MOLECULAR DIAGNOSTICS UNIT

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OVERVIEW

The Molecular Diagnostics Unit (MDU) is mainly dedicated to developing, implementing, standardising and making available a wide variety of highly sensitive and specific molecular diagnostics assays that are scarcely available in the Hospitals of the Spanish National Health System. MDU's portfolio of genetic tests enables the determination of alterations in the sequence or expression levels of key genes involved in cancer. In turn, these assays can be used for the early diagnosis of neoplasias, the detection of minimal residual disease in patients showing clinical remission, for monitoring the response to therapy in patients, as well as for facilitating decision-making amongst different treatment options. Furthermore, 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 portfolio. Finally, MDU is very much committed to disseminating knowledge in the field of molecular diagnostics by hosting and mentoring biomedical students.

"In this transition phase of precision medicine, MDU is increasingly focused on the implementation of assays for the detection of biomarker alterations that could grant a more selective diagnosis for cancer patients."

RESEARCH HIGHLIGHTS

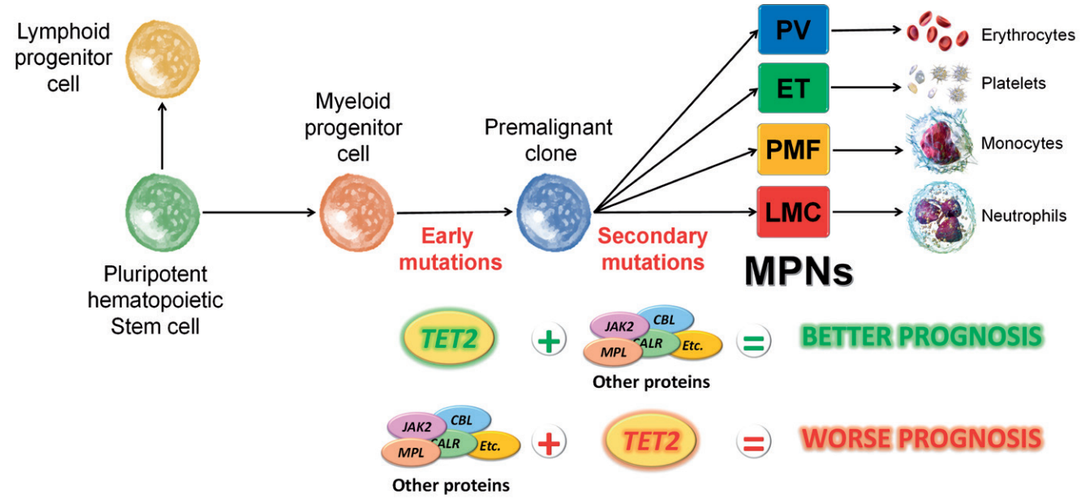

Figure The detection of mutations in *TET2* will improve the diagnostics algorithm by allowing prediction of the prognosis of patients with MPNs (MPN: myeloproliferative neoplasm; CML: chronic myeloid leukaemia; PV: polycythaemia vera; ET: essential thrombocythaemia; PMF: primary myelofibrosis).

Strengthening our support

During 2016, our catalogue has grown with the addition of a new molecular diagnostics test based on the detection, by bi-directional Sanger sequencing, of mutations in exons 4 and 5 of the *MYD88* gene. Waldenström's macroglobulinemia (WM) is a rare form of blood cancer that is characterised by an excess of malignant white blood cells (lymphoplasmacytic cells) in the bone marrow. It has been shown that WM is the result of a multistep transformation process that accumulates sequential oncogenic alterations. The most prominent is the *L265P* somatic activating mutation in the *MYD88* gene (present in 90% of WM). Hence, its detection would enable us to differentiate WM (but also diffuse large B-cell vitreoretinal lymphoma or marginal zone lymphomas) from indolent B-cell or other chronic lymphoproliferative disorders.

Additionally, because identification of several gene alterations involved in the onset of myeloproliferative neoplasms (MPNs) has revealed the huge complexity of these diseases and has challenged their accurate differential diagnosis, we started working on the implementation and validation of a new assay that will enable us to detect mutations in the *TET2* gene; this will complement the diagnosis of MPNs patients. Mutations in this tumour suppressor gene (present in 13% of MPNs) lead to genomic instability via epigenetic modifications and foster cancer progression. Recent studies have revealed that the order in which these mutations are acquired is critical. Thus, patients with early mutations in *TET2* were more likely to have better prognosis compared to patients who had previous mutations in others genes linked to MPNs (FIGURE).

Lastly, we have completed the initial experimental phase of a clinical trial sub project, FRAGANCE, led by the CNIO Gastrointestinal Cancer Clinical Research Unit, which is geared towards precision medicine for fragile patients with advanced pancreatic cancer.

Tutoring

MDU has also upheld its policy regarding training programmes in 2016 by welcoming one medical resident and one undergraduate student. ■