The Clinical Research Programme (CRP) has 2 main aims: 1) to translate preclinical research into novel clinical care standards; and 2) to address novel clinical oncology challenges with preclinical research. The specific areas of work include: 1) development of novel agents; 2) study of mechanisms of action of novel compounds and tackling drug resistance; and 3) moving forward in the field of biomarkers, functional taxonomy, and precision medicine. Currently, 2 functional objectives summarise the new operating model: A) generating synergies with ongoing research lines in the basic research programmes; and B) constituting a bi-directional bridge closing interactions between CNIO and tertiary cancer hospitals.

The clinical activity of the CRP’s Clinical Units takes place through agreements with tertiary hospitals: Hospital 12 de Octubre (H12O), Hospital La Paz (HLP), and Hospital de Fuenlabrada. These agreements foster the interaction between clinicians and scientists and allow scientists from all CNIO Programmes to participate in translational research studies. The number of ongoing collaborations between the Units of the CRP and CNIO Research Groups from other Programmes now involve 50 projects and 4 coordinated grants, which translate into the high translational research activity of the Centre. During the past year, 11 medical oncology residents from different Spanish hospitals completed their 3-month optional visiting stays at CNIO.

For 2023 we are pleased to mention the following research highlights. The Breast Cancer Clinical Research Unit, led by Miguel Quintela-Fandino, launched a large multi-centric, high-definition oncology project aiming to design the first cancer “Patient Digital Twin”. The H12O-CNIO Lung Cancer Clinical Research Unit, led by Luis Paz-Ares, contributed to several immunotherapy registration trials for new standards of care in lung cancer. The H12O-CNIO Haematological Malignancies Clinical Research Unit, led by Joaquín Martínez-López, developed a CAR-T therapy against multiple myeloma, a highly unmet clinical need, and made advances in the field of liquid biopsy, also in myeloma. The Molecular Diagnostics Unit, headed by Luis Lombardía, continued providing support to hospitals in the diagnosis of different malignancies, performing >500 diagnoses.

Of note, during 2023 we incorporated 2 new senior groups into the CRP: the H12O-CNIO Cancer Immunotherapy Clinical Research Unit, led by Luis Álvarez-Vallina; and the IdiPaz-CNIO Pediatric Onco-Haematology Clinical Research Unit, led by Antonio Pérez-Martínez. These 2 groups will cover 2 unmet needs at the CNIO: the development of novel cancer immunotherapy agents, and research in children’s cancers.

“The Clinical Research Programme aims to improve cancer care by developing novel agents and personalising therapeutic approaches on the basis of novel biomarkers.”
The Breast Cancer Clinical Research Unit (BCCRU) focuses on the translational interface of therapeutic development. Breast cancer is a heterogeneous disease and, thus, there are large inter-patient variations in terms of disease course, prognosis, relapse, and resistance to conventional or targeted therapeutics. Our activities are directed towards personalised treatment and range from preclinical models to correlative studies and clinical trials.

Our current research areas are to:

- Study the implications of hypoxia for immunotherapies.
- Understand the individual factors regulating response to immunotherapy in breast cancer, taking advantage of an advanced, personalised “tumouroid” platform.
- Tackle mechanisms of resistance against novel therapies in advanced breast cancer.
- Incorporate our findings into concept-driven clinical trials.
- Develop the new discipline of High-Definition Oncology.

“At the Breast Cancer Clinical Research Unit, we are focused on individualising therapy for patients with advanced breast cancer.”
In 2023, we started a new major line of research – High-Definition Oncology. Currently, precision oncology is largely based on genomics and performs poorly outside the context of matching targeted agents with oncogenic disease driving alterations. Outside this context, next-generation sequencing (NGS) panels are able to provide a solution in less than 10% of the cases. The problem is that many factors explain interpatient heterogeneity beyond genomics. These factors include, for example, the patient’s exosome (explained by factors such as diet or the environment, and translated into changes in the plasma metabolome), microbiome; plasma proteome; individual germline genetic variations that drive different pharmacodynamic or pharmacokinetic traits; co-morbidities or concurrent medications; and habits, mood or cognitive factors, among others. In addition, current medical approaches are based on single-point observations or probing at distant points in time, obtaining only snapshots of what it is in reality a disease trajectory. To take into account these factors, we launched a project consisting of longitudinal omic sampling, combined with electronic data capture from medical records and continuous physiologic monitoring via a smartphone, and habits/diet/quality of life tracking through an application built ad hoc and installed on the patients’ smartphones. The ultimate goals of this grant-supported research are to: 1) establish and understand female patients’ disease trajectories in advanced breast, lung or colorectal cancer; and 2) build a prototype of a cancer “Patient Digital Twin”.

Still in the area of precision medicine, we published a high-impact manuscript regarding the real-world impact of NGS panels outside the context of oncogenic disease. We established a set of indications according to clinical criteria for these genetic panels and compared the efficacy and personalisation of current treatment with previous studies and other situations, NGS panels are simply not ordered in other situations (green).

Another area of relevance within the field of treatment personalisation is the role of diet as an adjacent treatment in cancer management. Traditionally, cancer nutrition has focused only on cancer cachexia or other tangential aspects associated with anorexia or dysphagia. However, in recent years, robust evidence (at various preclinical and clinical levels) has been generated about how specific metabolic modulations can actually have therapeutic effect in cancer. Because of cancer mutations, tumours harbour metabolic alterations that render nutrients essential for the tumour but disposable for healthy cells; additionally, some nutrients can specifically damage the tumour and be innocuous to healthy cells. We have developed an algorithm that takes into account the tumour type, treatment type, known mutations, co-morbidities, certain microbiota parameters, and even patient dietary preferences, and that is able to deliver a unique set of dietary patterns for each patient. Through the translation of these patterns into a specific diet, we can deliver therapeutic nutrition to each patient so that efficacy is boosted and toxicity diminished. This algorithm – LUMICA V. 1.0 – was licensed to a spin-off company created at CNIO in 2023 – TNC Nutrición Terapéutica.

Finally, in the field of resistance against antiangiogenics, we completed our comprehensive model. In the past, we described how blocking SPP1 alleviates the development of hypoxia. (Single-cell RNA-seq CeDIAL analysis showing how in hypoxic conditions (right) there is increased communication through the SPP1 pathway between tumour cells and monocytes, compared with untreated tumours (left) or tumours that do not develop hypoxia (middle).)

Awards and recognition.

Creation of the CNIO Spin-off TNC Nutrición Terapéutica, Spain.
Personalised Precision Medicine Grant from the Carlos III Institute of Health (S3-01), awarded to Miguel Quintela-Fandino (CNIO). €2.5 million in funding over 3 years (2023–2025). Integrating longitudinal patient-generated data and multiple omic profiling for comprehensive precision oncology in women’s cancers. This project is led by CNIO, in partnership with 9 hospitals, 2 universities and the CRS Cancer Foundation, Spain.
AECF Project Award from the Scientific Foundation of the Spanish Association Against Cancer (AECC), Spain.
Advisory Board Member, Flagship ONLI-SU2I, Odyssey University Hospital and South Denmark University, Denmark.
Clinical Advisor, Kauffman Foundation, Spain.
OVERVIEW

The Molecular Diagnostics Unit’s (MDU) commitment to quality molecular testing, in both clinical and laboratory settings, ensures comprehensive support for cancer patient care and cancer research efforts by aligning with the growing needs of healthcare professionals and researchers. Thus, MDU plays a role in the Spanish healthcare system by offering a range of molecular diagnostic tests that aid clinicians in early cancer diagnosis, the detection of relapses, and monitoring therapy responses. These assays are constantly revised, integrating the latest diagnostic tests and upgrading the established ones. Likewise, the Unit provides support to CNIO’s Research Groups by analysing their samples for specific biomarker alterations or by providing specialised technical assistance. MDU is at the forefront of molecular diagnostics standardisation, collaborating with international and national organisations. Finally, through laboratory training, the Unit coaches biomedical students, technicians, and residents.

“IVDR implementation will improve the accuracy, reliability and efficiency of cancer diagnostics testing, thus ensuring improved patient care.” (FIGURE 1)

During 2023, our catalogue grew with the addition of a new assay. This assay will enable the detection, through direct sequencing, of p.C515S substitution in exon 15 of the BTK (Bruton tyrosine kinase) gene that mediates resistance to a BTK inhibitor, ibrutinib, by affecting its covalent binding to BTK. As a result, the detection of this mutation will help haematologists to switch the treatment of patients with chronic lymphocytic leukaemia by using second line non-covalent BTK inhibitors.

We have also improved the clinical utility of 2 assays listed in our catalogue. Firstly, to amend the diagnosis, prognosis and/or personalised therapy of cancer patients, especially those with acute myeloid leukaemia, we have extended the mutation detection scope in the TP53 gene - previously limited to exons 5, 6, 7 and 8 - to its whole sequence. Likewise, the detection of recurrent mutations already done in exons 9, 11, 13 and 17 of the KIT gene has been extended to exon 18. This upgrade will allow oncologists to offer new therapeutic options to their patients with gynaecological melanomas that harbour mutations in the KIT gene, not previously detected in cutaneous melanomas.

Additionally, last summer, aiming to replace the existing European In Vitro Diagnostic Directive (IVDD), we launched a key development that will lead us to implement a new In Vitro Diagnostic Regulation (IVDR) that is mandatory for all CNIO’s diagnostics support units in the midterm (FIGURE 1). To comply with IVDR requirements, our efforts address the upgrading and validation of the current assays to guarantee their safety and their analytical and clinical performance. With the aid of experts in Quality Management Systems, we are already beginning to establish robust quality control and assurance procedures, as well as documentation schemes that will warrant firm compliance with IVDR guidelines.

Finally, during 2023, in the framework of our training policy, we hosted an undergraduate student in biomedical engineering.
Immune evasion is a critical step in cancer progression in which tumour cells modulate the host immune system to evade destruction. Our Unit focuses on understanding the molecular and cellular mechanisms of cancer immune evasion to develop more effective and safer cancer immunotherapies. The Cancer Immunotherapy Clinical Research Unit has several areas of interest:

- Reactivation of tumour-specific endogenous T cell repertoires through the design of multi-specific antibodies against a combination of immunomodulatory targets. Preclinical and early clinical data show that this is a promising approach to enhance the clinical benefit of conventional checkpoint blockers.

- Generation of tumour reactive “artificial” T cell effectors by redirecting T cell activity towards cancer cells, targeting tumour-associated antigens (TAAa) with bispecific T cell-engaging (TCE) antibodies and/or membrane-anchored chimeric receptors (chimeric antigen receptors and/or chimeric costimulatory receptors).

- Development of multi-target approaches that simultaneously recognise extracellular and intracellular tumour antigens.

- Rational design of mRNA-based therapeutics.

- Provision of personalised cancer treatments by bringing new immuno-oncology drugs and adoptive cell therapies to the clinic.

“At the Cancer Immunotherapy Clinical Research Unit, we aim to develop immunotherapies that synergistically stimulate T cell immunity against cancer.”
**STAB-T cancer immunotherapy**

The "STAB-T strategy" is a novel adoptive cell therapy (ACT) developed by our Unit, based on the in vivo secretion of TCE Antibodies (STAB) by T cells (FIGURE 1). The secreted TCE antibodies redirect T cells against cancer cells expressing a predefined TAA. STAB-T cells offer several potential advantages over current T cell redirection strategies (FIGURE 1): in vivo endogenous secretion could result in effective concentrations of TCEs, and T cell recruitment is not restricted to engineered T cells, as in the case of CAR-T cell approaches. Polyclonal recruitment by TCEs of both engineered and unmodified bystander T cells, present in the tumour microenvironment, could lead to a significant boost in antitumour T cell responses (FIGURE 1). In 2023, we confirmed the remarkable therapeutic impact of single-targeted STAB-T cells in haematological cancers, B cell leukaemia, T cell leukaemia and multiple myeloma (Diez-Alonso L, Álvarez-Vallina L. Sci TransMed, in press), and showed that dual-targeted STAB-T Therapies (FIGURE 1) have superior control of leukaemia progression than dual-targeted CAR-T cells. We also showed that TCE-secreting tumour-infiltrating lymphocytes (STAB-TLs), but not conventional TIL, induce responses in solid tumours (non-small cell lung cancer) when administered intratumorally and systemically.

**Dendritic cell-mediated cross-priming by bispecific antibodies**

Dendritic cells (DCs) are professional antigen-presenting cells that play a central role in the induction of antigen-specific adaptive immune responses. DC natural killer (NK) group 2d receptors (DNKRs) are C-type lectin receptors (CLRs) selectively expressed at high levels by mouse CD1d+ and CD83+ DCs, and by their human equivalents. In this DC subset, defined as conventional type 1 DCs (cDC1s), DNKRs promote cross-priming of cytotoxic CD8+ T cell responses by diverting of necrotic cell cargo into a recycling endosomal compartment, resulting in preferential major histocompatibility complex (MHC) class I cross-presentation to CTLs. Our group developed a bispecific anti-RRB-x anti-DNGR-1 antibody (FIGURE 1) to target neutralised SARS-CoV-2 virions to CD1c+ and promote T cell cross-priming. Therapeutic administration of the bispecific antibody protected transgenic K18-hACE2 mice from lethal SARS-CoV-2 infection (Lázaro-Gorines R, Álvarez-Vallina L. (2023). Translational Research). This dual modulatory approach could lead to the unleashing and boosting of immune responses against tumours and protective immunity (Rubio-Pérez L, Álvarez-Vallina L. Oncosciomunology, 2023) (FIGURE 2b).

**Early clinical trials**

Our Unit, in collaboration with the Haematology and Medical Oncology Departments of the Hospital Universitario 12 de Octubre, has launched 2 independent clinical trials funded by the Carlos III Health Institute: a phase I, first-in-human clinical trial to evaluate the safety of STAB-T99 cells (genetically modified autologous T lymphocytes secreting CD19xCD30 bispecific antibodies) for B cell malignancies; and a phase I, first-in-human clinical trial to evaluate the safety of intratumoral administration of PIl2-specific Chimeric Antigen Receptor (CAR)-engineered T cells for progressive high-grade gliomas. A Phase I trial of a novel bispecific immunomodulating antibody for patients with EGFR-overexpressing cancer is also underway.

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**PUBLICATIONS**

**OVERVIEW**

Lung cancer remains the most frequent cause of cancer-related deaths worldwide. Our Unit focuses on the study of lung cancer, with a pragmatic orientation, always aiming to solve the problems of lung cancer patients. We specifically focus on 2 research areas: the identification of novel molecular biomarkers for diagnostic, prognostic, and predictive purposes; and the development of novel treatment strategies, including targeted therapies and immunotherapeutics. For example, we have contributed to elucidating the molecular determinants of EGFR or FGFR oncogenicity and have discovered biomarkers that may guide the efficacy of inhibitors of those receptors in lung cancer. We have continued developing an extensive platform of patient-derived xenografts (PDXs) and organoids (PDOs) of non-small-cell and small cell lung cancers to evaluate emerging therapeutic strategies. Finally, our Unit has extensive experience in taking new drugs (pemetrexed, erlotinib, nivolumab, tarlatamab and many others) to the clinic, as well as in conducting practice-changing trials in the fields of personalised cancer care and immuno-oncology.

“We have provided proof of concept that T cell engagers (TCEs) provide an efficacious strategy, at the cost of reasonable side effects, in cold solid tumours such as SCLC, including those lacking canonical T cell activation through antigen presentation (JCO 2023; NEJM 2023).”
Tarlatam showed promising antitumour activity in patients with small cell lung cancer (SCLC).

Two early trials led by our group demonstrated the efficacy of tarlatam, a bispecific T-cell engager targeting DLL3 and CD3, in patients with SCLC. In the first-in-human (FIH) clinical trial, 107 patients treated with tarlatam revealed a 23.4% objective response rate, a median response duration of 12.3 months and median survival of 13.2 months, with encouraging safety outcomes, despite treatment-related adverse events in 67%, mainly cytokine release syndrome (32%). In the second phase 2 clinical trial, involving 220 patients with previously treated SCLC, the administration of tarlatam at dosages of 10 mg or 100 mg every 2 weeks demonstrated antitumour activity with durable responses, showing 40% and 32% objective response rates, respectively. Median progression-free survival was 4.9 months and 3.9 months, with estimated 9-month overall survival rates of 68% and 66%, respectively. Cytokine-release syndrome was the most common adverse event, but a low percentage of patients discontinued treatment due to adverse events in both arms. These findings underscored tarlatam’s potential in preclinical SCLC, warranting further evaluation.

Efficacy of sotorasib compared to docetaxel for the treatment of non-small cell lung cancer (NSCLC).

In this clinical trial, we evaluated the efficacy and safety of sotorasib compared to docetaxel in the treatment of NSCLC with KRAS<sup>G12C</sup> mutation. Patients treated with sotorasib showed significant improvement in progression-free survival (HR 0.65) and overall response rate compared to patients receiving docetaxel, in addition, sotorasib-treated patients presented better toxicity profiles, providing better quality of life. As a result of this observation, the EMA recently approved the therapeutic use of tarlatam in pretreated patients with NSCLC harboring underlying KRAS<sup>G12C</sup> mutations.

ONCOS-102 combined with pembrolizumab and platinum chemotherapy for the treatment of malignant pleural mesothelioma (MPM).

In this early clinical trial, we showed the synergistic effect of combining a new immunotherapy agent, ONCOS-102 (an oncolytic adenovirus), with the conventional platinum chemotherapy regimen for the treatment of MPM. We evaluated both the clinical outcome of patients plus the impact of the novel strategy on the tumour microenvironment. The treatment resulted in a relevant median overall survival (up to 30 months), and the results were particularly promising in chemotherapy-naïve patients. We observed increased T-cell infiltration in ONCOS-102-treated patients, and differences in the transcriptome of several genes, including those associated with complement activation, humoral immune response, and regulation of acute inflammatory response. The results might shed light on new ways to tackle this very challenging disease.

**PUBLICATIONS**

The Haematological Malignancies Clinical Research Unit focuses on the identification of new molecular biomarkers and drivers of diseases and the development of novel therapeutic approaches. Moreover, we are developing novel strategies and cutting-edge technology tools to better characterise and monitor minimal residual disease to anticipate cancer outcomes. We have contributed to elucidating the molecular determinants of critical molecular processes in haematological malignancies such as splicing, ribosome biogenesis, nucleolus biology, and mechanoreception.

In the Haematological Malignancies Clinical Research Unit at CNIO we investigate:

- **Splicing**: Traditional haematological neoplasms (leukaemia, myeloma, lymphoma): new diagnostic approaches, biomarkers, and treatments.
- **Nucleolus biology and ribosome biogenesis**: Novel drivers of haematological malignancies such as bone marrow failures.
- **Mechanoreception**: Novel drivers of haematological neoplasms.
- **Ultra-deep sequencing**: Minimal residual disease (MRD) monitoring (LiqBio-MRD).
- **Immunotherapy**: NK-CARs, BITES, T-CARs and immune checkpoints inhibitors.

"Our results establish that RNA splicing inhibition, alone or combined with venetoclax, could be useful for the treatment of newly diagnosed or relapsed/refractory AML."
Post-translation splicing modifications play key roles in cellular metabolism and disease. They have been identified as key mechanisms in cytoskeleton resistance in acute myeloid leukemia (AML).

Despite the approval of several drugs for AML, cytoskeleton resistance is still widely used as a therapeutic approach. However, 85% of patients show resistance and only 10% overcome the disease. Using RNA-seq and phosphoproteomics, we show that RNA splicing and serine-arginine-rich (SR) protein phosphorylation were altered during cytoskeleton resistance. Moreover, phosphorylation of SR proteins at diagnosis was significantly lower in responders than in non-responders, pointing to their utility to predict response. These changes correlated with altered transcriptomic profiles of SR protein target genes. Notably, splicing inhibitors were therapeutically effective in treating sensitive and AML cells as monotherapy or in combination with other approved drugs. The E1BE-8800 and venetoclax combination showed the best efficacy in vitro, demonstrating synergistic effects in patient samples and no toxicity in healthy hematopoietic progenitors. Our results establish that RNA splicing inhibition, alone or combined with venetoclax, could be useful for the treatment of newly diagnosed or relapsed/refractory AML.

Real-life disease monitoring in follicular lymphoma patients using liquid biopsy ultra-deep sequencing and PET/CT

In this study, we screened 84 patients with follicular lymphoma (FL) for somatic mutations suitable as liquid biopsy MRD biomarkers using a targeted next-generation sequencing (NGS) panel. We found trackable mutations in 95% of the lymph node samples and 80% of the liquid biopsy baseline samples. We then used an ultra-deep sequencing approach with 2x10^9 sensitivity (LiqBio-MRD) to track those mutations on 151 follow-up liquid biopsy samples from 54 treated patients. The results demonstrated that LiqBio-MRD is a robust and non-invasive approach, complementary to metabolic imaging, for identifying patients with FL at high risk of having their treatment fail, and should be considered in future response-adapted clinical trials.

**Publications**


**Awards and Recognition**

- José Martínez-López: SanzCar Research Grant, IN2020, Spain.
- Laura Jerez and José Martínez-López (coordinators): ALMA Research Project, ISCIII-CI20, Spain.
- Santiago Barriga: Miguel Servet Research Contract, Spain.
- Ricardo Sánchez: Juan Pedió Grant, Spain.
- Pablo Blanco: Pre-doctoral Fellowship, Talavera Pino de Guzman and Buero Foundation, Spain.
- Maria Llanos: Scientific Image (Avances de la Ciencia) and Article of the Month, Spanish Society for Biochemistry and Molecular Biology. Best Presentation Award, XV Congreso de Investigación Estadística Gredos Ciencias de la Salud. XIV Congreso de Ciencias Veterinaria y Biomedicina, Spain.
- Laura Córdoba: Fullbright Pre-doctoral Research Grant.
- Jessica Encinas: Young Investigator Award, XI International Myeloma Workshop, Athens, Greece.
**OVERVIEW**

The Pediatric Onco-Hematology Clinical Research Unit, headed by Antonio Pérez-Martínez, comprises a multidisciplinary team of physicians, geneticists, biologists, biochemists, and bioinformaticians, who, for the past decade, have carried out projects ranging from knowledge generation to direct clinical application through the development of clinical trials. Our research, which is mostly funded by the Fundación Cris Contra el Cáncer, is largely focused on the design of therapies applied to pediatric oncology, infectious diseases, and paediatric transplantation. Briefly, our research interests include: 1) the use of haematopoietic stem cell transplantation as a platform for cell therapy; 2) the improvement of human and paediatric transplantation. Briefly, our research interests are focused on therapies applied to paediatric oncology, infectious diseases, and Sarcomas.

**RESEARCH HIGHLIGHTS**

Sarcomas represent approximately 10% of paediatric cancers. The survival rate for patients with high-risk disease, with metastasis at the time of diagnosis, or experiencing relapse, does not exceed 30%. In these cases, current treatments remain ineffective, and their administration is associated with acute and chronic effects that compromise the survival and quality of life of patients. There is an urgent need to find new therapeutic alternatives to improve the prognosis of patients with sarcoma.

In November 2023, a clinical trial for paediatric, adolescent, and young adult patients with advanced sarcoma, coordinated by Antonio Pérez Martínez and the Advanced Therapy Medicines Production Unit of La Paz University Hospital, received authorisation from the Spanish Association of Medicines and Medical Devices (Iudra CT 2019-004310-33, No. PII 20-001). Under the acronym CAR4SAR, this is the world’s first clinical trial with an allogeneic academic CART designed for paediatric patients with advanced sarcoma. It is an open-label, prospective, single-centre (HULP), non-randomised, dose-escalation trial aimed at determining the dose-limiting toxicity and maximum tolerated dose of systemically infused NKGD2-CAR memory T cells derived from donors (arm A) and a dual treatment involving both systemic and local infusions of NKGD2-CAR memory T cells derived from donors (arm B). This trial is the result of a collaboration between the La Paz Hospital Institute for Health Research, the CNIO, the Carlos III Health Institute, and the Central Hospital of Asturias, along with CRIS Cancer Foundation, which has been supporting this project for the past 6 years. The clinical trial initiation with the first patient will start in February 2024. In addition to its evident scientific impact, this trial will have a significant social impact. Over time it will enhance therapeutic options not only for paediatric patients with recurrent/refractory sarcoma but could also extend to other paediatric solid tumours with a poor success rate using conventional therapies. Study Details | A Phase I Trial of Memory T Cells Expressing an NKGD2 Chimeric Antigen Receptor in Children, Adolescents and Young Adults With Advanced Sarcoma | ClinicalTrials.gov.

**PUBLICATIONS**


**SELECTED PUBLICATIONS AT OTHER INSTITUTIONS**

- **García-Sols B et al.** (2023). Inherited human stem cell progenitors transplantation in children; 3) the use of both activated and memory-like NK cells and CART-T cells in paediatric oncology. Together with this, we led several projects aimed at studying the efficacy and feasibility of cell therapy against infectious diseases. Finally, we are also working on the induction of immunological tolerance in solid organ transplantation by inducing mixed haematopoietic chimeras through cell therapy. In this sense, we have several active academic clinical trials and collaborations with industry, with the objective of developing new and more effective therapies with fewer side effects.

**Post-Doctoral Fellows**

- Cristina Aguirre, Halin Barrié, Adela Escudero, Lucía Fernández, Elisa Izquierdo, Olakansu Latin, Adriana Martínez, Jordi Mingulín, Andrés Páez.

**Clinical Investigators**

- Karina Al Ajouri, Laura Clares, Adrián Barber, María Barzilai, Carmen Meneses, Alfonso Navarro, Patricia Rodríguez, Beatriz Ruiz, Clara Vergara.

**Technicians**

- Lidia Perníez (TS), Natalia Rios (TS)

**Student in Practice**

- Mahdiah Nughadi (October-December) Universidad de Studi [O] Painels, Italy

**Clinical Research Programme**

- IDIPAZ-CNIO PEDIATRIC ONCO-HEMATOLOGY CLINICAL RESEARCH UNIT

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