HISTOPATHOLOGY CORE UNIT

Vacant
Core Unit Head

Research Scientist
Eduardo José Caleiras

OVERVIEW

Pathology is the branch of science dedicated to the study of the structural, biochemical, and functional changes in cells, tissues, and organs that underlie disease. The Histopathology Unit offers support and expertise in a range of services from paraffin embedding and tissue sections to histochemical staining, research and diagnostic immunohistochemistry (IHC) testing, antibody validation, *in situ* hybridisation techniques (including mRNA *in situ* detection using RNAScope), and tissue microarray generation. Other value-added services offered by the Unit's highly skilled technicians include laser capture microdissection, slide digitalisation, image analysis, and quantification. The Unit also collaborates with CNIO researchers in the histopathological characterisation of animal models of disease, providing them with the necessary expert pathological advice. Finally, the Unit offers its portfolio of services to other institutions, including hospitals, research centres and private companies.

"The pathological analysis of mouse and human tissues provided by the Unit, applying a broad array of histochemical and immuno-histochemical techniques, is critical to the progress of oncology research projects run at the CNIO."

Technicians
Nuria Cabrera, María Gómez, Patricia González, Verónica Neva, Andrea Romero (PEJ)*, Zaira Vega

Student in Practice
Daniel Marban (March-June) (*Instituto Técnico de Estudios Profesionales*, Madrid, Spain)

**Plan de Empleo Joven* (Youth Employment Plan, until March)

RESEARCH HIGHLIGHTS

During 2022, the Unit significantly increased its workload compared to the previous years. Thus, about 30,000 paraffin blocks of tissue samples were generated, and nearly 25,000 histological techniques and over 22,000 immunohistochemistry techniques were delivered. This represents an increase of approximately 30% over the levels of 2021.

We also made significant progress in the digitisation of our material with about 15,400 slides, which represents approximately 54% of the stains generated. In addition, the Unit supports the CNIO Groups with the digital analysis of the images, training researchers in the use of the Zen imaging software.

Furthermore, we consolidated the application of *in situ* hybridisation technology to research projects at the CNIO, focusing on mRNA detection using RNAScope technology. As many as 402 cases were analysed, some of them with double staining, using the Ventana-Roche automated platform for IHC staining. This technique enables the detection of specific mRNAs directly in formalin-fixed, paraffin-embedded (FFPE) tissue sections, thus bringing a spatial dimension to gene expression analysis.

In 2022 the Unit was awarded a grant through the call *Ayudas a Proyectos de Colaboración Público-Privada* from the Ministry of Science and Innovation (*MCI*), for a project in collaboration with the company MedLumics and the *Universitat Pompeu Fabra*. The project focuses on the development of a system to treat auricular fibrillation using irreversible electroporation. The role of the Unit in the project focuses on the analysis of the pathological features and the mechanisms mediating cell death in the cardiac tissue upon auricular fibrillation ablation.

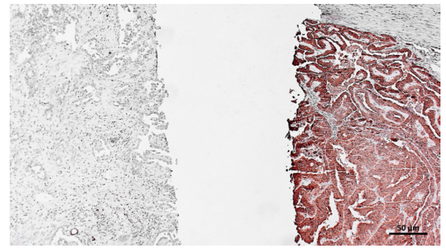

FIGURE 1 Detection of S-(2-Succinyl)-Cysteine (2SC) by immunohistochemistry in papillary carcinoma of the kidney. On the right, a case showing fumarate deficiency and the consequent accumulation of 2SC. On the left, another case of the same tumour type without fumarate deficiency. Courtesy of Cristina Rodríguez, Hereditary Endocrine Cancer Group.

The high quality of the techniques run by the Unit continues to be endorsed by External Quality Assessment Schemes. In this respect, our histochemical techniques were evaluated by UK NEQAS. Similarly, NordiQC and SEAP (*Sociedad Española de Anatomía Patológica*) evaluated a subset of our IHC techniques under different modules, including general markers, breast cancer markers, and PD-L1; these all obtained very good scores.

Training and outreach activities are also a key component of the Unit's activities. In the lab we hosted 1 vocational training student in anatomical pathology (*Formación Profesional de Grado Superior en Anatomía Patológica*) undertaking a practical module for 3 months. In addition, the Unit participated in a master's course in oncology research. ■

PUBLICATIONS

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- Mouron S *et al.* (incl. Bueno MJ, Caleiras E, Ximenénez-Embún P, Muñoz J, Gómez-López G, Fustero-Torre C, Sabroso-Lasa S, Malats N, Megias D, Malumbres M, Quintela-Fandino M) (2022). Phosphoproteomic analysis of neoadjuvant breast cancer suggests that increased sensitivity to paclitaxel is driven by CDK4 and filamin A. *Nat Commun* 13, 7529.
- González-Martínez J, Cwetsch AW, Gilabert-Juan J, Gómez J, Garaulet G, Schneider P, de Cárcer G, Mulero F, Caleiras E, Megías D, Porlan E, Malumbres M (2022). Genetic interaction between PLK1 and downstream MCPH proteins in the control of centrosome asymmetry and cell fate during neural progenitor division. *Cell Death Differ* 29, 1474-1485.
- Zhu L *et al.* (incl. Blanco-Aparicio C, Martínez S, Ortega-Paino E, Rodríguez-Perales S, Muñoz J, Caleiras E, Megías D, Quintela-Fandino M, Pastor J, Valiente M) (2022). A clinically compatible drug-screening platform based on organotypic cultures identifies vulnerabilities to prevent and treat brain metastasis. *EMBO Mol Med* 14, e14552.
- Fenor MD *et al.* (incl. Ruiz-Llorente S, Caleiras E) (2022). MEK inhibitor sensitivity in BRAF fusion-driven prostate cancer. *Clin Transl Oncol* 24, 2432-2440.
- Montero-Conde C *et al.* (incl. Currás-Freixes M, Gonzalez-Neira A, Megías D, Blasco MA, Caleiras E, Rodríguez-Perales S, Robledo M) (2022). Comprehensive molecular analysis of immortalization hallmarks in thyroid cancer reveals new prognostic markers. *Clin Transl Med* 12, e1001.