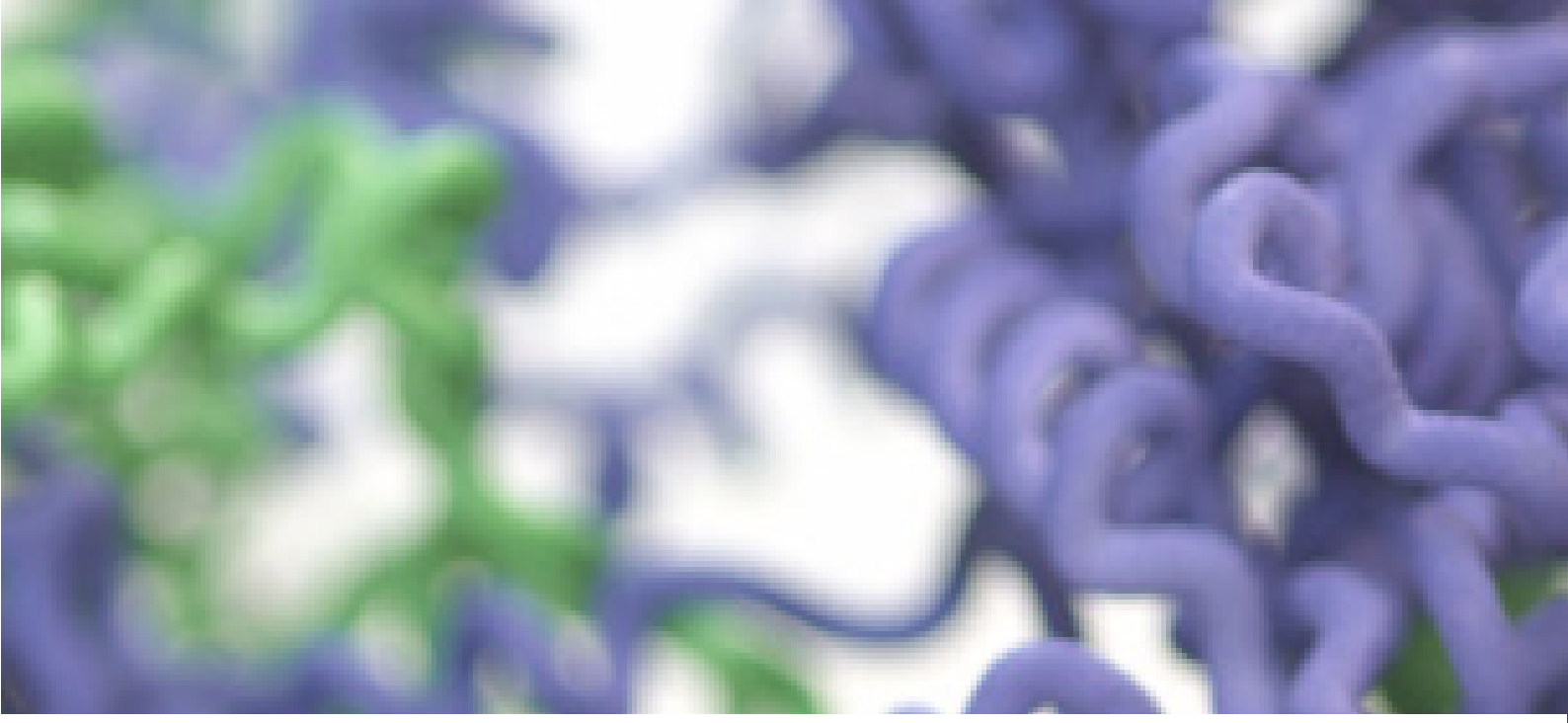


IRB BARCELONA

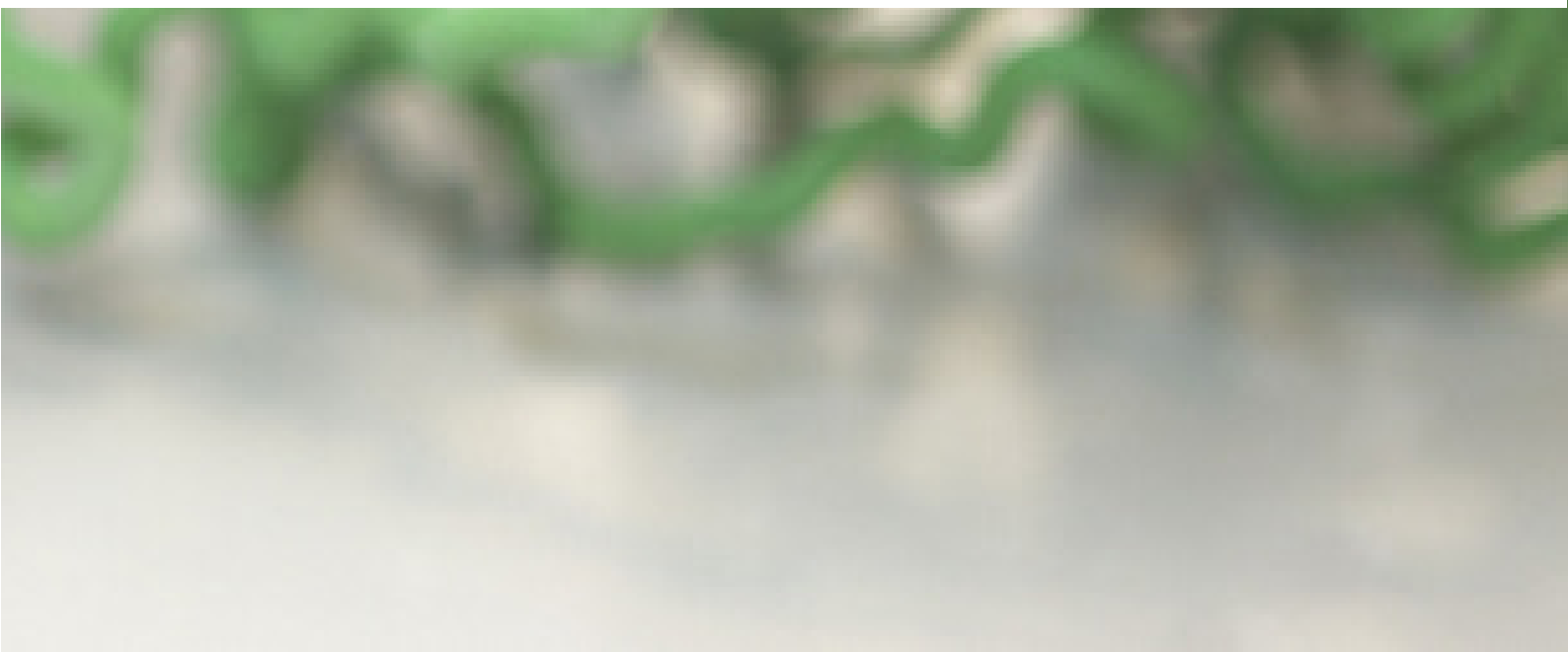
INSTITUTE FOR RESEARCH IN BIOMEDICINE

## Advancing the frontiers of biomedical research

The Institute for Research in Biomedicine (IRB Barcelona) is an independent, non for-profit research center engaged in basic and applied biomedical science. The convergence of biology, chemistry, medicine, physics and computer science at IRB Barcelona provides a unique opportunity for the translation of basic biomedical research into innovation.

# CGI

# CANCER GENOME INTERPRETER



# CGI
# Cancer Genome Interpreter

***Cancer Genome Interpreter*** **is a powerfull bioinformatics tool to assess both the biological and clinical significances of alterations in tumor genomes. By combining extensive expert curation and computational analysis, *Cancer Genome Interpreter* is of great advantage to support the rationale design and application of genomic-driven oncologic therapies.**

## TECHNOLOGY

The CGI bioinformatics tool comprehensively gathers the state-of-the-art knowledge of the biological and clinical relevance of genomic variants in cancer. For the remaining variants of unknown significance, the CGI uses an ensemble of bioinformatics methods that predict their oncogenic potential.

This unique approach combines mutation-specific metrics with the knowledge retrieved from the analysis of the sequencing data of more than 10,000 tumors across 32 cancer types. Furthermore, CGI is in constant update, which leads to more accurate results as the knowledge in the field evolves.

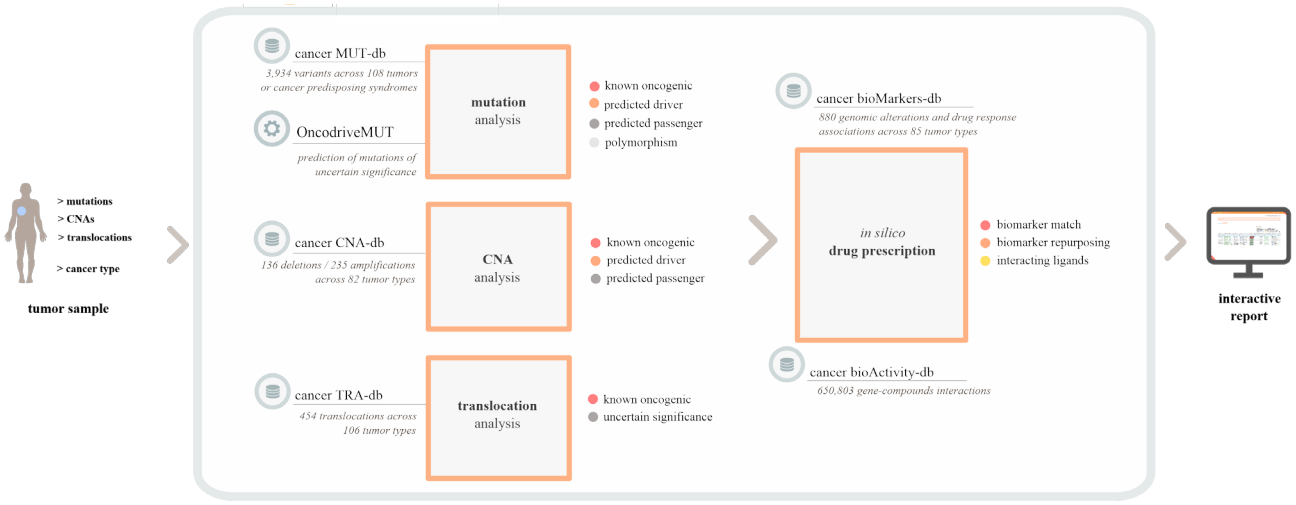
## CURRENT STAGE OF DEVELOPMENT

CGI is already registered and **available for use**. The **early-adopters includes top-tier oncology centers** that use the technology to support the allocation of patients to early clinical trials and for the identification of potential drug-repurposing opportunities.

## COMPETITIVE ADVANTAGE

CGI supports a **broad range of applications** in both research and clinical settings, such as the **identification of novel biomarkers of drug response** and the **prioritization of genome-guided clinical trials.**

The technology is **available for licensing** or **co-development** and the feasibility of novel, tailor-made applications might be assessed.




*Scheme of the Cancer Genome Interpreter.* The input is a list of genomic alterations and the cancer type of the tumor(s) to analyze. The platform firstly identifies validated oncogenic events and predicts the relevance of the remaining variants of unknown signficance by using an ensemble of bioinformatics tools . The CGI then retrieves (i) all anti-cancer therapies affected by the genetic alterations of the tumor (supported by different levels of clinical evidence) according to the state-of-the-art knowledge; and (ii) available small chemical compounds that interact with driver genes according to available bioactivity assays data. The user receives interactive reports suitable for various applications.

## RESEARCH TEAM


Prof. Núria Lopez-Bigas (IRB Barcelona / Pompeu Fabra University /ICREA)

Dr. David Tamborero (IRB Barcelona / Pompeu Fabra University)

BIOMEDICAL GENETICS


## MORE INFORMATION

**Cancer Genome Interpreter Annotates The Biological And Clinical Relevance Of Tumor Alterations**

Tamborero D, *et al.* Genome Medicine 2018, *in press*

doi: https://doi.org/10.1101/140475

## CONTACT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IRB BARCELONA
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## IN COLLABORATION WITH

upf. Universitat Pompeu Fabra Barcelona

ICREA

# A Cancer Genome Interpreter framework

> mutations
> CNAs
> translocations

> cancertype

tumor(s) input data

**annotation** of alterations

- format recognition
- remapping
- standardization

identification of putative **oncogenic events**

**mutation** analysis
- known oncogenic
- predicted driver
- predicted passenger
- polymorphism

**CNA** analysis
- known oncogenic
- predicted driver
- predicted passenger

**translocation** analysis
- known oncogenic
- uncertain significance

identification of potential **actionable events**

in silico **drug prescription**
- biomarker match
- biomarker repurposing

**ligand** exploration
- interacting ligands

### Catalog of Cancer Genes

genes **validated** or **predicted** as oncogenic in 193 tumor types

680 with mutations
170 with amplifications
93 with deletions
160 with translocations

### Catalog of Validated Oncogenic Mutations

**validated** oncogenic mutations in driver genes

2,495 somatic mutations
2,819 germline variants

### OncodriveMUT

**estimation** of the oncogenic effect of variants of uncertain significance in driver genes

### Cancer Biomarkers Database

genomic alterations influencing drug response according to distinct levels of **clinical relevance**

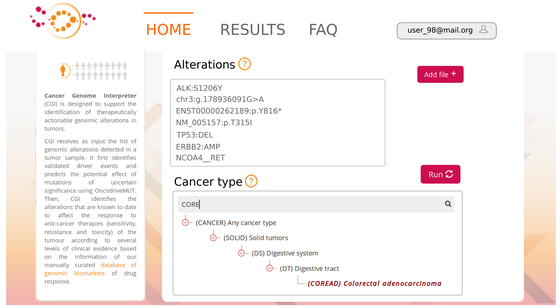
1,624 genomic biomarkers
130 drugs
310 cancer types

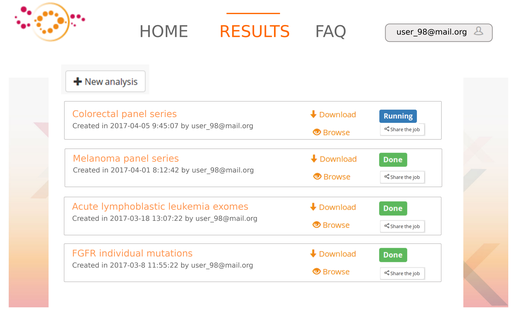
### Cancer Bioactivities Database

interactions of driver protein products with existing chemical compounds according to **binding affinity** data

20,243 protein-ligand interactions

# B Online interface




# C Alteration analysis interactive report

ALTERATIONS | PRESCRIPTIONS

Mutations | CNAs | Fusions

**Show entries with:** mutations **demonstrated** to be oncogenic; mutations **predicted** as drivers (according to OncodriveMUT); other mutations

| Sample id | Gene | Protein change | Consequence | GDNA | Domain | Exon | Tumor driver | Role | delicate dom | Pathogenicity | in cluster | Oncogenic classification |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| coread_01 | BRAF | p.V600E | Missense | chr7:g.140453136A>T | Pkinase Tyr | 15 | ✓ | OG | ✓ | High | ✓ | known in: COREAD, OV, LUAD, .. |
| coread_32 | APC | p.R1450* | Nonsense | chr5:g.112175639C>T | | 16 | ✓ | TSG | | High | | known in: COREAD |
| coread_32 | APC | p.G1120E | Missense | chr5:g.112174650G>A | | 16 | ✓ | TSG | | Medium | | known in: ST |
| coread_45 | RNF43 | p.A169T | Missense | chr17:g.56440713C>T | | 14 | ✓ | TSG | | High | ✓ | predicted driver - tier 1 |
| coread_57 | FGFR2 | p.L618M | Missense | chr10:g.123256060A>T | Pkinase Tyr | 13 | ✓ | OG | ✓ | Medium-high | | predicted driver - tier 2 |
| coread_82 | PIK3CA | p.A1020V | Missense | chr3:g.178952004C>T | | 4 | ✓ | OG | | Medium | | predicted passenger |
| coread_86 | MLL3 | p.I455M | Missense | chr7:g.151949735T>C | | 10 | ✓ | TSG | | Low | | polymorphism |

# D In silico prescription interactive report

ALTERATIONS | PRESCRIPTIONS

Biomarkers | Bioactivities

**Show entries with:** mutations described as biomarkers for the selected tumor type; mutations described as biomarkers for a different tumor type; mutations in genes described as biomarkers with a different aminoacid change; mutations in genes described as biomarkers upon other alteration types

| Sample id | Observed alteration | Drugs | Effect | Tumor type | Level of evidence | Reference | Tumor match | Biomarker match |
|---|---|---|---|---|---|---|---|---|
| coread_01 | BRAF V600E | Cetuximab, Panitumumab | Resistant | COREAD | Late trials | PMID: 20619739 PMI... | ✓ | C |
| coread_01 | BRAF V600E | Vemurafenib | No responsive | COREAD | Early trials | PMID: 26287849. | ✓ | C |
| coread_01 | BRAF V600E | Irinotecan + Cetuximab + Vemurafenib | Responsive | COREAD | Guidelines | NCNN guidelines | ✓ | C |
| coread_01 | BRAF V600E | Panitumumab + Dabrafenib + Trametinib | Responsive | COREAD | Early trials | ASCO 2015 (abstr 103...) | ✓ | C |
| coread_01 | BRAF V600E | Panitumumab + Dabrafenib + Alpelisib | Responsive | COREAD | Early trials | PMID:28363909 | ✓ | C |
| coread_32 | APC R1450* + G.. | Tankyrase inhibitor | Responsive | COREAD | Pre-clinical | PMID: 22440753 PMI... | ✓ | C |
| coread_45 | RNF43 A169T | Porcupine inhibitor | Responsive | COREAD | Case report | ENA 2015 (abstr C45...) | ✓ | C |