MOLECULAR DIAGNOSTICS UNIT

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CORE UNIT HIGHLIGHTS

Extending our portfolio

During 2021, we expanded our offer of assays by adding a new one that will enable the detection of activating mutations in exons 14 and 17 of the *CSF3R* gene encoding the receptor for colony-stimulating factor 3, a cytokine that controls the production, differentiation, and function of granulocytes. Alterations in *CSF3R*, commonly found in patients with chronic neutrophilic leukaemia (CNL) or some atypical chronic myeloid leukaemia (aCML), have been reported as useful prognostic and predictive markers, since patients with altered *CSF3R* showed an aggressive course of CNL and some sensitivity to ruxolitinib, a nonselective JAK inhibitor.

We also increased the detection coverage of a test implemented more than 10 years ago. This test uses qRT-PCR to detect BCL2-IgH fusion gene variants necessary for the diagnosis of follicular lymphoma and some cases of large B-cell lymphomas, as well as to monitor for minimal residual disease after treatment. The former assay detected only 50-60% of the cases with the MBR (major breakpoint region) variant and 5-10% with the mcr (minor cluster region) variant. However, recent findings have revealed new variants that had not been previously used to evaluate patients with follicular lymphoma. As a result, with the current test, we have improved our capability to notify those patients with follicular lymphoma sharing 3'MBR or ICR variants (10-15% of) and 5'mcr (15-20%) variants (FIGURE 1).

Finally, we also started a pilot study to evaluate the feasibility of implementing a test using Next Generation Sequencing technology that will enable us to analyse the mutational status of the *IGHV* (immunoglobulin heavy chain variable region) gene; this analysis is crucial for the prognosis and response to therapy of patients with chronic lymphocytic leukaemia.

Training

During the first semester of 2021, MDU hosted 2 undergraduate students who carried out their end-of-degree projects. ∎

OVERVIEW

The activity of the Molecular Diagnostics Unit (MDU) is primarily aimed at providing an array of reliable and time/cost-efficient molecular diagnostic assays to help our National Health System's clinicians make early diagnosis, detect possible relapses, and/or monitor the response to therapy in patients with different cancers. Therefore, we devote effort to strengthening, updating and expanding the assays that are currently offered by implementing the latest tests available, or by upgrading the most established ones. Likewise, the Unit also provides support to the research needs of CNIO's Clinical Research Units and Research Groups by checking their samples for alterations in the biomarkers included in our catalogue. Furthermore, MDU collaborates with several international and national organisations focused on the standardisation and improvement of molecular diagnostics in cancer. Finally,

"During the last 15 years, MDU has supported over 300 clinicians by providing nearly 7000 specific and sensitive assays, with the aim of improving the diagnosis, prognosis, and response to therapy of more than 3000 cancer patients."

the MDU is also involved in disseminating knowledge in the field of molecular diagnostics by instructing biomedical students in our techniques and methods.
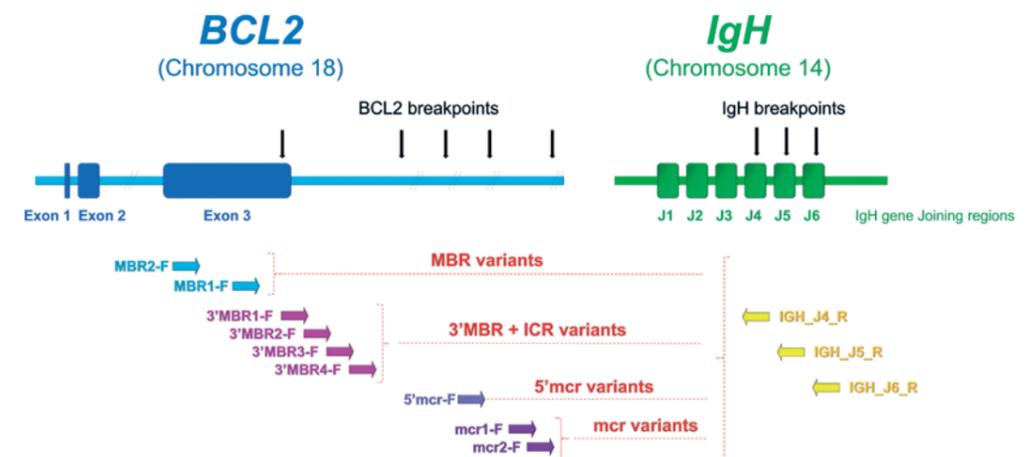

FIGURE 1 Location of primers and probes used in the new assay. Primers and probes were designed to include all known breakpoints in BCL2 and IgH sequences and thus allow us to detect the different variants of the BCL2-IgH fusion gene. MBR, major breakpoint region; mcr, minor cluster region; ICR, intermediate cluster region.