Medicina Personalizada en Cáncer: Perspectiva Bioinformática

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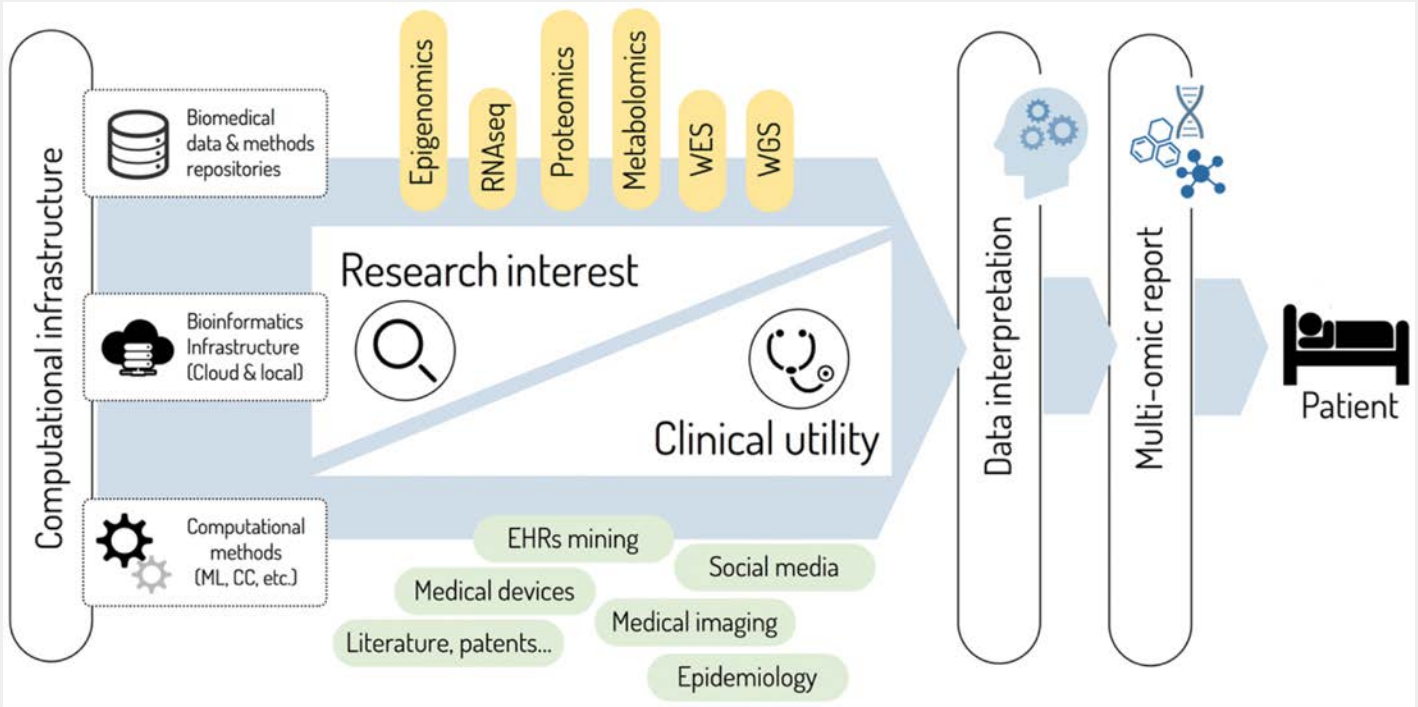
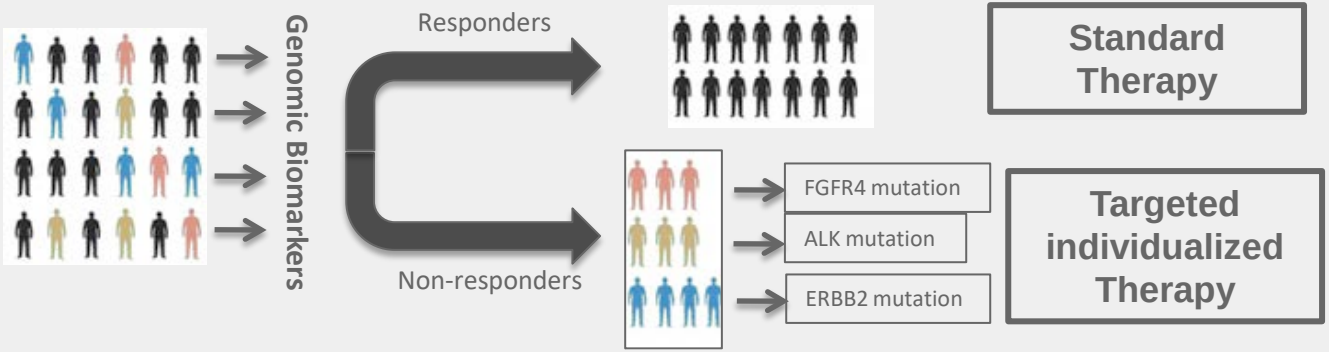
Precision medicine (PM) workflow



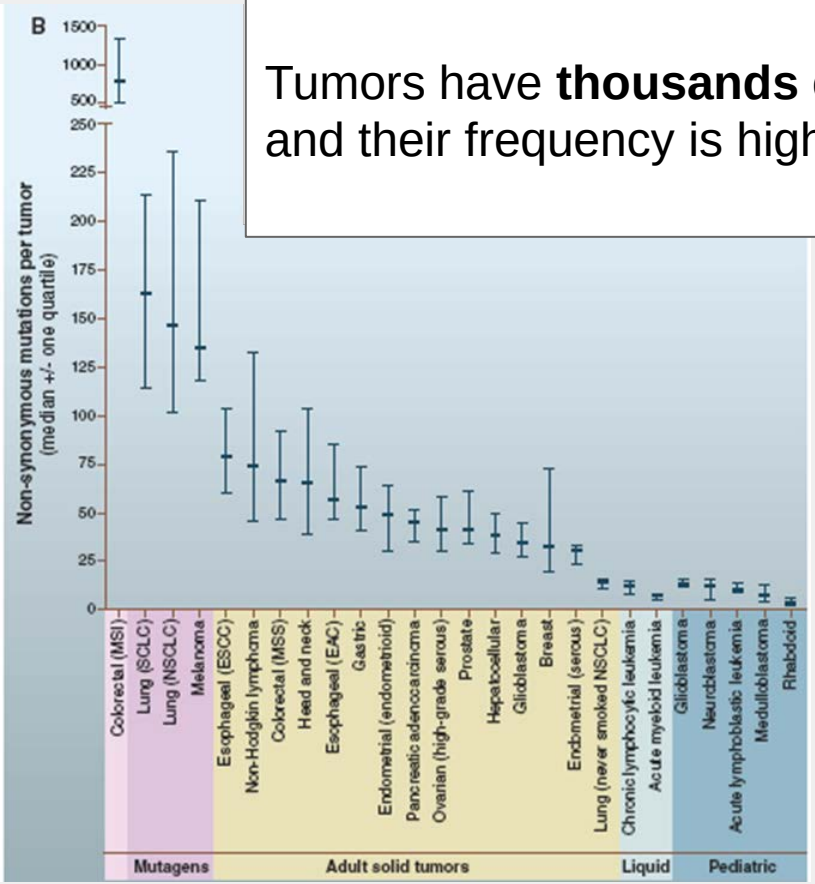
The Goal of Cancer Personalized Medicine

•To fulfill the promise of delivering the right dose for the right indication to the right patient at the right time.

•Personalized medicine uses an individual's genetic profile and individual information to guide decisions made in regard to the prevention, diagnosis, and treatment of cancer.



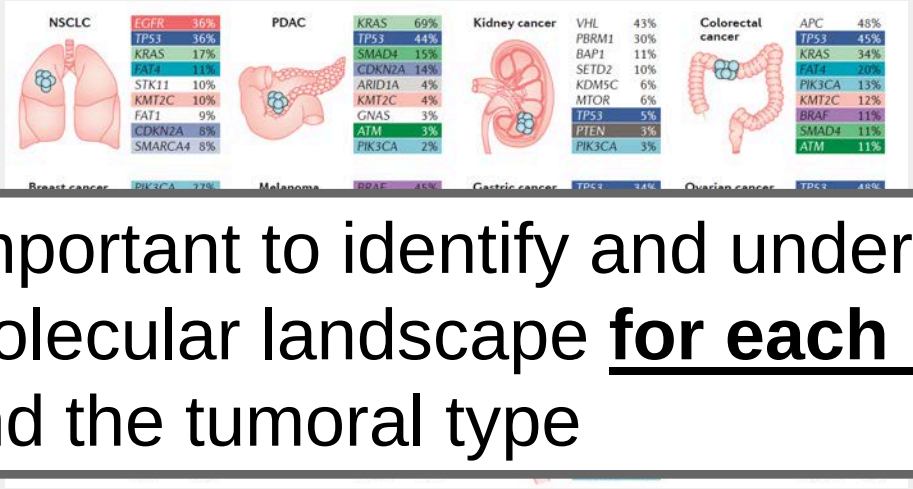
Cancer Genome Landscape



Tumors have **thousands** of molecular alterations and their frequency is highly **heterogeneous**.

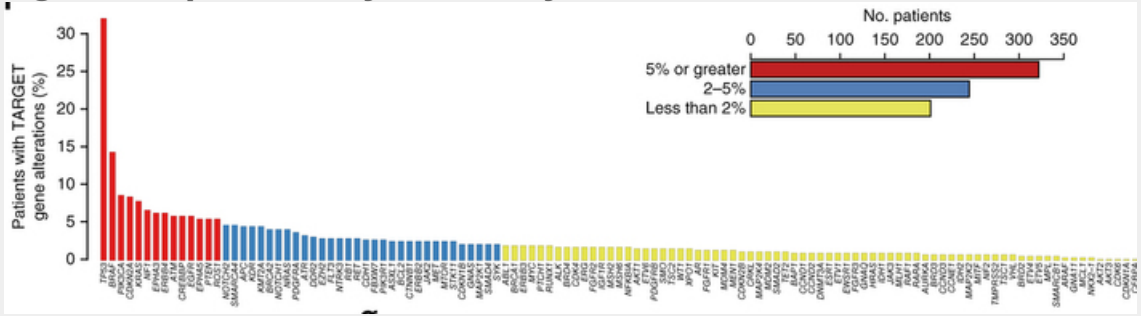
Vogelstein et al., *Science* 2013

Top genes frequently mutated in cancer



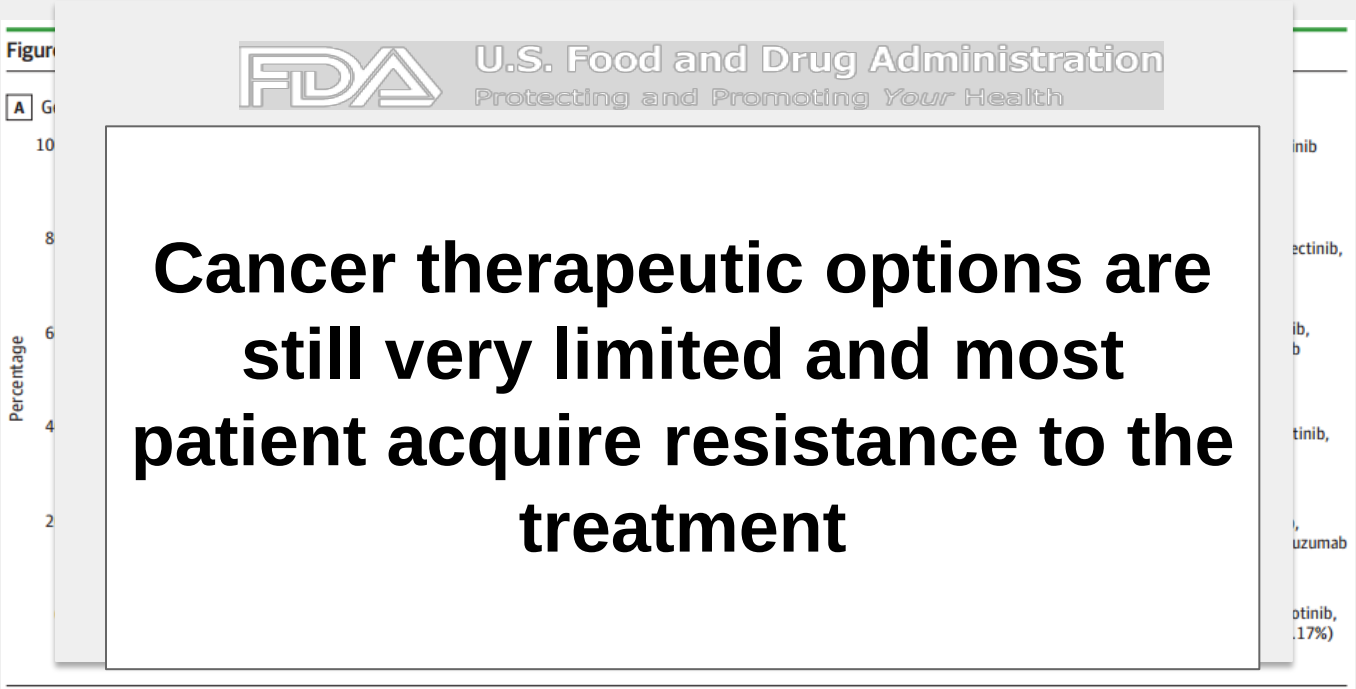
It is important to identify and understand the molecular landscape **for each patient** beyond the tumoral type

Long-tail of potentially clinically relevant alterations in cancer genes



Van Allen et al. Nat Med 2014

Genetic Biomarkers and new targeted therapies



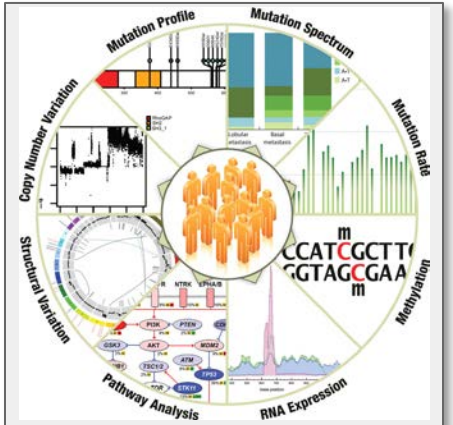
In 2006: elegible, 5.09 %
In 2018: elegible, 8,33%

In 2006: benefit, 0.70 %
In 2018: benefit, 4.90 %

Marquart J et al. **JAMA oncol**. 2018

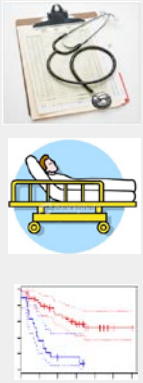
Integrative Genomics Tools Needed for Prediction and Personalized Care

Discovery of novel oncogenes, tumor suppressor genes, oncogenic pathways & Biomarkers



Patient's tumor genomic data

Experimental data
in vitro and *in vivo*
(xenografts & GEMM)



Clinical data

PubMed GEO OMIM CCLE Cancer Cell Line Encyclopedia COSMIC Genomes Catalogue of somatic mutations in cancer THE CANCER GENOME ATLAS International Cancer Genome Consortium International HapMap Project 1000 Genomes ENCODE

Literature and
Biological Databases

Bioinformatic analyses + Data warehouse/Framework

Variant prediction

Gene/protein function prediction

Pharmacogenomics: Druggable targets

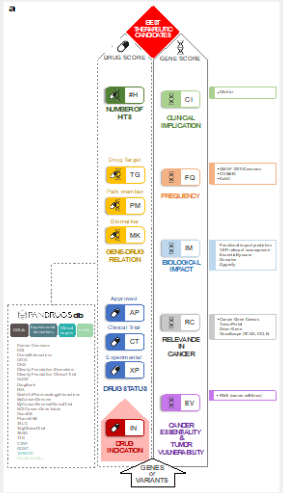
Application → Clinical interpretation → Personalized Medicine

Knowledge-driven hypothesis generation for cancer treatment
CNIO Bioinformatics Unit approach

Target: TUMOR IMMUNOCONTEXTURE

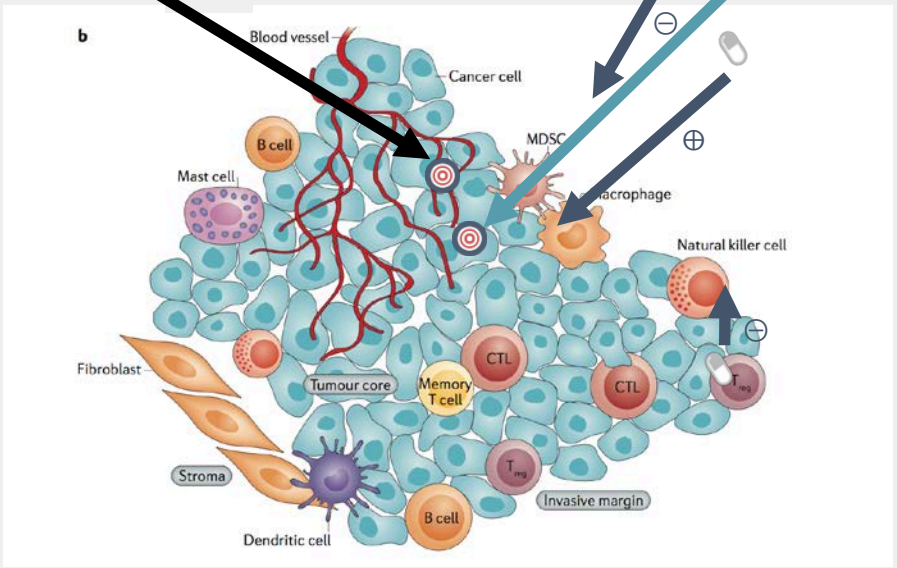
PANDRUGS

In silico prescription based on **genomic alterations**



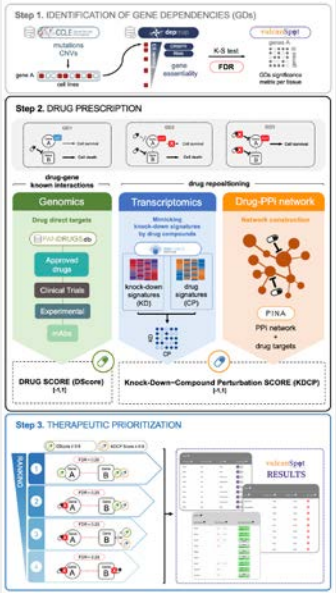
Dreimt

In silico prescription based on **immune cell populations**



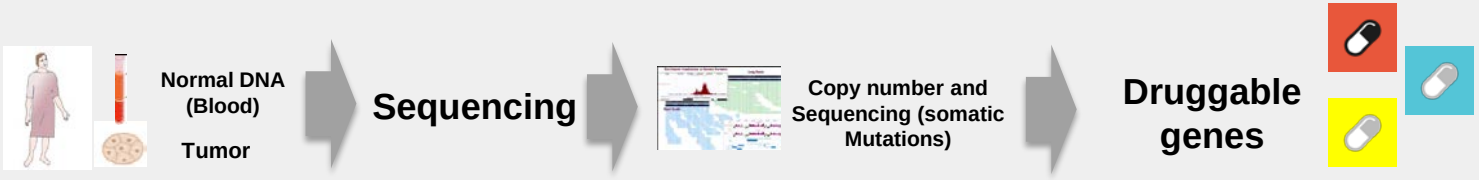
vulcanSpot

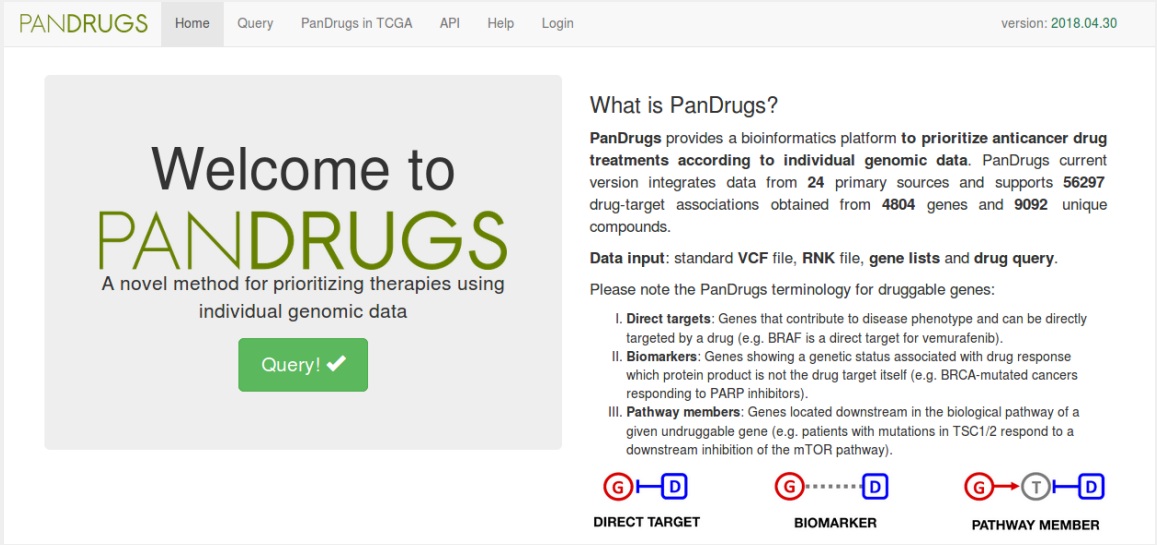
In silico prescription based on **genetic dependencies**



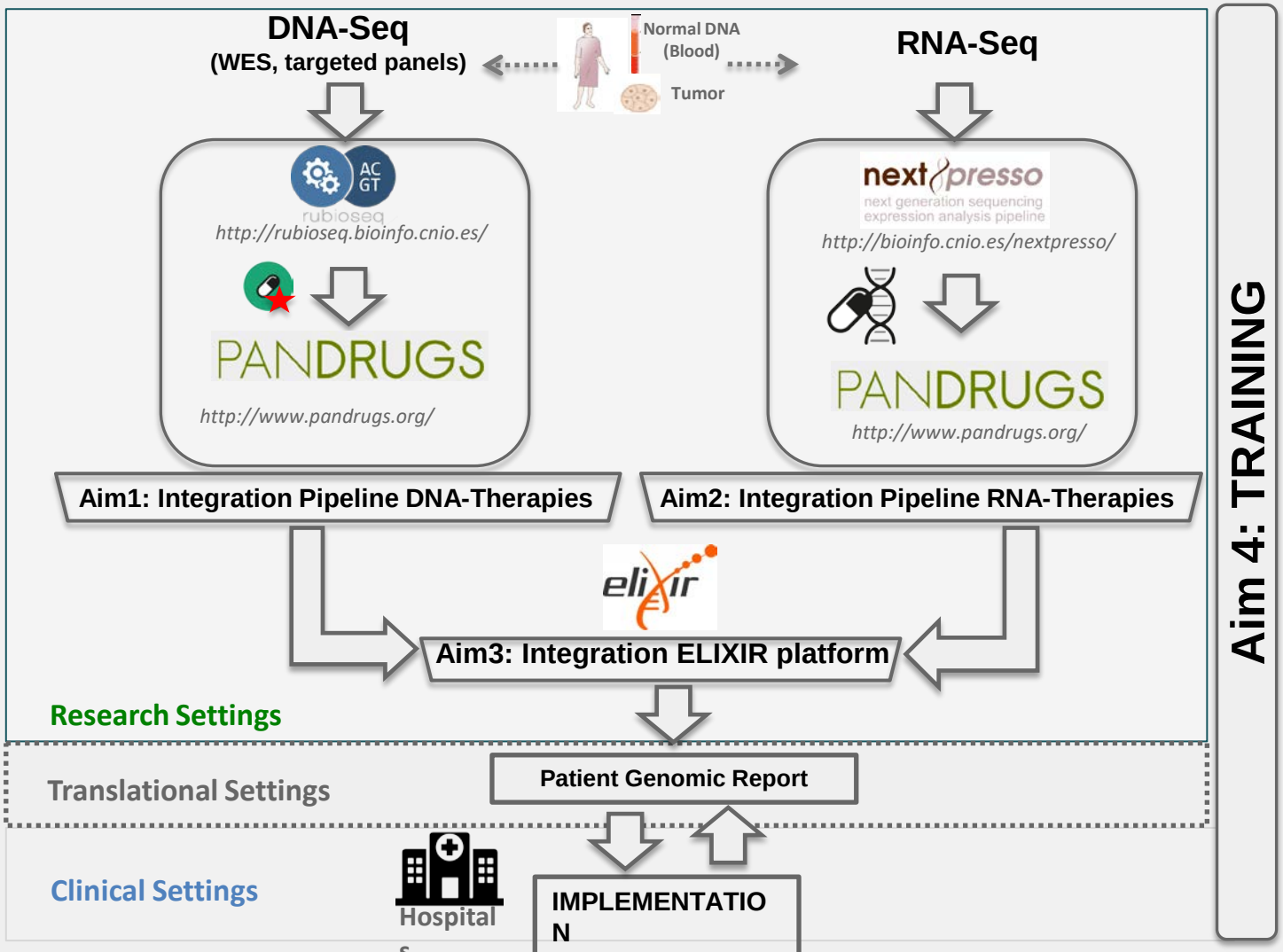
PanDrugs: in silico drug prescription http://www.pandrugs.org

A tool to guide the selection of therapiesfrom the results of genome-wide studies in cancer disease.

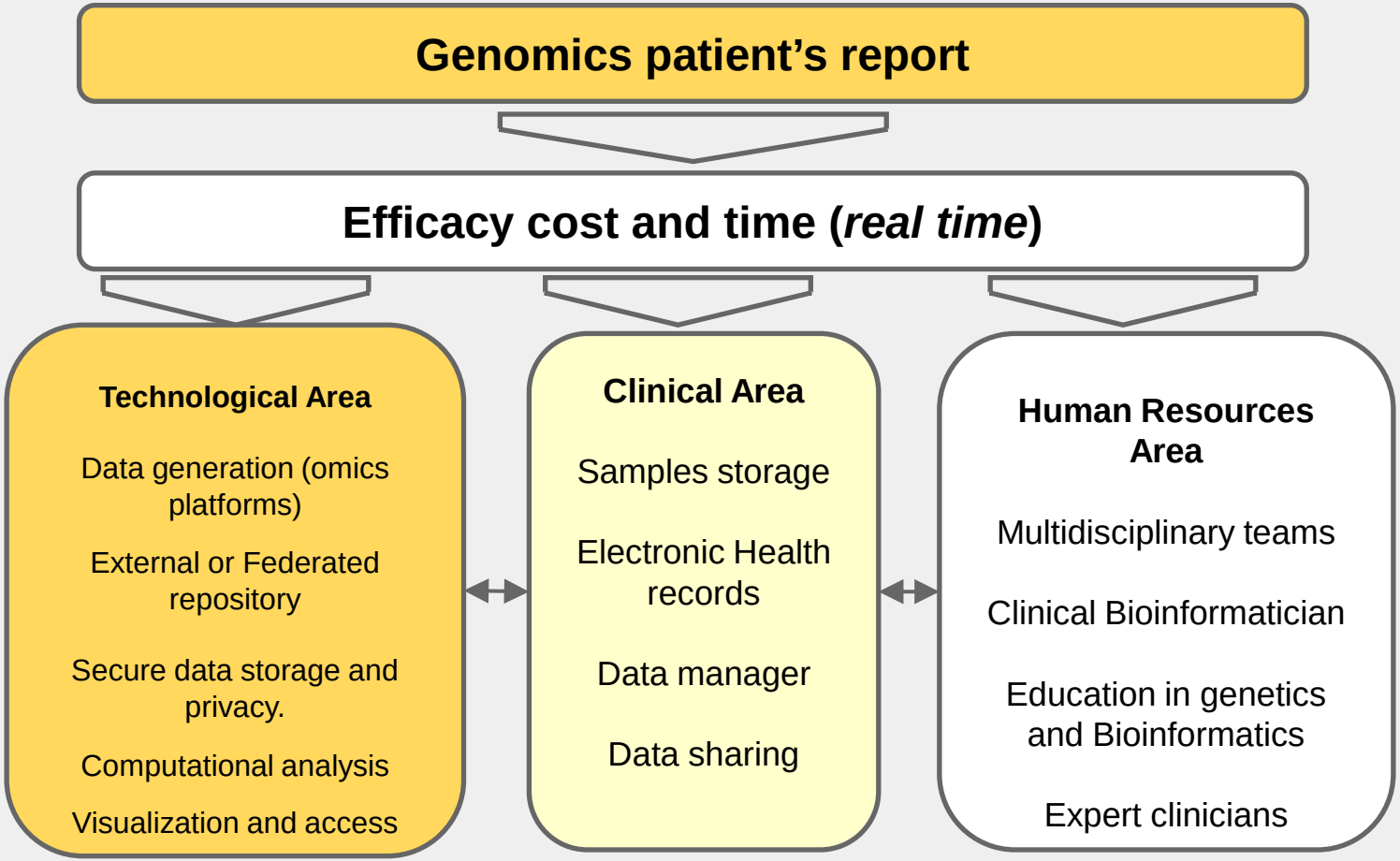




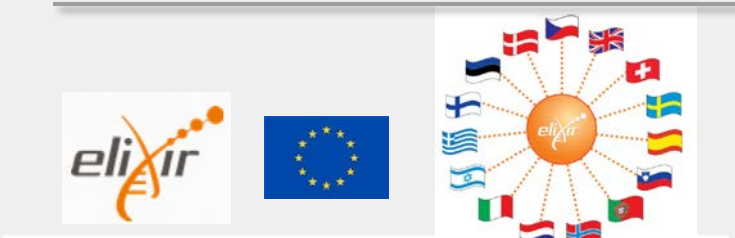
Piñeiro-Yáñez, E, Reboiro-Jato M *et al.* Genome Medicine. 2018


DNA-Seq
(WES, targeted panels)
Normal DNA
(Blood)
Tumor
RNA-Seq
rubioseq
http://rubioseq.bioinfo.cnio.es/
PANDRUGS
http://www.pandrugs.org/
nextpresso
next generation sequencing
expression analysis pipeline
http://bioinfo.cnio.es/nextpresso/
PANDRUGS
http://www.pandrugs.org/
Aim1: Integration Pipeline DNA-Therapies
Aim2: Integration Pipeline RNA-Therapies
elixir
Aim3: Integration ELIXIR platform
Research Settings
Translational Settings
Patient Genomic Report
Clinical Settings
Hospital
IMPLEMENTATIO
N
Aim 4: TRAINING

PM requires coordination across multiple stakeholders

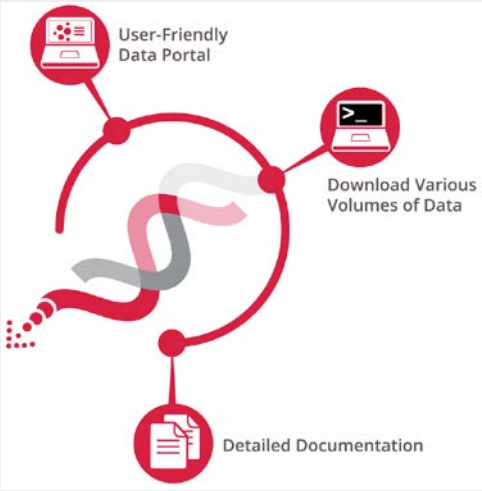


1. Infrastructure and technological area



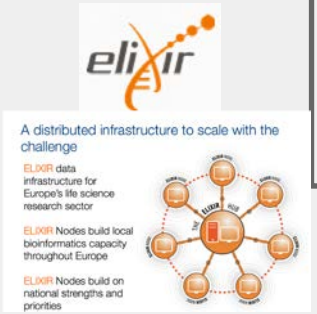
EUROPEAN GENOME-PHENOME ARCHIVE

NIH NATIONAL CANCER INSTITUTE Genomic Data Commons



https://www.elixir-europe.org/

2. Clinical Area

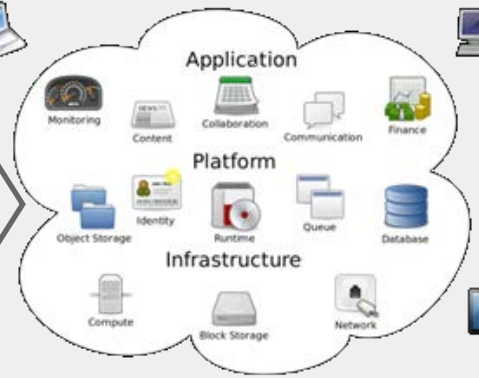


Prospective and retrospective cohorts, clinical trials, basket trials, umbrella trials, 200,000 patients in 2024

EUROPEAN GENOME-PHENOME ARCHIVE

NIH NATIONAL CANCER INSTITUTE Genomic Data Commons

- **Demographic data**
- **Enviromental factors**
- **Genomic data**
- **Clinical data**
- **Treatments**
- **Evolution**



Correlation between genomic data (biology) and disease evolution

Knowledge will come from the agregation of the diversity (diseases, ethnicities, geography, exposures, treatment…. And Sharing!

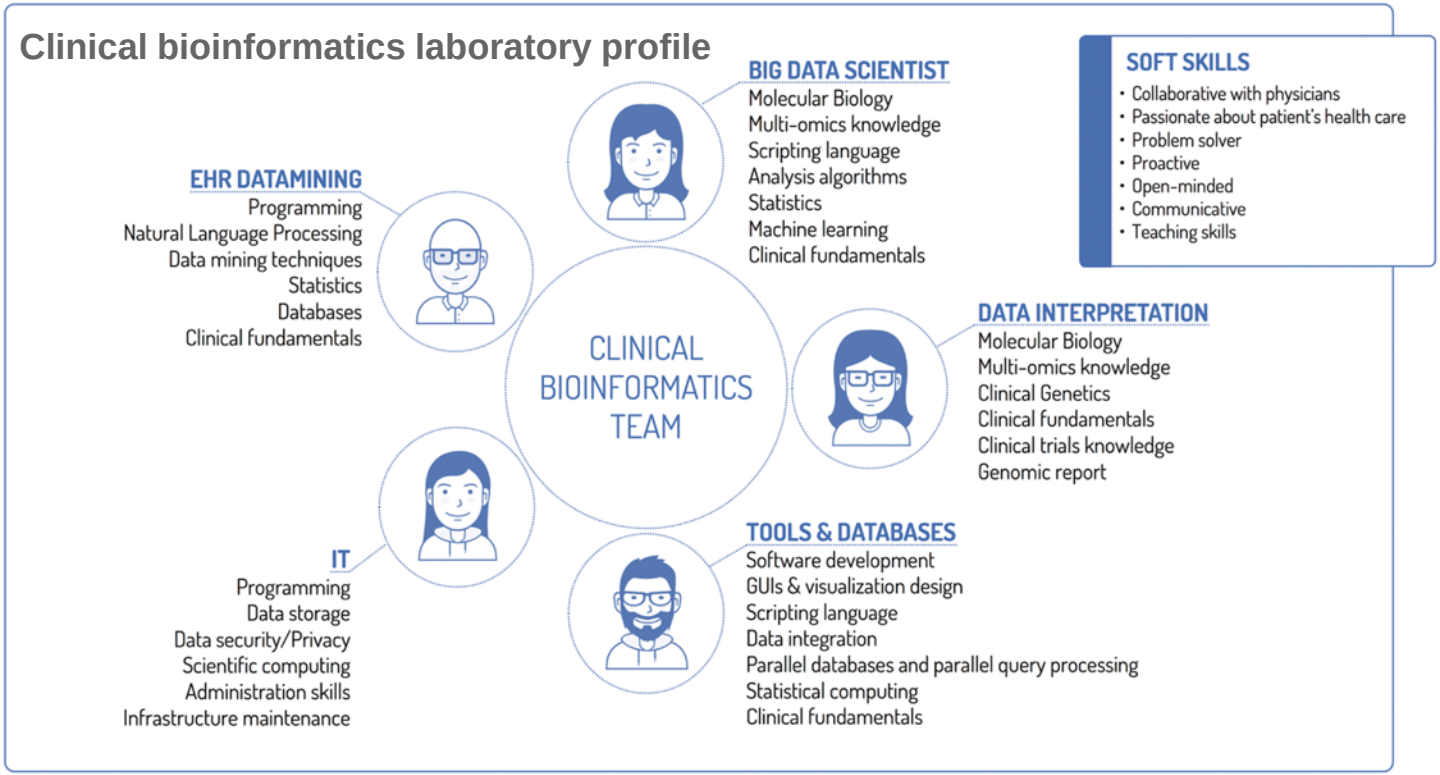
International Cancer Genome Consortium for Medicine

https://icgcmed.org/

Courtesy Fabien Calvo

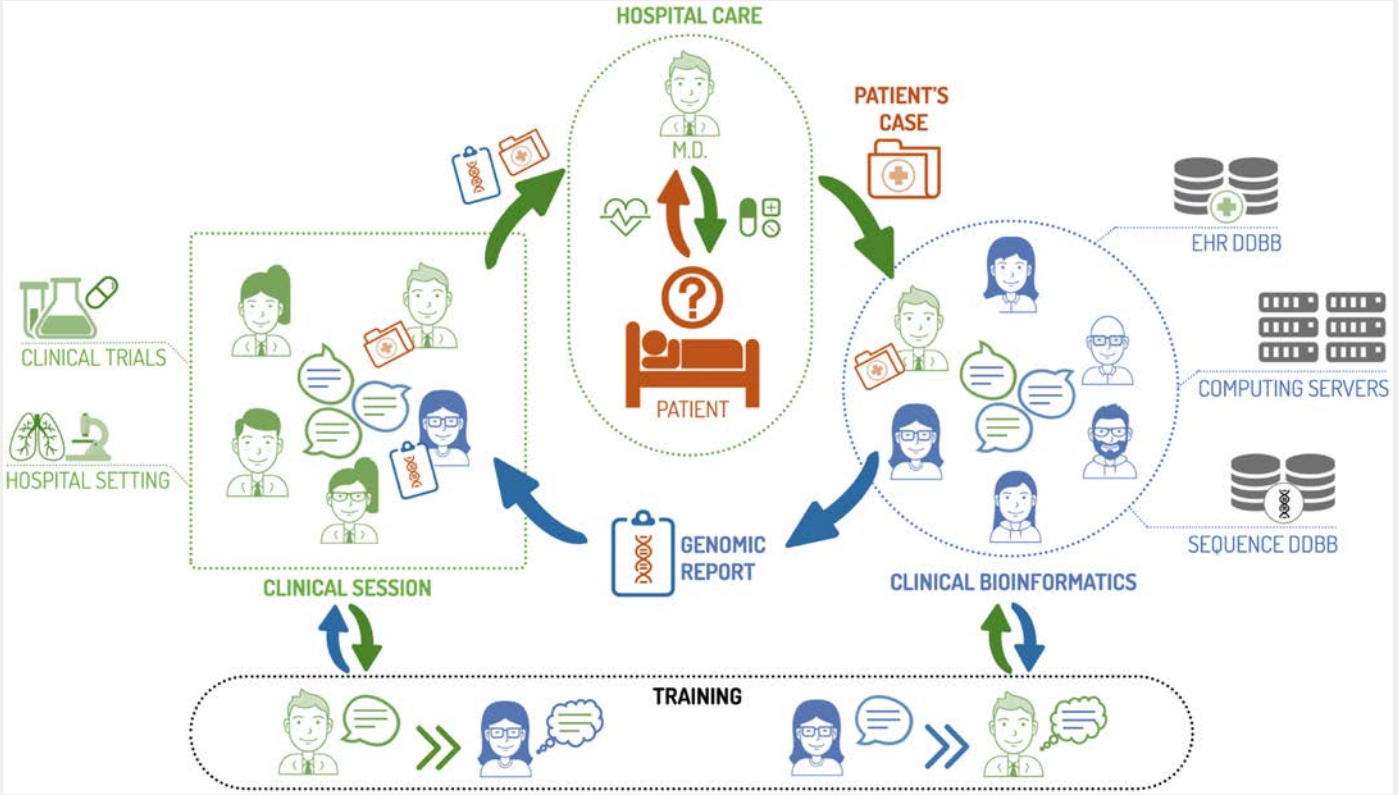
3. Human Resources Area

Clinical bioinformatics teams require multidisciplinary experts to perform regular tasks.



Gómez-López G, et al. Precision medicine needs pioneering clinical bioinformaticians. Brief Bioinform. 2017

Multidisciplinary team: Training



Bioinformatics Training

http://www.masterbioinformatica.com/

2ª edición del Máster en Bioinformática Aplicada a Medicina Personalizada y Salud (Curso 2018-2019), organizado por la Escuela Nacional de Sanidad – ISCIII. Colabora el Centro Nacional de Investigaciones Oncológicas y Barcelona Supercomputing Center.

Abierto el plazo de inscripciones Curso 2019-2020.

Programa de clases

Asignatura
GENÉTICA CLÍNICA
INTRODUCCIÓN A LA INVESTIGACIÓN CLÍNICA
HERRAMIENTAS PARA EL MANEJO DE DATOS EN SALUD
ANÁLISIS E INTERPRETACIÓN DE DATOS 'ÓMICOS'
SEMINARIOS BIOINFORMÁTICA APLICADA A MEDICINA PERSONALIZADA Y SALUD

Ayudas Acción estratégica de Salud - ISCIII
Clinical Bioinformaticians

Conclusions

- More genomic efforts should define markers to predict response and outcome (cure!) …. and prevention.

- **Clinical – Pharma actions:**
  - Genomic-driven clinical trials recruitment are needed.
  - Retrospective studies will allow the identification of new predictive biomarkers of drug response.
  - **Sharing data** (molecular and clinical) is the key.

- Guarantee the implementation of **omics platforms** in the National Health System network.

- High-performance **computing infrastructures**.

- **Training multidisciplinary teams.**

Thanks and….

Please

SUPPORT CANCER RESEARCH

ONCONET-SUDOE Workshop on Innovative IT for healthcare

"The patient journey: Information Technologies focused on the cancer patient"

3rd- 4th April, 2019

CNIO Auditorium. C/ Melchor Fernández Almagro 3, Madrid, Spain

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