

MOLECULAR DIAGNOSTICS UNIT

Luis Lombardía
Unit Head

Technician
Diana Romero

Students in Practice
Paula Broncano and Giselle Coronel
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OVERVIEW

The Molecular Diagnostics Unit (MDU) is primarily engaged in providing support to oncologists, haematologists and pathologists of our National Health System, by offering quality molecular tests for cancer patients. In this regard, the Unit has developed a catalogue with a broad variety of sensitive and specific assays to determine changes in sequences or expression levels of crucial genes that are involved in cancer, and that help to monitor minimal residual disease in patients showing clinical remission as well as to follow-up on their response to therapy. Consequently, MDU is also committed to implementing novel diagnostic solutions, not only to improve clinical practice but also to resolve periodic inquiries from CNIO's Research Units and Groups. MDU also forms part of several international and national groups aimed at normalising and improving molecular tests in cancer. Finally,

“The ongoing accumulation and combination of actionable biomarkers included in molecular diagnostics tests is bringing us closer to precision medicine, especially for haematological tumours.”

an essential part of our mission is to contribute to academic programmes by hosting clinical post-residents and pre/post graduate students.

Inmaculada - Ríos Rosas, Madrid, Spain), Silvia Novo (September-October) (*Universidad Autónoma de Madrid, Spain*)

Visiting Scientist
Ana Jambrina (*Hospital General Universitario Gregorio Marañón, Madrid, Spain*)

CORE UNIT HIGHLIGHTS

During 2022, our catalogue grew with the addition of a new assay, which will enable the detection, through bi-directional Sanger sequencing, of structural alterations in exon 3 of the β -catenin gene, *CTNNB1*. High frequencies of *CTNNB1* activating mutations and in-frame deletions have been spotted in 3% of all cancers, including melanoma, lung, endometrium, colon, kidney, and ovarian tumours. Since they have been associated with altered sensitivity to specific drugs, their analysis can be useful as a predictive marker by suggesting different therapy options.

We also improved the clinical utility of *KRAS* gene testing by supplementing the detection of the recurrent mutations already implemented in exons 2 and 3 to exon 4. The extended assay is intended to enable clinicians to manage their patients with colorectal, pancreatic, or lung adenocarcinomas, since somatic mutations in exon 4 have been linked to a better prognosis, and they can also be used as an inclusion criterion to enrol patients in active or forthcoming clinical trials.

Additionally, in the context of our partnership with *GBMH* (*Grupo de Biología Molecular y Hematología*), we are participating in the development of comprehensive national guidelines for the management of patients with different haematological cancers. Our initial contribution was to complete a list of diagnostic, prognostic, and predictive markers that should be systematically analysed using Next Gene Sequencing (NGS) in order to manage patients with acute myeloid leukaemia (AML). To evaluate the clinical and analytical utility of this diagnostic tool, the next step will be to design a panel containing at least the markers required for the analysis, and then to establish the feasibility of using RNAseq technology to be able to analyse simultaneously both single and fusion genes (FIGURE 1).

Finally, during 2022, in the framework of our training policy, we hosted a medical resident, an undergraduate student, and 2 future technicians in anatomical pathology. ■

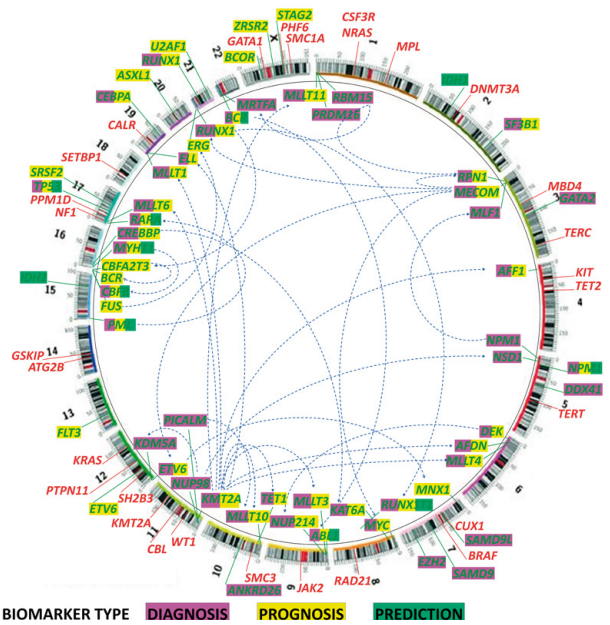


FIGURE 1 The comprehensive massive sequencing of validated markers (green), yet to be validated, are expected to complete the whole panel required for full precision medicine of AMLs, prognosis, and treatment of patients