Recently, the field of haematology has been gaining traction in cancer research, not only for the study of critical disease affecting human health, but also for its implications in solid cancers and the applicability of haematological tools to other areas.

In terms of cancer implications, immune cells play a remarkable role in metastasis, inflammation, and immune surveillance. In fact, this concept triggered the development of the most promising cancer therapy of the 21st century, immunotherapy.

Moreover, the haematology research area has been developing cutting-edge applications such as liquid biopsy, an easy peripheral blood/plasma analysis that can anticipate the appearance of disease, or the emergence of tumour clones in relapsed patients.

The following main lines of research define our laboratory:

- Liquid biopsy, minimal residual disease, and next-generation sequencing.
- Immunotherapy: NK/T-CAR, BITES and immune checkpoints in haematological and paediatric cancers.
- Role of hnRNP K, master regulator of tumorigenesis.
- Viral infection and cancer.

“We improved our in-house deep-sequencing analysis for measurable residual disease (MRD), revealing its value in decision-making for clinical trials and as a prognosis marker.”
Next-generation sequencing of measurable residual disease in multiple myeloma by immunoglobulin repertoire analysis

Measurable residual disease (MRD) is a poor study variable in routine practice. The most common measure of MRD was developed through low cytometry, of which our laboratory has conducted previous studies in multiple myeloma (MM) and other haematological malignancies. However, preliminary next-generation sequencing data from MRD studies show an increase in sensitivity, specificity, and applicability. In 2020, we measured MRD by next-generation sequencing of immunoglobulin genes with a sensitivity of 10−6. Here we present our single-institution experience assessing MRD in 234 MM patients, both newly diagnosed (159) and relapsed (75). We describe the impact of depth, duration, and direction of response on prognosis. Those patients achieving MRD negativity at 10−6 were, as well, those with aggressive MRD with higher progression-free survival (PFS). In the MM diagnosis cohort, 40% of the patients achieved MRD negativity at 10−6 and 59% at 10−7. Median PFS in this cohort was superior in those achieving MRD at 10−6 vs 10−7 (PFS: 87 months vs 32 months, P < 0.01). In the MM relapsed cohort, 36% achieved MRD negativity at 10−6 and 47% at 10−7. Median PFS was superior for the cohort achieving MRD at 10−6 vs 10−7 (PFS: 42 months vs 17 months, P < 0.01). Serial MRD monitoring identified 3 categories of MM patients at diagnosis: (A) patients with <3 MRD 10−6 negative samples, (B) patients with detectable but continuously declining clonal numbers, and (C) patients with stable or increasing clonal number (≥10log). PFS was superior in groups A and B vs C (P < 0.01).

This work validates the importance of MRD evaluation as part of clinical care, both as an important prognostic marker at diagnosis and at relapse in multiple myeloma disease. Our data support its use as an endpoint in future clinical trials as well as for clinical decision-making. (Work published in Blood Advances).

Impact of prolonged maintenance of the immunomodulatory drug lenalidomide in multiple myeloma

Lenalidomide is an immunomodulatory drug approved for maintenance treatment in newly diagnosed multiple myeloma, and it has been shown to improve progression-free survival (PFS) and, in several studies, overall survival. Nevertheless, the impact of prolonged maintenance on lenalidomide on the kinetics of minimal residual disease (MRD) and its prognostic impact have not been studied in depth. To obtain better knowledge in this regard, we retrospectively analysed 139 patients who received lenalidomide maintenance in real-world clinical practice and whose MRD levels were observed during the treatment period by multiparametric flow cytometry or next-generation sequencing with a sensitivity of at least 10−4.

Lenalidomide maintenance correlated with an increased depth of the disease response, with 38% of patients achieving continuously declining MRD status (MRD-negative), 34.3% of patients who were MRD positive after induction treatment achieved MRD-negative status during maintenance and ultimately had improved PFS. Serial MRD assessments identified patients with progressively decreasing MRD levels who also had better PFS outcomes, compared with patients not showing a decreasing pattern of MRD. These results support the role of maintenance therapy, not only to sustain, but also to increase the depth of disease response with a PFS benefit. In addition, MRD monitoring during maintenance identifies patients with better prognosis and may help in their clinical management. (Work published in Blood Advances).