR7A3	SNV	C / T	C / C	C / C	missense_variant	tolerated	benign	18.62	0.194	0.263	3.040	■■■■■■■	■■■■■■■	■■■						
<input type="checkbox"/>	1:25256444 G/A	rs71514255	RUNX3	SNV	G / A	G / G	G / G	intron_variant 2KB_upstream_variant regulatory_region_variant	-	-	12.75	0.186	0.370	2.020	■■■■■■■	■■■■■■■	■■■						
<input type="checkbox"/>	1:29037241 -T	rs11415888	GMEB1	INDEL	- / T	- / -	- / -	intron_variant regulatory_region_variant	-	-	-	0.650	0.067	0.875	■■■■■■■	■■■■■■■	■■■						
<input type="checkbox"/>	1:36884530 G/A	rs72663495	OSCP1,SNORA63	SNV	G / A	G / G	G / G	intron_variant 2KB_downstream_variant 2KB_upstream_variant	-	-	4.83	-0.965	0.086	0.613	■■■■■■■	■■■■■■■	■■■						

Showing 1 to 10 of 1810 rows 10 rows per page

1 2 3 4 5 ... 181 >

Variant: 1:19612477:C:T

Advanced Annotation | File Metrics | Beacon Network

Summary

Consequence Types (2)

Population Frequencies (70)

Variant Trait Association ()

Gene Trait Association ()

ID: rs2231198
HGVS: ENST00000361640(ENSG00000162482):c.412G>A
Alleles: C/T
Location: 1:19612477
Most Severe Consequence: missense_variant (Gene: AKR7A3, Transcript: ENST00000361640)
Most Severe Deleterious Score: Sift: tolerated (Gene: AKR7A3, Transcript: ENST00000361640)
Polyphen: benign (Gene: AKR7A3, Transcript: ENST00000361640)
CADD Scaled: 18.62

Front-end: MMP-SAS

Genomic

Chromosomal Location

3:444-55555,1:1-100000

Feature IDs (gene, SNPs, ...)

Search for Gene Symbols

BRCA2,ENSG00000139618,ENST0000544455,rs28897700

Gene Disease Panels

Intellectual disability (1262)

AARS,AASS,ABCC9,ABCD1,ABCD4,ABHD5,ACAD9,ACADM,ACO2,ACOX1,ACSL4,ACTB,ACTG1,ACY1,...

Biotype

Nothing selected

Variant Type

- SNV
- MNV
- CNV
- SV
- INDEL

Population Frequency

Select Population MAF

- + 1000 Genomes
- + gnomAD Genomes
- + ESP6500
- + MGP

Deleteriousness

Conservation

<input type="checkbox"/>	1:25256444 G/A	rs71514255	RUNX3	SNV	G / A	G / G	G / G	intron_variant 2KB_upstream_variant regulatory_region_variant	-	-	12.75	0.186	0.370	2.020			
<input type="checkbox"/>	1:29037241 -T	rs11415888	GMEB1	INDEL	- / T	- / -	- / -	intron_variant regulatory_region_variant	-	-	-	0.650	0.067	0.875			
<input type="checkbox"/>	1:36884530 G/A	rs72663495	OSCP1,SNORA63	SNV	G / A	G / G	G / G	intron_variant 2KB_downstream_variant 2KB_upstream_variant	-	-	4.83	-0.965	0.086	0.613			

Showing 1 to 10 of 1810 rows 10 rows per page

1 2 3 4 5 ... 181

Variant: 1:19612477:C:T

Advanced Annotation | **File Metrics** | **Beacon Network**

Summary

ID rs2231198

HGVS ENST00000361640(ENSG00000162482):c.412G>A

Alleles C/T

Location 1:19612477

Most Severe Consequence Type missense_variant (Gene : AKR7A3, Transcript : ENST00000361640)

Most Severe Sift tolerated (Gene:AKR7A3, Transcript: ENST00000361640)

Deleterious Polyphen benign (Gene:AKR7A3, Transcript: ENST00000361640)

Score CADD Scaled 18.62

Consequence Types (2)

Population Frequencies (70)

Variant Trait Association ()

Gene Trait Association ()

Front-end: MMP-SAS

Chrom	Pos	Ref	Alt	Gene	Variant Type	Consequence	Consequence	Consequence	Consequence	missense_variant	tolerated	benign	18.62	0.194	0.263	3.040	Progression	Progression	Progression
1	19612477	C/T	T/C	AKR7A3	SNV	C / T	C / C	C / C	C / C	missense_variant	-	-	18.62	0.194	0.263	3.040	██████████	██████████	██████████
1	25256444	G/A	A/G	RUNX3	SNV	G / A	G / G	G / G	G / G	intron_variant 2KB_upstream_variant regulatory_region_variant	-	-	12.75	0.186	0.370	2.020	██████████	██████████	██████████
1	29037241	-T	T-	GMEB1	INDEL	- / T	- / -	- / -	- / -	intron_variant regulatory_region_variant	-	-	-	0.650	0.067	0.875	██████████	██████████	██████████
1	36884530	G/A	A/G	OSCP1,SNORA63	SNV	G / A	G / G	G / G	G / G	intron_variant 2KB_downstream_variant 2KB_upstream_variant	-	-	4.83	-0.965	0.086	0.613	██████████	██████████	██████████

Showing 1 to 10 of 1810 rows | 10 rows per page

Navigation: < 1 2 3 4 5 ... 181 >

Variant: 1:19612477:C:T

Advanced Annotation
File Metrics
Beacon Network

Summary

Consequence Types (2)

Population Frequencies (70)

Variant Trait Association ()

Gene Trait Association ()

ID: rs2231198

HGVS: ENST00000361640(ENSG00000162482):c.412G>A

Alleles: C/T

Location: 1:19612477

Most Severe Consequence Type: **missense_variant** (Gene: AKR7A3, Transcript: ENST00000361640)

Most Severe Sift: **tolerated** (Gene: AKR7A3, Transcript: ENST00000361640)

Deleterious Polyphen Score: **benign** (Gene: AKR7A3, Transcript: ENST00000361640)

CADD Scaled: **18.62**

Genomic

Population Frequency

Deleteriousness

Protein Substitution Score

SIFT: Deleterious < []

Polyphen: Probably ds < []

Logical Operator: OR AND

CADD

Raw: < []

Scaled: < []

Conservation

Conservation Score

PhyloP: < []

PhastCons: < []

Gerp: < []

Logical Operator: OR AND

Consequence Type

Gene Ontology

Phenotype-Disease

VCF Metrics

Front-end: MMP-SAS

Consequence Type

Select SO terms 1

Loss-of-Function (LoF) terms:

- LoF terms

Consequence Type terms:

- Intergenic
 - upstream_gene_variant (SO:0001631)
 - 2KB_upstream_variant (SO:0001636)
 - downstream_gene_variant (SO:0001637)
 - 2KB_downstream_variant (SO:00020)
 - intergenic_variant (SO:0001628)
- Regulatory
 - mature_miRNA_variant (SO:0001620)
 - regulatory_region_ablation (SO:0001630)
 - regulatory_region_amplification (SO:0001631)
 - regulatory_region_variant (SO:0001632)
 - TF_binding_site_variant (SO:000178)
 - TFBS_ablation (SO:0001895)
 - TFBS_amplification (SO:0001892)
- Coding
 - coding_sequence_variant (SO:00015)
 - feature_elongation (SO:0001907)
 - feature_truncation (SO:0001906)
 - frameshift_variant (SO:0001589)
 - incomplete_terminal_codon_variant (SO:0001822)
 - inframe_deletion (SO:0001822)
 - inframe_insertion (SO:0001821)
 - missense_variant (SO:0001583)
 - NMD_transcript_variant (SO:0001621)
 - protein_altering_variant (SO:0001818)
 - synonymous_variant (SO:0001819)
 - start_lost (SO:0002012)
 - stop_gained (SO:0001587)
 - stop_lost (SO:0001578)
 - stop_retained_variant (SO:0001567)
- Non-coding
 - 3_prime_UTR_variant (SO:0001624)
 - 5_prime_UTR_variant (SO:0001623)
 - intron_variant (SO:0001627)
 - non_coding_transcript_exon_variant (SO:0001627)
- Splice
 - splice_acceptor_variant (SO:0001574)
 - splice_donor_variant (SO:0001575)
 - splice_region_variant (SO:0001630)
- transcript_ablation (SO:0001893)
- transcript_amplification (SO:0001889)

Variant ID	RefSeq	Gene	Variant Type	Alleles	Effect	Impact	Score	Other Scores	Annotations			
1:1509825 A/G	rs6666293	SSU72,AL645728.1	SNV	A / G	A / A	A / A	5.09	-2.220	0.049	-4.570	intron_variant, 2KB_upstream_variant, regulatory_region_variant, TF_binding_site_variant	
1:5940092 CA/-	rs140612295	NPHP4	INDEL	CA / -	CA / CA	CA / CA	-	-	0.113	0.005	-0.338	intron_variant, NMD_transcript_variant, regulatory_region_variant
1:11156046 T/-	rs374028571	EXOSC10,RP4-635E18.6	INDEL	T / -	T / T	T / T	-	-	-1.193	0.108	1.070	intron_variant, NMD_transcript_variant, regulatory_region_variant
1:17570466 T/C	rs2293921	PADI1	SNV	T / C	T / T	T / T	3.54	-0.282	0.003	-0.769	intron_variant, regulatory_region_variant	
1:16974869 G/C	rs4570422	CROCCP2,MST1P2	SNV	G / C	G / G	G / G	6.23	0.000	0.000	0.000	0.000	non_coding_transcript_exon_variant, regulatory_region_variant
1:19611487 A/T	rs59348345	AKR7A3	SNV	A / T	A / A	A / A	0.39	-1.496	0.017	-1.350	intron_variant	
1:19612477 C/T	rs2231198	AKR7A3	SNV	C / T	C / C	C / C	18.62	0.194	0.263	3.040	missense_variant, tolerated, benign	
1:25256444 G/A	rs71514255	RUNX3	SNV	G / A	G / G	G / G	12.75	0.186	0.370	2.020	intron_variant, 2KB_upstream_variant, regulatory_region_variant	
1:29037241 -/T	rs11415888	GMEB1	INDEL	- / T	- / -	- / -	-	0.650	0.067	0.875	intron_variant, regulatory_region_variant	
1:36884530 G/A	rs72663495	OSCP1,SNORA63	SNV	G / A	G / G	G / G	4.83	-0.965	0.086	0.613	intron_variant, 2KB_downstream_variant, 2KB_upstream_variant	

Showing 1 to 10 of 1810 rows rows per page

Variant: 1:19612477:C:T

Advanced Annotation | File Metrics | Beacon Network

Summary

ID: rs2231198

HGVS: ENST00000361640(ENSG00000162482):c.412G>A

Alleles: C/T

Location: 1:19612477

Most Severe Consequence Type: **missense_variant** (Gene: AKR7A3, Transcript: ENST00000361640)

Most Severe Sift: **tolerated** (Gene: AKR7A3, Transcript: ENST00000361640)

Most Severe Deleterious Score: **benign** (Gene: AKR7A3, Transcript: ENST00000361640)

Score: CADD Scaled **18.62**

Consequence Types (2)

Population Frequencies (70)

Variant Trait Association ()

Gene Trait Association ()



Consequence type: the location or effect of a sequence variation on a transcript

Front-end: MMP-SAS

Gene Ontology

GO Accessions ⓘ

GO:0000145

Add GO Term Q

Phenotype-Disease

HPO Accessions ⓘ

HP:0000001, HP:3000079

Add HPO Term Q

ClinVar Accessions ⓘ

RCV000058226

Full-text search on HPO, ClinVar, protein domains or keywords. Some OMIM and Orphanet IDs are also supported ⓘ

Full-text search, e.g. *melanoma*

VCF Metrics

VCF FILTER ⓘ

PASS

PASS

QualByDepth

FisherStrand

RMSMappingQuality

MappingQualityRankSumTest

ReadPosRankSumTest

StrandOddsRatio

Variant ID	Ref	Alt	Gene	Type	Impact	Consequence	Annotations	Score 1	Score 2	Score 3	Score 4	Score 5	Score 6	Score 7	Score 8	Score 9	Score 10	Score 11	Score 12	Score 13	Score 14	Score 15	Score 16	Score 17	Score 18	Score 19	Score 20		
1:5940092 CA/-	rs140612295	NPHP4	INDEL	CA / -	CA / CA	CA / CA	intron_variant 2KB_upstream_variant regulatory_region_variant TF_binding_site_variant	-	-	-	0.113	0.005	-0.338																
1:11156046 T/-	rs374028571	EXOSC10,RP4-635E18.6	INDEL	T / -	T / T	T / T	intron_variant NMD_transcript_variant regulatory_region_variant	-	-	-	-1.193	0.108	1.070																
1:17570466 T/C	rs2293921	PADI1	SNV	T / C	T / T	T / T	intron_variant regulatory_region_variant	-	-	3.54	-0.282	0.003	-0.769																
1:16974869 G/C	rs4570422	CROCCP2,MST1P2	SNV	G / C	G / G	G / G	non_coding_transcript_exon_variant regulatory_region_variant	-	-	6.23	0.000	0.000	0.000																
1:19611487 A/T	rs59348345	AKR7A3	SNV	A / T	A / A	A / A	intron_variant	-	-	0.39	-1.496	0.017	-1.350																
1:19612477 C/T	rs2231198	AKR7A3	SNV	C / T	C / C	C / C	missense_variant	tolerated	benign	18.62	0.194	0.263	3.040																
1:25256444 G/A	rs71514255	RUNX3	SNV	G / A	G / G	G / G	intron_variant 2KB_upstream_variant regulatory_region_variant	-	-	12.75	0.186	0.370	2.020																
1:29037241 -/T	rs11415888	GMEB1	INDEL	- / T	- / -	- / -	intron_variant regulatory_region_variant	-	-	-	0.650	0.067	0.875																
1:36884530 G/A	rs72663495	OSCP1,SNORA63	SNV	G / A	G / G	G / G	intron_variant 2KB_downstream_variant 2KB_upstream_variant	-	-	4.83	-0.965	0.086	0.613																

Showing 1 to 10 of 1810 rows rows per page ⏪ 1 2 3 4 5 ... 181 ⏩

Variant: 1:19612477:C:T

Advanced Annotation **File Metrics** Beacon Network

Summary

ID: rs2231198

HGVS: ENST00000361640(ENSG00000162482):c.412G>A

Alleles: C/T

Location: 1:19612477

Most Severe Consequence Type: missense_variant (Gene: AKR7A3, Transcript: ENST00000361640)

Most Severe Deleterious Score: Sift tolerated (Gene: AKR7A3, Transcript: ENST00000361640)

Most Severe Polyphen Score: benign (Gene: AKR7A3, Transcript: ENST00000361640)

CADD Scaled: 18.62

Front-end: MMP-SAS

OpenCB IVA v1.1.3 Variant Browser Variant Interpretation Clinical Facets Panels Beacon Tools test Studies About Logout

Approximate Count
 Select all multi-allelic variants

Genomic
Population Frequency
Deleteriousness
Conservation
Consequence Type
Gene Ontology
Phenotype-Disease
VCF Metrics

Variant ID	RefSeq ID	Gene	SNV	C/T	C/C	C/T	Consequences		
10:81318578 T/C	rs17880662	SFTPA2	SNV	T / C	T / T	T / T	intron_variant 2KB_downstream_variant regulatory_region_variant	-	-	0.35	-1.578	0.000	-1
10:82331437 C/T	rs45526031	SH2D4B	SNV	C / T	C / C	C / C	intron_variant regulatory_region_variant	-	-	2.27	-0.768	0.002	-5
10:85899115 A/G	-	RP11-338I21.1,GHITM	SNV	A / G	A / A	A / A	non_coding_transcript_exon_variant 2KB_upstream_variant regulatory_region_variant TF_binding_site_variant	-	-	8.05	0.496	0.068	1
10:89118125 C/T	rs77153116	LINC00863,NUTM2D	SNV	C / T	C / C	C / C	missense_variant	deleterious	possibly damaging	18.27	0.175	0.040	0

Showing 61 to 70 of 1517 rows rows per page < 1 ... 6 **7** 8 ... 152 >

Variant: 10:89118125:C:T

Advanced Annotation **File Metrics** Beacon Network

Summary
Consequence Types (4)
Population Frequencies (66)
Variant Trait Association (8)
Gene Trait Association (0)

Clinvar
No ClinVar data available

Cosmic

Mutation Id	Primary Site	Site Subtype	Primary Histology	Histology Subtype	Sample Source	Tumour Origin	Gene Name	Mutation Somatic Status
COSM3752025	thyroid		other	neoplasm			FAM22D_ENST00000381697	Confirmed somatic variant
COSM3752024	breast		carcinoma	ER-positive carcinoma	surgery fresh/frozen		NUTM2A	Confirmed somatic variant
COSM3752024	thyroid		other	neoplasm			NUTM2A	Confirmed somatic variant
COSM3752025	pancreas		carcinoma	ductal carcinoma			FAM22D_ENST00000381697	Confirmed somatic variant
COSM3752024	large intestine	colon	carcinoma	adenocarcinoma			NUTM2A	Confirmed somatic variant
COSM3752025	breast		carcinoma	ER-positive carcinoma	surgery fresh/frozen		FAM22D_ENST00000381697	Confirmed somatic variant
COSM3752024	pancreas		carcinoma	ductal carcinoma			NUTM2A	Confirmed somatic variant
COSM3752025	large intestine	colon	carcinoma	adenocarcinoma			FAM22D_ENST00000381697	Confirmed somatic variant

Front-end: MMP-SAS



☰ Prioritization

genotype = 0/1,1/1
gene
Consequence Types

Showing 1-10 of 16 variants

Study

Samples

Select Sample Genotypes:

Inheritance Mode:
Select...

Sample	0/0	0/1	1/1	.I.
██████████	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>

Genomic

Chromosomal Location

3:444-55555,1:1-100000

Feature IDs (gene, SNPs, ...)

Search for Gene Symt

BRCA2,ENSG00000139618,ENST00000544455,rs28897700

Variant	SNP Id	Genes	Type	Samples	Consequence Type	Deleteriousness			Conservation			Population Freq	
						SIFT	Polyphen	CADD	PhyloP	PhastCons	GERP	1000 Genomes	gnomAD Genomes
<input checked="" type="checkbox"/> 16:68853296 C/G	COSM159879	CDH1,RP11-354M1.2,FTLP14	SNV	C / G	missense_variant	deleterious	probably damaging	23.70	0.555	0.190	4.570	-	-
<input type="checkbox"/> 16:68771372 C/T	rs3743674	CDH1	SNV	T / T	splice_region_variant	-	-	10.26	-1.988	0.005	-1.510	██████████	██████████
<input type="checkbox"/> 16:68771419 -/GCCCCAGCCCGT	rs147838237	CDH1,RNA5SP429	INDEL	GCC... / GCC...	intron_variant NMD_transcript_variant regulatory_region_variant TF_binding_site_variant	-	-	-	-0.339	0.009	-0.555	██████████	██████████
<input type="checkbox"/> 16:68857441 T/C	rs1801552	RP11-354M1.2,CDH1,FTLP14	SNV	T / C	synonymous_variant	-	-	6.21	-0.213	0.000	2.580	██████████	██████████
<input type="checkbox"/> 16:68867612 T/-	rs369254048	CDH1	INDEL	T / -	3_prime_UTR_variant NMD_transcript_variant 2KB downstream variant	-	-	-	0.533	0.003	-6.620	██████████	██████████

Front-end: MMP-SAS

CBA MMP-SAS v1.1.9 Start test Studies About Logout

Clinical Analysis

Upload Analysis **Prioritization** Report

Search

Clear genotype = [redacted]:0/1,1/1 gene Consequence Types

Table Result Genome Browser (Beta)

Back to Clinical Analysis Selector Save Interpretation...

Save Interpretation

Positive Diagnosis

ID: my_interpretation

Name: sample_interpretation

Description: Description of this interpretation ...

Comment: Add a comment ...

View Save

Study

Samples

Select Sample Genotypes:

Inheritance Mode: Select...

Sample	0/0	0/1	1/1	./.
[redacted].1	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>

Genomic

Chromosomal Location

3:444-55555,1:1-100000

Feature IDs (gene, SNPs, ...)

Front-end: MMP-SAS



Clinical Analysis AN-5046

Select analysis:

[Browse...](#)

Clinical Interpretation

Select Interpretation:

3182_68_interpretation

Interpretation Analysis: my_interpretation

Summary		
Sample Name: ██████████ Somatic: false Phenotypes: Mucinous gastric carcinoma (HP:0031498)	Subject Name: fake_patient2 Sex (karyotype): FEMALE (XX) Date of Birth: 1982 (ALIVE) Parental Consanguinity: false Phenotypes: Mucinous gastric carcinoma (HP:0031498)	Family Name: Phenotypes: Pedigree:
Analysis Name (date): my_interpretation (2 May 18) Type: SINGLE Analyst: () Description:	Software Name: TEAM (website) Version: 2.0 (commit) Dependencies: CellBase (v4.5.0)	Variant Filters genotype: ██████████/1, 1/1 alternate_frequency: 1kG_phase3-ALL<0.01, MGP-ALL<0.01 protein_substitution: sift==deleterious, polyphen==probably damaging annot-ct: coding_sequence_variant, feature_elongation, feature_truncation, frameshift_variant, incomplete_terminal_codon_variant, inframe_deletion, inframe_insertion, missense_variant, NMD_transcript_variant, protein_altering_variant, synonymous_variant, start_lost, stop_gained, stop_lost, stop_retained_variant studies: mmp_admin@misc_grch37:miscellaneous

Reported Variants

Showing 1-1 of 1 variants [Create Report](#)

Variant	Genes	Type	Gene Annotation	Prediction	Zigosity		Max allele freq	File metrics	Custom Annotations	Interpretation
					fake_patient2					
16:68853296 C/G	CDH1, RP11-354M1.2, FTLP14	SNV	missense_variant		● ○		Quality: 6085.77 Filter: PASS DP: 560		Add to Report Comments (0)	

Front-end: MMP-SAS

CBA MMP-SAS v1.1.9 Start test Studies About Logout

Projects / mmp_admin@misc_grch37 / miscellaneous

Clinical Analysis

Upload Analysis Prioritization Report

Personal Information

Service petitioner: Unidad de Oncología

Department: _____

City: _____

Patient: _____

NUHSA: _____

Family Number: _____

Analysis type: _____

Entry date: _____

Birth Year: _____

Relationship: _____

Physician one: _____

Physician two: _____


Analysis

Interpretation

Other Information ⓘ

Save report

Export report



Solicitante: Unidad de Oncología

Departamento / Unidad: Sección de Genética y Genómica

Centro: HUVR UGC Medicina Maternofetal, Genética y Reproducción

Ciudad: HU virgen del Rocío

Avda. Manuel Siurot s/n, 41013 Sevilla

Paciente: _____

NUHSA: _____

Nº ADN: _____

Nº de familia: _____

Tipo de Análisis: _____

Tipo de Muestra: Sangre

Fecha de entrada: _____

Año de Nacimiento: _____

Sexo: FEMENINO

Parentesco: _____

Estatus: AFECTO

Fecha de informe: 5/7/2018, 4:31:14 PM

INFORME DE ANÁLISIS GENÉTICO MOLECULAR DE ENFERMEDAD DE Cáncer gástrico

Motivo de la consulta
Cáncer gástrico

Información de Análisis

ID Análisis: 3182

Descripción: _____analysis

Información de Priorización

Resultado

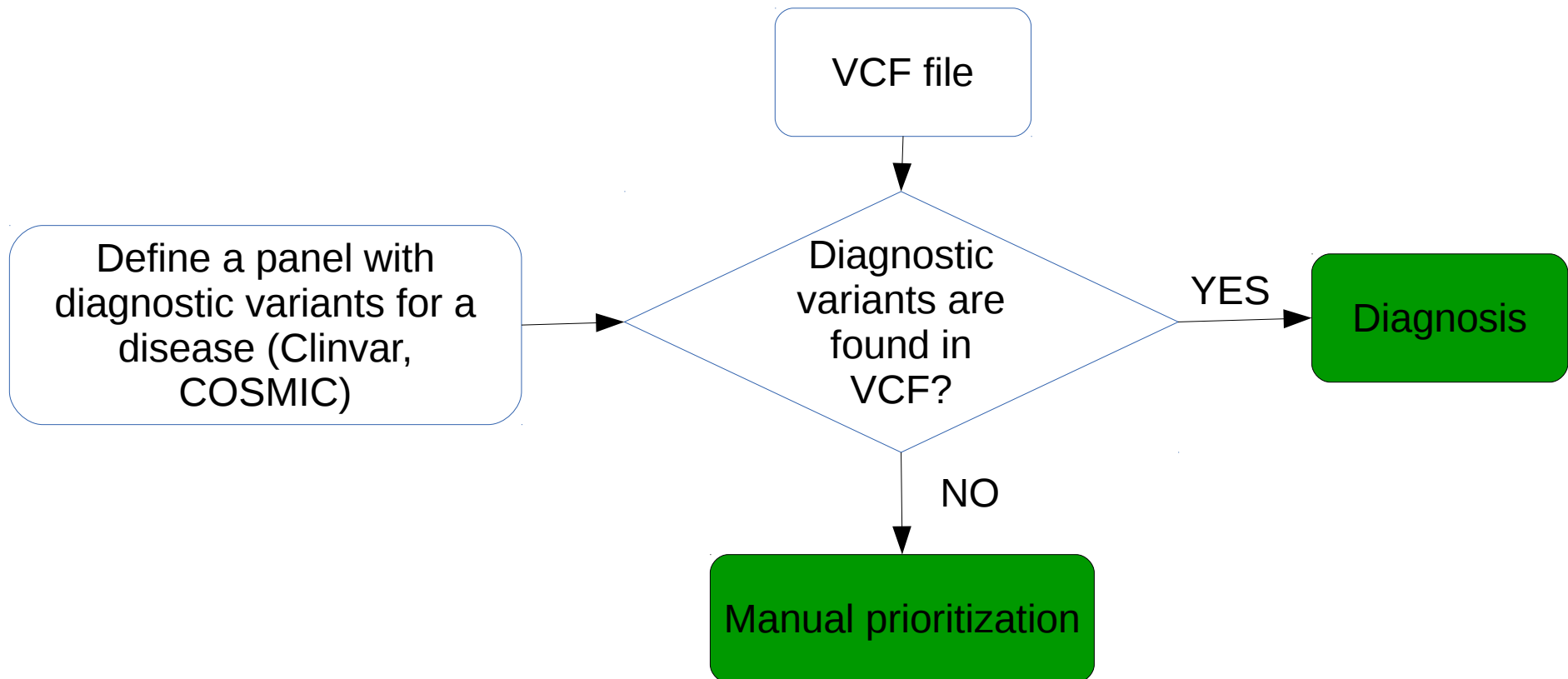
Variante	ID SNP	Genes	Tipo	Tipo de consecuencia
16:68853296:C:G	16:68853296:C:G	CDH1,RP11-354M1.2,FTLP14,	SNV	missense_variant

Resumen

- presenta la mutación 16:68853296:C:G del gen CDH1,RP11-354M1.2,FTLP14, en Heterocigosis

IVA. Upcoming improvements (available soon)

- Gene panel component
 - Design and management of panels of genes
 - Goal: Diagnostic purposes



IVA. Upcoming improvements (available soon)

- Gene panel component
 - Essential for defining (informed consent is necessary):
 - **Pharmacogenetic variants:** variability in genes implicated in drug response can modulate treatment efficacy or predispose to adverse drug reactions
 - **Secondary findings:** reporting of known pathogenic or expected pathogenic variants in the 56 ACMG genes even when unrelated to the primary medical reason for testing

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ACMG STATEMENT | Genetics
inMedicine

Recommendations for reporting of secondary findings in clinical exome and genome sequencing, 2016 update (ACMG SF v2.0): a policy statement of the American College of Medical Genetics and Genomics

Sarah S. Kalia, ScM¹, Kathy Adelman²,
Christine Eng, MD⁵, James P. Evans, MD, PhD⁶,
Teri E. Klein, PhD¹⁰, Bruce R. Korf, MD, PhD¹¹,
C. Sue Richards, PhD¹⁴, Christopher N. Vango,
David T. Miller, MD, PhD¹⁸; on behalf of the /

Genetics
inMedicine | LETTER TO THE EDITOR

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ACMG secondary findings 2.0

To the Editor: The authors of the recent American College of Medical Genetics and Genomics secondary findings

leads to an inconsistency in that many EP novel predicted loss of function variants would score as “likely pathogenic” in the new pathogenicity criteria, while it is unclear whether expected pathogenic missense variants should be reported as secondary findings. The second issue is that an explicit decision should be made as to the pathogenicity threshold

IVA.Upcoming improvements (available soon)

- Variant classification according to ACMG Standards:
 - Pathogenic, likely pathogenic, benign, likely benign, uncertain significance

© American College of Medical Genetics and Genomics **ACMG STANDARDS AND GUIDELINES** | **Genetics
inMedicine**

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, PhD¹, Nazneen Aziz, PhD^{2,16}, Sherri Bale, PhD³, David Bick, MD⁴, Soma Das, PhD⁵, Julie Gastier-Foster, PhD^{6,7,8}, Wayne W. Grody, MD, PhD^{9,10,11}, Madhuri Hegde, PhD¹², Elaine Lyon, PhD¹³, Elaine Spector, PhD¹⁴, Karl Voelkerding, MD¹³ and Heidi L. Rehm, PhD¹⁵; on behalf of the ACMG Laboratory Quality Assurance Committee

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- Antonio Rueda (*Genomics England*)



Clinical Bioinformatics Area

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



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