BIOINFORMATICS UNIT

Fátima Al-Shahrour
Unit Head

Research Scientist
Michael Tress

Gradutate Students
Santiago García (PEJ, CAM)*, María José Jiménez, Laura Martínez, Fernando Pozo (until September)

Plan de Empleo Joven de la Comunidad de Madrid (Youth Employment Plan, Madrid)

OVERVIEW

Bioinformatics is a key discipline for understanding the cancer genome and for the future of cancer therapeutics. Bioinformatics-based approaches have the ability to transform the vast amount of biological data into comprehensible models that provide a deep understanding of cancer disease and the complex genotype-phenotype relationships needed to identify molecular cancer-driving alterations and novel therapeutic targets.

The CNIO Bioinformatics Unit (BU) has several objectives: (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 to identify new biomarkers and drug response mechanisms, (iii) to provide bioinformatics support with data analysis and interpretation using computational and statistical methods, (iv) to maintain the scientific computing facilities at the CNIO, and (v) to provide training in bioinformatics tools and methods.

"We develop bioinformatics methods to therapeutically characterise differentially drug-responsive tumour cell subpopulations, proposing cell-specific anticancer treatments at single-cell resolution."

Bioinformaticians
Ruth Álvarez (since Nov.) (TS)**, Daniel Cerdán (TS)**, Tomas Di Domenico (TS)**, Coral Fustero (until June) (TS)**, Gonzalo Gómez (TS)**, Osvaldo Graña (until Aug.) (TS)**, Elena Piñeiro (TS)**, Francisco J Soriano (since Oct.) (TS)**

**Titulado Superior* (Advanced Degree)

Students in Practice
Lucas Friedman (June-Dec.) (Master's in Biocomputing, *ENS-ISCIII*, Madrid, Spain), Paula Gómez (June-Aug.) (Summer Trainee, *Univ. Carlos III de Madrid*, Spain), Adel Samir Saleh (June-Aug.) (Summer Trainee, Nile University, Abuja, Nigeria), Víctor Sánchez (June-Dec.) (*ENS-ISCIII*, Madrid, Spain)

Visiting Scientist
Carlos Carretero (*Hosp. 12 de Octubre*, Madrid, Spain)

RESEARCH HIGHLIGHTS

In 2022, the Bioinformatics Unit published more than 10 peer-reviewed articles as a result of our ongoing research projects and scientific collaborations (see the full list of our activities in our website: https://bioinformatics.cnio.es/). We studied cancer cell biology, inter- and intra-tumour heterogeneity, and drug response, using single-cell and spatial transcriptomics. In particular, we reviewed current approaches for the selection of anticancer therapies based on the type of tumour heterogeneity being targeted and the type of sequencing data available (FIGURE 1, Jiménez-Santos *et al.* 2022).

During 2022, our group participated in whole-genome screenings, identifying N-glycosylations as a genetic and therapeutic vulnerability in calreticulin-mutant myeloproliferative neoplasms, thus advancing the development of clonally selective treatments for this disease (Jutzi *et al.* 2022). We also collaborated in identifying the deficiency in the FBXW7 tumour suppressor gene that leads to multi-drug resistance (Sanchez-Burgos *et al.* 2022). In addition, our laboratory released an updated version of the APPRIS database (Rodríguez *et al.* 2022), which selects principal protein isoforms according to protein structure, function features and conservation.

Beyond the above-mentioned activities, the BU is an active node of the European network ELIXIR (https://www.elixir-europe.org/), leading the ELIXIR Cancer Data Focus Group to provide the framework and expertise for the systematic analysis and interpretation of cancer genomes. BU also co-coordinates the *ISCIII* IMPaCT-Data project (https://impact-data.bsc.es/), in which our activity focuses on leading training activities and genomics data management. Our training and knowledge-transfer activities include the co-organisation of the MSc in "*Bioinformática aplicada a la medicina personalizada y la salud*" at the *ISCIII*. ■

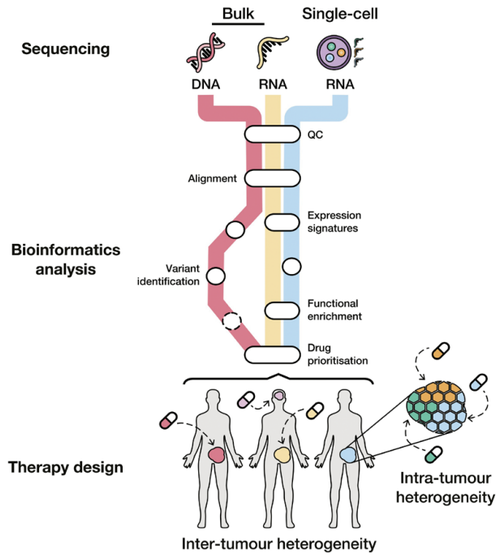

FIGURE 1 Summarised roadmap for drug prioritisation and therapy design to address inter- and intra-tumour heterogeneity using multi-omics data.

SELECTED PUBLICATIONS*

- Rodriguez JM, Pozo F, Cerdán-Vélez D, Di Domenico T, Vázquez J, Tress ML (2022). APPRIS: selecting functionally important isoforms. *Nucleic Acids Res* 50, D54-D59.
- Sanchez-Burgos L, Navarro-González B, García-Martín S, Sirozh O, Mota-Pino J, Fueyo-Marcos E, Tejero H, Antón ME, Murga M, Al-Shahrour F, Fernandez-Capetillo O (2022). Activation of the integrated stress response is a vulnerability for multidrug-resistant FBXW7-deficient cells. *EMBO Mol Med* 14, e15855.
- Jiménez-Santos MJ, García-Martín S, Fustero-Torre C, Di Domenico T, Gómez-López G, Al-Shahrour F (2022). Bioinformatics roadmap for therapy selection in cancer genomics. *Mol Oncol* 16, 3881-3908.
- Pozo F, Rodriguez JM, Martínez Gómez L, Vázquez J, Tress ML (2022). APPRIS principal isoforms and MANE Select transcripts define reference splice variants. *Bioinformatics* 38(Supplement_2), ii89-ii94.
- Sanchez-Burgos L, Gómez-López G, Al-Shahrour F, Fernandez-Capetillo O (2022). An in silico analysis identifies drugs potentially modulating the cytokine storm triggered by SARS-CoV-2 infection. *Sci Rep* 12, 1626.
- Rogado J, Pozo F, Troulé K, Sánchez-Torres JM, Romero-Laorden N, Mondejar R, Donnay O, Ballesteros A, Pacheco-Barcia V, Aspa J, Al-Shahrour F, Alfranca A, Colomer R (2022). Excess weight and anti-PD-1 immune checkpoint inhibitor's outcomes in non-small cell lung cancer. *Clin Transl Oncol* 24, 2241-2249.

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