Medicina Personalizada en Cáncer: Perspectiva Bioinformática

Fátima Al-Shahrour, PhD
Bioinformatics Unit - Spanish National Cancer Research Centre (CNIO)
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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**.
Long-tail of potentially clinically relevant alterations in cancer genes

It is important to identify and understand the molecular landscape **for each patient** beyond the tumoral type.
Genetic Biomarkers and new targeted therapies

Cancer therapeutic options are still very limited and most patients acquire resistance to the treatment.

In 2006: eligible, 5.09%
In 2018: eligible, 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

- Patient’s tumor genomic data
- Experimental data in vitro and in vivo (xenografts & GEMM)
- Clinical data
- 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

\textbf{PANDRUGS}

\textit{In silico} prescription based on genomic alterations

\textbf{Dreimt}

\textit{In silico} prescription based on immune cell populations

\textbf{vulcanSpot}

\textit{In silico} prescription based on genetic dependencies
PanDrugs: in silico drug prescription http://www.pandrugs.org

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

Welcome to PANDRUGS
A novel method for prioritizing therapies using individual genomic data

What is PanDrugs?
PanDrugs provides a bioinformatics platform to prioritize anticancer drug treatments according to individual genomic data. PanDrugs current version integrates data from 24 primary sources and supports 56,287 drug-target associations obtained from 4,804 genes and 9,092 unique compounds.

Data input: standard VCF file, RNAK file, gene lists and drug query.

Please note the PanDrugs terminology for druggable genes:
I. Direct targets: Genes that contribute to disease phenotype and can be directly targeted by a drug (e.g. BRAF is a direct target for vemurafenib).
II. Biomarkers: Genes showing a genetic status associated with drug response, which protein product is not the drug target itself (e.g. BRCA-mutated cancers responding to PARP inhibitors).
III. Pathway members: Genes located downstream in the biological pathway of a given undruggable gene (e.g. patients with mutations in TSC1/2 respond to a downstream inhibition of the mTOR pathway).

Aim 1: Integration Pipeline DNA-Therapies

DNA-Seq (WES, targeted panels)

RNA-Seq

Normal DNA (Blood)

Hospital

Translational Settings

Clinical Settings

Aim 2: Integration Pipeline RNA-Therapies

Aim 3: Integration ELIXIR platform

Aim 4: TRAINING

Hospital

Research Settings

Patient Genomic Report

IMPLEMENTATION

http://bioinfo.cnio.es/nextpresso/

http://rubioseq.bioinfo.cnio.es/

http://www.pandrugs.org/

http://www.pandrugs.org/
PM requires coordination across multiple stakeholders

Genomics patient’s report

Efficacy cost and time (*real time*)

**Technological Area**
- Data generation (omics platforms)
- External or Federated repository
- Secure data storage and privacy.
- Computational analysis
- Visualization and access

**Clinical Area**
- Samples storage
- Electronic Health records
- Data manager
- Data sharing

**Human Resources Area**
- Multidisciplinary teams
- Clinical Bioinformatician
- Education in genetics and Bioinformatics
- Expert clinicians

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1. Infrastructure and technological area

**ELIXIR** data infrastructure for Europe’s life science research sector

**ELIXIR** Nodes build local bioinformatics capacity throughout Europe

**ELIXIR** Nodes build on national strengths and priorities

[Visit ELIXIR website](https://www.elixir-europe.org/)
2. Clinical Area

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

- Demographic data
- Environmental factors
- Genomic data
- Clinical data
- Treatments
- Evolution

Correlation between genomic data (biology) and disease evolution

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

https://icgcmed.org/
Courtesy Fabien Calvo
Clinical bioinformatics teams require multidisciplinary experts to perform regular tasks.

Multidisciplinary team: Training
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.
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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