BIOINFORMATICS UNIT

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Head of Unit

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OVERVIEW

Bioinformatics is a key discipline for furthering our understanding of the cancer genome and for the future of cancer therapeutics. Bioinformatics-based approaches have the ability to transform the huge amount of biological data into comprehensive models that provide an in-depth understanding of cancer disease and the complex relationships among genotype and phenotype that are needed to identify cancer driver molecular alterations and new therapeutic targets.

The CNIO Bioinformatics Unit (BU) has several goals: i) to develop new computational methodologies and bioinformatics tools to enable the integration of biological and clinical data; ii) to achieve genome analysis in cancer patients' data in order to identify new biomarkers and mechanisms of drug response; iii) to provide bioinformatics support with data analysis and interpretation using computational and statistical methods; and iv) to maintain the CNIO's scientific computing facilities and provide training in bioinformatics tools and methods.

"VulcanSpot is a novel computational method used to prioritise drugs that can target cancer-specific gene dependencies, unlocking therapeutic options beyond known actionable driver genes."

Graduate Students
Laura Martínez (since February)
Guillermo Martín-Serrano, Javier Perales, Fernando Pozo (since February), Kevin Troulé

Technicians
Andrés Cañada (until July) (TS)*, Diana De La Iglesia (since April) (TS)*, Tomas Di Domenico (TS)*, Coral Fustero (TS) *, Gonzalo Gómez(TS)*, Osvaldo Graña (TS) *, Elena Piñeiro (TS)*

Titulado Superior (Advanced Degree)

RESEARCH HIGHLIGHTS

In 2018, the CNIO Bioinformatics Unit published 16 peer-reviewed articles (see full list on our web site https://bioinformatics.cnio.es/) as a result of our ongoing research projects and scientific collaborations with CNIO Research Groups and other national and international research institutions.

During this year, we developed several bioinformatics tools for *in silico* prescription of anticancer drugs: PanDrugs (https://www.pandrugs.org/) in collaboration with SING group (*Universidad de Vigo*), and VulcanSpot (http://vulcanspot.org/) for detecting and targeting cancer genetic dependencies. All our tools are freely available and have been applied in different genomic studies from our numerous scientific collaborations such as: transcriptomics analysis using our tool nextpresso (Djurec M *et al.*, 2018) or in collaboration with M. Robledo's Group from the Human Cancer Genetics Programme to study pheochromocytoma and paraganglioma (*PPGLs*) tumours. In addition, the Bioinformatics Unit has published an update of the APPRIS database (http://appris.bioinfo.cnio.es/). The principal and alternative isoforms annotated in the APPRIS database are being used to refine and extend the Ensembl/GENCODE human reference set. APPRIS annotations have now also been expanded to cover both the human and mouse proteomes in UniProtKB as well as the clinically relevant RefSeq human and mouse gene sets.

The Bioinformatics Unit, as a new node of INB/ELIXIR-ES (https://inb-elixir.es/), aims to provide the tools, infrastructure and expertise for the systematic analysis and interpretation of cancer genomes. Importantly, the Bioinformatics Unit is extensively involved in teaching activities – with an important focus on the translational bioinformatics area – to train bioinformatics users and developers. We co-organise the *Master en Bioinformática Aplicada a Medicina Personalizada y Salud* (ISCIII-ENS) as well as advanced Bioinformatics courses for sequencing analysis (visit our web page for a full list of activities). ■

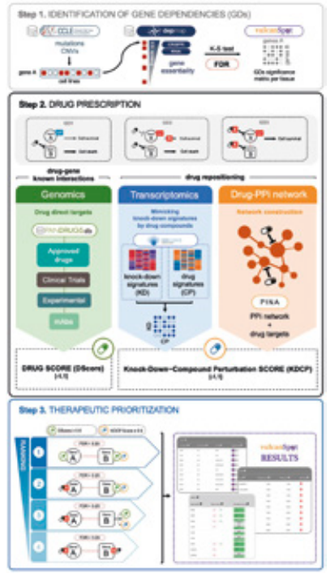

Figure VulcanSpot workflow: 1) identification of genome-wide vulnerable Gene Dependencies (GD) integrating functional genomics datasets; 2) to propose drugs to target GDs following a dual strategy; and 3) therapeutic prioritisation as a final output targeting GDs detected in the user's gene list.

SELECTED PUBLICATIONS*

- Zagorac I *et al.* (incl. Al-Shahrour F ... Quintela-Fandino M) (2018). In vivo phosphoproteomics reveals kinase activity profiles that predict treatment outcome in triple-negative breast cancer. *Nat Commun* 9, 3501.
- Rodriguez JM, Rodriguez-Rivas J, Di Domenico T, Vázquez J, Valencia A, Tress ML (2018). APPRIS 2017: principal isoforms for multiple gene sets. *Nucleic Acids Res* 46, D213-D217.
- Abascal F, Juan D, Jungreis I, Martinez L, Rigau M, Rodriguez JM, Vazquez J, Tress ML (2018). Loose ends: almost one in five human genes still have unresolved coding status. *Nucleic Acids Res* 46, 7070-7084.
- Djurec M, Graña O, Lee A, Troulé K, Espinet E, Cabras L, Navas C, Blasco MT, Martín-Díaz L, Burdiel M, Li J, Liu Z, Vallespinós M, Sanchez-Bueno F, Sprick MR, Trumpp A, Sainz B Jr., Al-Shahrour F, Rabadan R, Guerra C, Barbacid M (2018). Saa3 is a key mediator of the protumorigenic properties of cancer-associated fibroblasts in pancreatic tumors. *Proc Natl Acad Sci U S A* 115, E1147-E1156.
- Piñeiro-Yáñez E, Reboiro-Jato M, Gómez-López G, Perales-Patón J, Troulé K, Rodríguez JM, Tejero H, Shimamura T, López-Casas PP, Carretero J, Valencia A, Hidalgo M, Glez-Peña D, Al-Shahrour F (2018). PanDrugs: a novel method to prioritize anticancer drug treatments according to individual genomic data. *Genome Med* 10, 41.
- Paumard-Hernández B *et al.* (incl. Al-Shahrour F ... Benítez J) (2018). Whole exome sequencing identifies PLEC, EXO5 and DNAH7 as novel susceptibility genes in testicular cancer. *Int J Cancer* 143, 1954-1962.
- López-Nieva P *et al.* (2018). RNA-Seq reveals the existence of a CDKN1C-E2F1-TP53 axis that is altered in human T-cell lymphoblastic lymphomas. *BMC Cancer* 18, 430.

* please see BU's web site for a list of all publications.