BIOINFORMATICS UNIT

Fátima Al-Shahrour
Unit Head

Post-Doctoral Fellow
Hector Tejero

OVERVIEW

Bioinformatics is a key discipline for understanding the cancer genome and, therefore, essential 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 between genotype and phenotype that are needed to identify cancer driver molecular alterations and new therapeutic targets.

"We have developed SATIE, a tool that enables us to predict sequential treatments in cancer. SATIE can propose sensitising treatments, second-line therapies or therapeutic interventions for acquired drug resistance."

Our Unit has several goals:

- → To provide bioinformatics support with data analysis and interpretation using computational and statistical methods.
- → To achieve genome analysis in cancer patients' data in order to identify new biomarkers and mechanisms of drug response.
- → To develop new computational methodologies and bioinformatics tools for cancer research.
- → To maintain CNIO's scientific computing facilities and to provide training in bioinformatics tools and methods.

Graduate Student
Javier Perales

Technicians
Ángel Carro (TS)*, Coral Fustero (PEJ-L)**, Gonzalo Gómez (TS)*, Osvaldo Graña (TS)*, Elena Piñeiro (TS)*, Miriam Rubio (TS)*, Kevin Troulé (PEJ-L)**

**Titulado Superior* (Advanced Degree)
***Plan de Empleo Joven-Licenciado* (Youth Employment Plan-Graduate)*

RESEARCH HIGHLIGHTS

During 2016, the Bioinformatics Unit (former Head, David G. Pisano), and the Translational Bioinformatics Unit headed by Fátima Al-Shahrour from the Clinical Research Programme, were reorganised and merged into one single Bioinformatics Unit (BU). BU was established with the aim of providing resources to enable the integration of biological and clinical data, using computational biology approaches, as well as to contribute to research projects in need of bioinformatics support.

In 2016, BU published 22 peer-reviewed articles as a result of our ongoing research projects and scientific collaborations with CNIO Research Groups as well as other national and international research institutions. We developed several bioinformatics tools for the analysis of next-generation sequencing data in collaboration with the SING group from the University of Vigo – RubioSeq+ (Rubio-Camarillo *et al.*, 2017), nextpresso (Graña *et al.*, 2016) – and 2 web tools to guide the selection of therapies from genome-wide studies in cancer disease – PanDrugs (http://pandrugs.bioinfo.cnio.es) and SATIE (http://satie.bioinfo.cnio.es). RubioSeq+ has been used in several projects, such as the analysis of the lynx genome (Abascal *et al.*, 2016), and for the whole-exome sequencing analysis of patient-derived xenografts for lung cancer (Pereira *et al.*, 2016).

Regarding our scientific collaborations, we helped to unveil mechanisms of cellular reprogramming and senescence (Mosteiro *et al.*, 2016), and also to describe the role of p21 in fasting adaptation (Lopez-Guadamillas *et al.*, 2016) in collaboration with Manuel Serrano's Group (CNIO). Other bioinformatics analyses were performed together with Mariano Barbacid's Group (CNIO) (Ambrogio *et al.*, 2016); these identified DDR1/Notch inhibition as a novel therapy for KRAS-driven lung adenocarcinoma. Finally, within the context of our international collaborations with Harvard associated institutions, we have contributed to the study of leukaemia stem cells in AML (Puram et al. 2016) and the mechanisms of CALR mutations in MPN cells (Elf *et al.*, 2016). ■

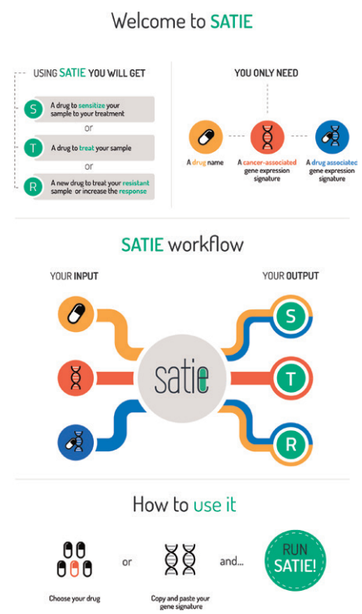

Figure SATIE-Sequential Antitumour Treatment Inference and Enrichment tool. http://satie.bioinfo.cnio.es

SELECTED PUBLICATIONS*

- Mosteiro L, Pantoja C, Alcazar N, Marión RM, Chondronasiou D, Rovira M, Fernandez-Marcos PJ, Muñoz-Martin M, Blanco-Aparicio C, Pastor J, Gómez-López G, De Martino A, Blasco MA, Abad M, Serrano M (2016). Tissue damage and senescence provide critical signals for cellular reprogramming in vivo. *Science* 354, 6315. pii: aaf4445.
- Ambrogio C, Gómez-López G, Falcone M, Vidal A, Nadal E, Crosetto N, Blasco RB, Fernández-Marcos PJ, Sánchez-Céspedes M, Ren X, Wang Z, Ding K, Hidalgo M, Serrano M, Villanueva A, Santamaría D, Barbacid M (2016). Combined inhibition of DDR1 and Notch signaling is a therapeutic strategy for KRAS-driven lung adenocarcinoma. *Nat Med* 22, 270-277.
- Puram RV *et al.* (incl. Al-Shahrour F) (2016). Core Circadian Clock Genes Regulate Leukemia Stem Cells in AML. *Cell* 165, 303-316.
- Elf S Abdelfattah NS *et al.* (incl. Al-Shahrour F) (2016). Mutant Calreticulin Requires Both Its Mutant C-terminus and the Thrombopoietin Receptor for Oncogenic Transformation. *Cancer Discov* 6,368-381.
- Montero JJ, López de Silanes I, Graña O, Blasco MA (2016). Telomeric RNAs are essential to maintain telomeres. *Nat Commun* 17, 12534.
- Pérez-Guijarro E, Karras P, Cifdaloz M, Martínez-Herranz R, Cañón E, Graña O, Horcajada-Reales C, Alonso-Curbelo D, Calvo TG, Gómez-López G, Bellora N, Riveiro-Falkenbach E, Ortiz-Romero PL, Rodríguez-Peralto JL, Maestre L, Roncador G, de Agustín Asensio JC, Goding CR, Eyras E, Megías D, Méndez R, Soengas MS (2016). Lineage-specific roles of the cytoplasmic polyadenylation factor CPEB4 in the regulation of melanoma drivers. *Nat Commun* 7, 13418.
- Abascal F *et al.* (incl. Tress ML, Valencia A) (2016). Extreme genomic erosion after recurrent demographic bottlenecks in the highly endangered Iberian lynx. *Genome Biol* 17, 251.

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