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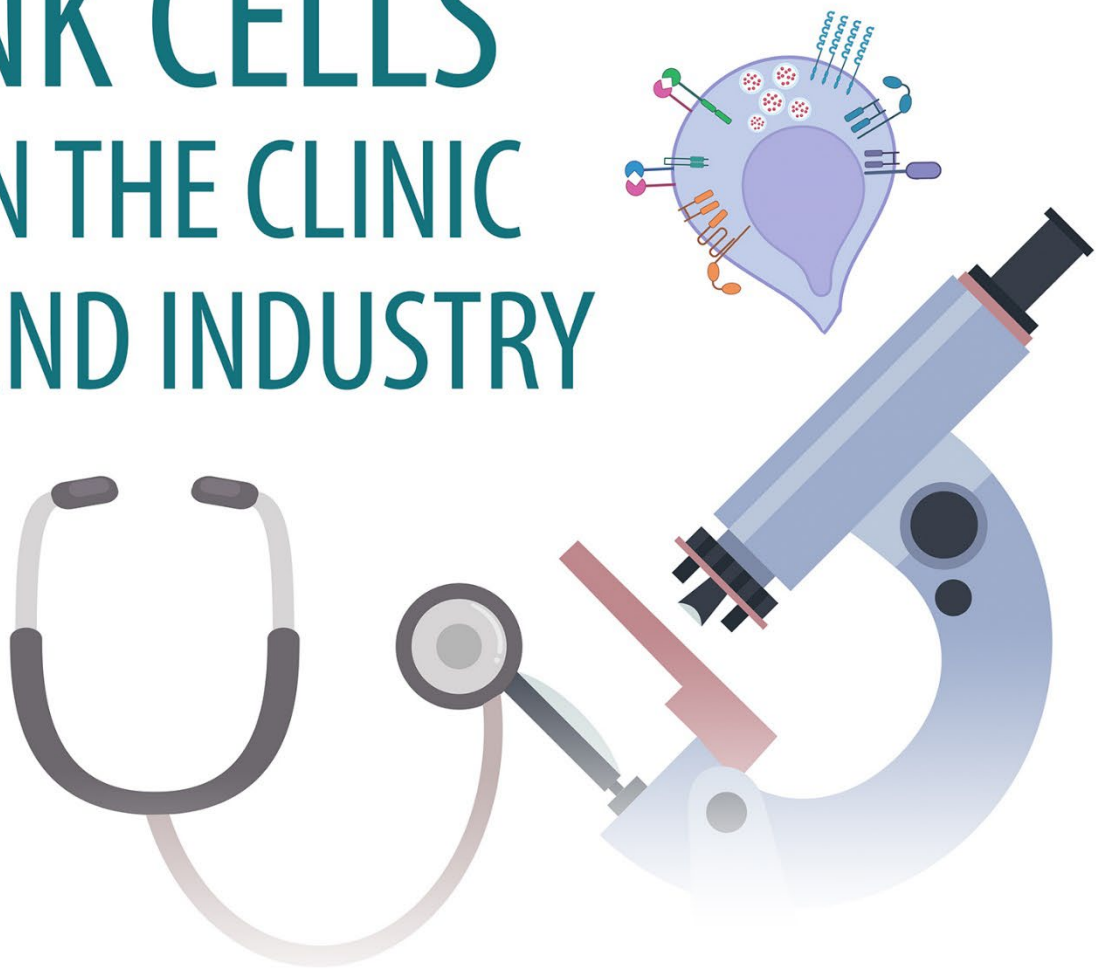
EXCELENCIA SEVERO OCHOA

Centro Nacional de Biotecnología

MODELS, CHALLENGES AND PROMISES OF ADVANCED THERAPIES FOR CANCER:

NK CELLS IN THE CLINIC AND INDUSTRY



INTERNATIONAL WORKSHOP

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ABSTRACT BOOK

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ORAL PRESENTATIONS

O1. TARGETING SIRT2: NOVEL INHIBITORS FOR IMPROVED ANTITUMOR IMMUNE RESPONSE.

Ilic, Aleksandra; Djokovic, Nemanja; Djikic, Teodora.

University of Belgrade Faculty of Pharmacy Department of Pharmaceutical Chemistry, research group prof. Katarina Nikolic.

SIRT2 is an NAD^+-dependent deacetylase involved in metabolic regulation, genomic stability, and immune modulation. Emerging evidence suggests that SIRT2 significantly shapes tumour progression by influencing the tumour microenvironment, particularly through effects on natural killer (NK) cells. Altered SIRT2 expression can disrupt NK-cell infiltration and tumouricidal activity, highlighting SIRT2 as a promising target for enhancing antitumor immune responses. In this work, a 3D-QSAR model based on nicotinamide-derived SIRT2 inhibitors was developed and supported by GRIND pharmacophore analysis. External validation confirmed the model's reliability and enabled the rational design of new inhibitor candidates. Molecular docking across SIRT1–3 isoforms allowed the construction of machine-learning classification models for predicting SIRT2 selectivity. Integration of 3D-QSAR, docking-based selectivity modeling, and ADMET profiling led to the identification of several selective SIRT2 inhibitor candidates. These compounds will be synthesized and evaluated in vitro to verify their efficacy and potential in improving antitumor immune responses.

Keywords: Computational

O2. GLIOBLASTOMA SPHEROIDS UNCOVER DISTINCT NK CELL INTERACTIONS WITH DIFFERENTIATED AND STEM-LIKE GLIOBLASTOMA CELLS.

Habič, Anamarija[1]; Kolenc, Milavec Tina[1]; Žižek, Pia[2]; Kladnik, Špela[3]; Majc, Bernarda[3]; Senjor, Emanuela[4]; Perišić, Nanut Milica[4]; Porčnik, Andrej[5]; Prestor, Borut[5]; Švajger, Urban[6]; Novak, Metka[7]; Breznik, Barbara[8].

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Natural killer (NK) cell-based immunotherapeutic approaches hold great promise for the treatment of glioblastoma, an aggressive and incurable type of brain cancer with poor patient prognosis. Notably, NK cells can eliminate glioblastoma stem cells, which drive glioblastoma recurrence. However, the complex crosstalk between glioblastoma and NK cells remains incompletely understood. In our study, we optimised a protocol for reproducible production and dynamic culture of glioblastoma spheroids from differentiated glioblastoma cells and glioblastoma stem-like cells in the Celvivo reactor system. NK cell infiltration into spheroids and NK cell cytotoxicity were then investigated in direct co-cultures as well as in an advanced dynamic organ-on-chip system. Spheroids derived from differentiated glioblastoma cells secreted higher levels of immunomodulatory cytokines compared to spheroids from glioblastoma stem-like cells and were highly resistant to NK cell killing. Finally, the CD155-DNAM1/TIGIT axis was identified as an important regulator of the profound NK cell cytotoxicity against glioblastoma stem-like cells.

Subject area: In vitro

O3. DEVELOPMENT OF CAR-NK CELL THERAPIES FOR DIFFICULT-TO-TREAT TUMOURS FROM BENCH TO BEDSIDE.

Van Audenaerde, Jonas; Smits, Evelien;Weidensee, Brian; Peeters, Emma, Van den Eynde, Astrid; Gehrcken, Laura; Van Der Heijden, Sanne; Vanheeswijck, Liesbeth; Gevaerts, Charlotte; Quatannens, Delphine; Lardon, Filip; Deben, Christophe; Zaryouh, Hannah; Verswyvel, Hanne; De Waele, Jorrit.

Center for Oncological Research, Univeristy of Antwerp.

Chimeric Antigen Receptor (CAR)-T cell therapies have achieved unprecedented results in treating B-cell malignancies but their use is often limited by severe toxicities. In contrast, CAR natural killer-(NK) cells represent a substantially safer and off-the-shelf alternative. We have established a platform for systematic screening of multiple CAR targets in difficult-to-treat tumours, including pancreatic cancer, metastatic colorectal cancer, and (paediatric) brain tumours. We study them in vitro using e.g. real-time killing assays on 2D cell lines and 3D patient-derived organoids models, multiplex cytokine and chemokine secretion analysis and in-depth phenotyping using spectral flow cytometry. Also in vivo validation is performed in several relevant orthotopic mouse models. Our platform has already produced strong preclinical data on the use of CD70-targeting CAR-NK cells in solid tumours with CD70 as promising pan-cancer target. Moreover, we have initiated the development of GMP-compliant manufacturing processes to bring this promising cell therapy to the clinic.

Subject area: In vitro/3D

O4. TOWARD CLINICAL TRANSLATION OF BCG-PRIMED NK CELL IMMUNOTHERAPY.

Felgueres, María-José; Muniesa, Inés; Morales, Lucía; Martínez, Víctor; Córdoba Laura; Suárez, Cristian; Turón, Martina; López, Eduardo; Del-Fresno, Carlos; Paramio, Jesús; Valés, Mar.

National Centre for Biotechnology, Spanish National Research Council (CNB-CSIC).

Natural killer (NK) cell–based immunotherapies are very promising, but complex manufacturing, activation regimes and reduced activity in solid tumours limit their success. We present a clinically oriented strategy to generate potent anti-tumour NK cells by priming peripheral blood mononuclear cells with Bacillus Calmette-Guérin (BCG, tuberculosis vaccine) and stimulating with low-dose IL-12, IL-15, and IL-21. Unlike many existing NK cell platforms, this approach achieves robust NK cell expansion without cell sorting and is fully compatible with cryopreserved starting material, supporting an off-the-shelf manufacturing model. BCG-primed NK (BIL-NK) cells demonstrate consistent cytotoxicity across multiple solid tumour types in 2D and 3D patient-derived organoid systems, with effective tumour infiltration and significant *in vivo* efficacy. These features address key limitations of current NK cell therapies, including scalability, reproducibility and translational feasibility. Together, our findings position BIL-NK cells as a clinically viable and competitive immunotherapy derived from an already approved drug.

Subject area: In vitro/3D

O5. CAR T CELLS BASED ON NK CELL RECEPTORS EXERT POTENT ANTI-TUMOR ACTIVITY AGAINST PEDIATRIC MALIGNANT CNS TUMORS.

Ibáñez-Navarro, Marta; De la Hoz, Marta; De Santisteban-Tara, María Octavia; Clares-Villa, Laura; De Pablos, Ana; Velasco, María; Mañas, Adriana; Pérez-Martínez, Antonio; **Fernández Casanova, Lucía**.
CNIO.

NKG2D and CD16 are activating receptors of Natural Killer cells that mediate anti-tumor cytotoxicity either by recognizing the NKG2D ligands or binding the Fc fragment of antibodies mediating Antibody Dependent Cell Cytotoxicity (ADCC).

We have engineered T cells with three CAR constructs: NKG2D, CD16, and NKG2D-CD16 and tested their anti-tumor ability as monotherapy, or combined with Dinutuximab-β(anti-GD2) against seven pediatric CNS tumor cell lines.

In vitro, all the tested cell lines were sensitive to NKG2D-CAR T cells lysis, especially SJ-GBM2 (glioblastoma) and DAOY (medulloblastoma) cells. CD16-CAR T cells combined with Dinutuximab-β, targeted SJ-GBM2 and DAOY cells, and this effect was more pronounced with NKG2D-CD16 CAR T cells. Mice engrafted with SJ-GBM2 or DAOY cells showed reduced tumor burden and prolonged survival upon treatment with an intracranial infusion of NKG2D-CAR T cells.

Our data suggests that this NK-T-CAR approach could be a promising therapeutic strategy for pediatric CNS tumors.

References

[1] Natural Killer Cells in Cancer Immunotherapy, Jeffrey S. Miller and Lewis L. Lanier, Annual Review of Cancer Biology, 2019.
[2] Towards Immunotherapy for Pediatric Brain Tumors. Stacie Shiqi Wang,e t al. Trends in Immunology, 2019

Subject area: Other(Please specify your area in the comments section)
Keywords: NKG2D, CD16, CAR T cells, pediatric malignan brain tumors

O6. THE KEY ROLE OF NK CELLS CONTROLLING LUNG METASTASIS FROM GASTROINTESTINAL TUMORS.

Martín Rubio, Paula; Raigón-Gómez, Ester; Encabo, Marimar; Giraldo, Cindy; Moreno-Manuel, Andrea; Hidalgo, Sandra; Pardo, Julián; Aguiló, Nacho; Sancho, Patricia; Sanz-Pamplona, Rebeca.
IIS Aragon; Cancer Heterogeneity and Immunomics; Metabolism and Cancer Stem Cells.

Metastatic disease is the main cause of cancer-related deaths. Although immunotherapy is a promising strategy, its success against metastases remains limited. We previously identified a cluster of “High-Immune” metastases, susceptible to immunotherapy, mainly composed of lung metastases.

Transcriptomic analyses revealed that lung metastases from gastrointestinal tumors have increased NK cell infiltration and expression of NK-related genes, compared to liver metastases or primary tumors. In vitro, NK-92 exhibited dose-dependent cytotoxicity against patient-derived organoids and mouse-derived cell cultures from lung metastases. RNA-seq analyses of organoids and matched tissues are underway to identify markers involved in NK cell resistance and metastatic progression. Preliminary data in cell lines indicated high HLA-E expression in ASPC1, correlating with increased NK resistance in vitro and lung tumor burden in vivo.

Overall, lung metastases present a characteristic immune microenvironment in which NK cells have an essential role, supporting NK-based immunotherapy as a potential strategy against lung metastases.

Subject area: Other(Please specify your area in the comments section)
Keywords: NK cells, lung metastases, immunotherapy

POSTER PRESENTATIONS

P1. PRECLINICAL DEVELOPMENT OF BB-NK-001: AN ACADEMIC IL-12/15/18-PREACTIVATED NK CELL PRODUCT FOR THE TREATMENT OF ACUTE MYELOID LEUKEMIA.

Sandá, Víctor[1]; Gartzia-Aranaga, Itxaso[2]; Calvo-Martínez, Susana[2]; Luzuriaga-Álvarez, Alba[2]; Pérez-López, Ana María[2]; Amarilla-Irusta, Ainhoa[1]; López-Pardo, Ainara[1]; San Juan, Itxaso[1]; Iturbe-Larrondo , Ainhoa[1]; Galdona-Yeregi, Nerea[3]; Álvarez-Rodríguez, Maite[3]; Mateos-Mazón, Juan José[4]; Amutio, Elena[4]; García-Ruiz, Juan Carlos[4]; Martín-Antonio, Beatriz5; Sánchez-Pernaute, Rosario6; Zenarruzabeitia, Olatz[7]; Amo, Laura; Borrego, Francisco[8].

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Preactivation of NK cells with IL12/15/18 induces the development of cytokine-induced memory-like NK cells that exhibit enhanced anti-tumor activity, making them a promising option for treating AML. We have manufactured an academic IL12/15/18preactivated NK cell product, named BBNK001, using the CliniMACS Prodigy (Miltenyi) and characterized the obtained products and paired control (non-activated) NK cells. Flow cytometry analysis revealed that BBNK001 products were highly pure in NK cells (99%), enriched in activation markers (CD25/69/137). scRNAseq analysis showed the clustering of 9 different subpopulations and highlighted key genes driving the transcriptional program of BBNK001 cells (IL2RA, TNFRSF9 or IFNG). Additionally, BBNK001 cells were functionally superior to control NK cells, showing higher degranulation, production of IFNγ and TNFα, and greater cytotoxicity against K562 and AML blasts. Finally, K562-xenograft NSG mice treated with BBNK001 demonstrated an increased survival and reduced leukemia burden. In conclusion, BBNK001 cells could be a promising treatment for AML.

Subject area: clinical trial

Keywords: Cytokine-Induced Memory-Like (CIML) NK cells, GMP-manufacturing, Acute Myeloid Leukemia (AML)

P2. HLA-B*44 AND BW4 ALLOTYPES HINDER THE EFFICACY OF BCG TREATMENT IN BLADDER CANCER.

Rosique, Claudia; López, Pedro; Campillo, José Antonio ; Galindo, Francisco; Martínez, María Victoria ; Martínez, Mª Dolores ; Ruíz, Inmaculada; Gimeno; Lourdes ; López, Alicia ; Minguela, Alfredo.

Immunology Service, Virgen de la Arrixaca University Clinical Hospital (HCUVA)

Introduction: Bacille Calmette-Guerin (BCG) is the immunotherapy of choice for high-risk non-muscle invasive bladder cancer (BC), although recurrence eventually occurs in 50% of patients and 20% progress to advanced stages. Methods: Predictive value of KIR/HLA interactions was evaluated in 325 BC patients treated with BCG. Proliferation, cytotoxicity, production of cytokines and intracellular nitric oxide (icNO) were assessed in peripheral blood mononuclear cells after stimulation with anti-CD3/CD28 or BCG. **Results:** HLA-B*44 and other KIR3DL1 Bw4 ligands were associated with unfavorable outcomes. Bw4 ligands were associated with weaker NK cell proliferation, lower IL-1□, IL-6, and icNO production after BCG stimulation in vitro, revealing an inhibitory role of KIR3DL1. **Conclusion:** Mechanisms by which KIR3DL1/Bw4 interaction interferes with BCG-induced NK cell proliferation and the production of cytokines and icNO, warrant further investigation. HLA-I genotyping should be investigated as a useful biomarker to personalize BCG immunotherapy in BC.

Subject area: Clinical Trial

P3. ACTIVATING KIR–LIGAND INTERACTIONS DRIVE NK CELL PROGRAMS LINKED TO CANCER CLINICAL OUTCOMES.

Ruiz Lorente, Inmaculada; Vallejo-Pulido, Andrés; López-Abad, Alicia; López Cubillana, Pedro ; Barozi, Víctor; Khakoo, Salim; Minguela, Alfredo; Gimeno, Lourdes.

Immunology Service, Virgen de la Arrixaca University Clinical Hospital (HCUVA), Biomedical Research Institute of Murcia (IMIB), Murcia, Spain

Cancer remains a major global health burden. Although cure rates are improving, recurrence and refractory disease require alternative strategies, where NK cells could play pivotal roles if their antitumor activity is enhanced. To assess the impact of KIR/HLA-I interactions on circulating NK cell transcriptomes and patient outcomes. KIR and HLA-I genotyping and flow cytometry of circulating NK cells were performed in patients with bladder (n=328), melanoma (n=311), ovarian cancer (n=89), plasma-cell neoplasms (n=323), and childhood leukemia (n=102). Single-cell transcriptomic analyses of NK and T cells were conducted in donors with genotypes associated with short or long survival. Activating KIRs (aKIR) rather than inhibitory KIRs correlated with patient outcomes. Accumulation of aKIR interactions was linked to shorter survival, while KIR2DS1/C2 alone associated with longer survival. Single-cell data revealed an adaptive NK subset enriched in long-surviving patients. Specific aKIR/HLA-I interactions shape adaptive NK profiles and antitumor immunity, offering strategies for refractory cancers.

Subject area: In vitro

P4. PRECLINICAL EVALUATION OF NKG2D-CD44V6 CAR-NK-92 MI CELL-BASED IMMUNOTHERAPY IN AN ORTHOTOPIC MOUSE MODEL OF BLADDER CANCER.

Turón Orra, Martina; Lodewijk, Iris ; García Gómez, Laura; Pérez Escavy, Mercedes ; Suárez Cabrera, Cristian; Montesinos, Esther; Casado Olea, José Antonio; Río, Paula; Valeri, Antonio; Dueñas, Marta ; Paramio González, Jesús Maria ; Morales Rodríguez, Lucía.

Molecular and Translational Oncology Division, Centro de Investigaciones Energéticas, Medioambientales y Tecnológicas (CIEMAT). Madrid, Spain. Cellular and Molecular Oncology and Genitourinary Tumor Group, Biomedical Research Institute Imas12, Hospital Universitario "12 de Octubre". Madrid, Spain. Centro de Investigación Biomédica en Red de Cáncer (CIBERONC). Madrid, Spain.

Bladder cancer (BC) ranks as the 9th most common cancer worldwide, and current treatments benefit only a small subset of patients. Chimeric Antigen Receptor – Natural Killer (CAR-NK) immunotherapy offers a promising alternative, though data in solid tumors remain limited. Building on our previous *in vitro* findings showing strong cytotoxicity of NKG2D-CD44v6 CAR-NK-92 MI cells, we evaluated their activity *in vivo*. An orthotopic murine model was generated by intramural bladder injection of Firefly luciferase-expressing RT112 cells for non-invasive tumor monitoring. CAR-NK-92 MI cells were engineered to express Cypridina luciferase to assess biodistribution, persistence, and tumor targeting. CAR-NK-92 MI cells persisted for at least seven days, accumulated preferentially in tumors, and showed greater specificity than parental NK-92 MI cells. Treated mice exhibited significantly reduced tumor growth, and CAR-NK cells were observed intratumorally. These results support NKG2D-CD44v6 CAR-NK-92 MI cells as a promising therapeutic strategy for BC.

Subject area: In vitro

Keywords: bladder cancer - immunotherapy - CAR-NK - NKG2D - CD44v6 - murine model

P5. CELL FACTORIES OF NK-CELL ENGAGERS: A NEXT-GENERATION STAB-T IMMUNOTHERAPY.

Franco-Mansilla, Jaime; Lázaro, Rodrigo; Zagorac, Ivana; Carrasco, Carlos; Sanz, Laura; Roda, Pedro; Álvarez, Luis.
Unidad de Investigación Clínica en Inmunoterapia del Cáncer CNIO-HMarBCN

Bispecific antibodies have advanced cancer immunotherapy by redirecting immune cells toward tumor targets, but their short half-life limits clinical applicability. To address this, the STAb-T platform enables engineered T cells to secrete immune engagers in vivo for sustained local activity. In this study, we describe NKCE-HA, a novel NK cell engager designed to recruit NKR^+ immune cells, including NK cells, against HA-expressing tumors. Purified NKCE-HA demonstrated potent, antigen-dependent NK-mediated cytotoxicity, high specificity for HA, monomeric stability, and resistance to competition from serum immunoglobulins, while preserving surface antigen availability. NKCE-HA also engaged multiple NKR^+ immune subsets. When secreted by STAb-T cells, NKCE-HA retained full biological activity and effectively recruited circulating NK cells, achieving cytotoxicity comparable to a HA-specific T cell engager. Importantly, co-expression of NKCE-HA and a TCE-HA in a dual STAb-T configuration resulted in synergistic tumor killing. These findings support NKCE-HA as a promising component of next-generation combinatorial cancer immunotherapies.

References

[1] CNIO-HMRIB Cancer Immunotherapy Clinical Research Unit, Spanish National Cancer Research Centre (CNIO), Madrid; Hospital del Mar Research Institute Barcelona (HMRIB), Barcelona, Spain 2STAb Therapeutics, Madrid, Spain. 3Banc de Sang i Teixits, Barcelona, Spain. 4Complutense University of Madrid, Madrid, Spain.

Subject area: In vitro

P6. MICROWAVE-SYNTHESIZED IRON NANOPARTICLES TO IMPROVE ADOPTIVE CELL TRANSFER THERAPIES.

Blanco Arribas, Elena; Barber Castaño, Domingo F.
National Centre for Biotechnology (CNB-CSIC).

Adoptive cell transfer (ACT) is a promising immunotherapeutic strategy for cancer treatment, aimed at enhancing the immune system's ability to selectively eliminate tumor cells. However, its clinical efficacy is often limited by poor immune cell infiltration into tumors and insufficient activation within the tumor microenvironment. To address these limitations, we investigated the use of iron oxide magnetic nanoparticles (MNPs) to guide and localize immune cells using an external magnetic field (EMF), thereby improving their accumulation and function at the tumor site.

We employed microwave-synthesized 14 nm iron oxide MNPs (MW14) functionalized with two different surface coatings: 3-aminopropyl-triethoxysilane (APS) and dimercaptosuccinic acid (DMSA). Their interaction with murine natural killer (NK) cells was systematically evaluated. Following nanoparticle treatment, NK cell viability, nanoparticle association, and functional activity were assessed.

Using a flow chamber microscopy system, we demonstrated that MNP-treated NK cells can be effectively retained under a localized magnetic field, confirming their responsiveness to magnetic guidance. Importantly, low concentrations of MNPs did not induce cytotoxic effects under any of the tested conditions. Among the coatings evaluated, APS-functionalized MNPs showed higher cellular association and superior magnetic retention, highlighting their potential for tumor-directed immune cell mobilization. Furthermore, MNP treatment did not impair NK cell cytotoxic function.

Together, these findings establish a foundation for the use of MNP-loaded immune cells in ACT-based cancer immunotherapy. By preserving key immune effector functions while enabling precise magnetic guidance, this strategy offers a promising approach to enhance immune cell targeting and therapeutic efficacy within solid tumors.

References

1 Sanz-Ortega, Laura et al. "Magnetic Nanoparticles Attached to the NK Cell Surface for Tumor Targeting in Adoptive Transfer Therapies Does Not Affect Cellular Effector Functions." Frontiers in immunology vol. 10 2073. 30 Aug. 2019, doi:10.3389/fimmu.2019.02073

Subject area: In vitro

P7. A COMBINATORIAL THERAPY FOR BLADDER CANCER: EPIGENETIC INHIBITOR AND CAR-NK CELLS.

Morales Rodríguez, María Lucía ; Turon-Orra, M; Nunes, S.P. ; Río, P. ; Valeri, A.; San José-Enériz, E.; Agirre, F. Prosper, X.; Paramio, J.M.

Molecular and Translational Oncology Division, Centro de Investigaciones Energéticas, Medioambientales y Tecnológicas (CIEMAT). Madrid, Spain. Cellular and Molecular Oncology and Genitourinary Tumor Group, Biomedical Research Institute Imas12, Hospital Universitario "12 de Octubre". Madrid, Spain. Centro de Investigación Biomédica en Red de Cáncer (CIBERONC). Madrid, Spain.

Natural Killer cells expressing chimeric antigen receptors (CAR-NKs) are being tested as a promising cell-based immunotherapy against different solid tumors. Epigenetic modifications are drivers of bladder cancer (BC) and their modulation by inhibitors is a promising approach for BC management. Here, we explore NK cell-based immunotherapy combined with an epigenetic inhibitor as a therapeutic strategy for advanced BC patients. A novel inhibitor of epigenetic machinery against histone deacetylases, CM-1758, induced surface expression of NK cell ligands (NKG2DLs) in four human BC cell lines. Cytotoxic effects of NKG2D CAR-NK cells in co-culture with BC tumor cells were significantly potentiated as compared with parental NK-92 MI cells. In particular, BC cells treated with CM-1758, that augmented its NKG2DLs levels, increased their sensitivity to NKG2D CAR-NK cells in co-culture. Our results support that treatment with epigenetic inhibitors may facilitate the use of CAR-NK-based cell therapies as a promising strategy for BC management.

Subject area: In vitro/ 3D

P8. EXTRACELLULAR VESICLE–BASED DELIVERY OF GENE-MODULATING RNA CARGO TO ENHANCE ANTI-TUMOUR IMMUNITY.

Esenkaya, Hatice.

Karolinska Institute and Kilis 7 Aralik University.

The development of advanced therapies in cancer immunology requires safe, precise, and programmable systems capable of modulating tumour cell behaviour and improving immune responsiveness. In this project, we explore engineered extracellular vesicles (EVs) as a next-generation platform for delivering functional RNA cargo designed to restore or enhance immunogenic molecular pathways in cancer cells. By incorporating optimized RNA-binding scaffolds, our approach enables EVs to selectively package small nuclear RNA or gene-modulatory sequences that can influence RNA processing, transcript stability, or downstream signalling events relevant to immune recognition. Initial results demonstrate efficient loading and transfer of functional RNA into recipient tumour cells, leading to measurable correction of RNA-processing defects and enhanced expression of immunologically relevant targets. This provides a foundation for future strategies in which EV-delivered RNAs could increase NK-cell recognition, promote immunogenic transcript variants, or sensitise tumour cells to cytotoxic responses.

Subject area: In vitro/ 3D

P9. TOXOPLASMA INFLUENCES ON THE NATURAL KILLER (NK) CELLS FUNCTIONS AGAINST CANCER CELLS.

Nozad Charoudeh, Hojjatollah ; Aghayan, Sargis ; Daryani, Ahmad.

Scientific Center of Zoology and Hydroecology, NAS, RA, Yerevan, Armenia.

NK cells are promising effector cells for antibody-based immunotherapy and HLA-KIR-dependent anticancer activity against stem cell-derived cancers, malignant tumors, and drug-resistant cancers. In particular, donor NK cells do not activate graft versus host disease (GVHD) in recipients; on the contrary, they increase graft versus leukemia (GVL). They kill cells with altered HLA expression and, by inducing cell-cell interaction, trigger antibody-dependent cell cytotoxicity (ADCC) against cancers. Both cells are safe in allogeneic and haploidentical transplantation. Parasitic infections are one challenge to keeping these cells functional against cancers. For instance, Toxoplasma gondii may infect immune cells and reduce their activity; however, it has been reported that weakened Toxoplasma has a positive effect on NK cells. Therefore, it is important to evaluate Toxoplasma gondii's influence on these types of immune cells. Searching for any influence of Toxoplasma gondii on KIR-positive and ADCC activity of NK cells against leukemia. The type of KIR receptors that respond to Toxoplasma on NK and gamma delta T cells will be explored. Toxoplasma lysate antigen (TLA) of different strains of Toxoplasma gondii could have therapeutic effects on these cells without remaining alive will be defined. HLA-C polymorphism will be evaluated in response to Toxoplasma infection. The level of HLA-C expression can be controlled with a single nucleotide polymorphism (SNP) in an NK cell-specific promoter region, because it affects NK cell activity and, consequently, the immune response to Toxoplasma infections.

Subject area: In vitro/ 3D

P10. THIAZOLE-BASED PYRIDINES AS SELECTIVE ANTICANCER CANDIDATES TARGETING LUNG CANCER CELLS.

Nuha, Demokrat ; Dawbaa, Sam; Evren, Asaf Evrim ; Çiyanci, Zennure Şevval ; Teme, Halide Edip ; Çiftçi, Gülşen Akalin; Yurttaş, Leyla.
University for Business and Technology, Faculty of Medical Biochemistry, Prishtina, Kosovo.

This work presents the synthesis and biological evaluation of a new series of hydrazonothiazole-based pyridines designed as targeted agents against lung cancer. All compounds were structurally confirmed through NMR and HRMS analyses and demonstrated favorable physicochemical profiles in silico, consistent with drug-like criteria. Their anticancer potential was assessed in the A549 lung carcinoma cell line, where several molecules displayed strong cytotoxic activity, surpassing the reference drug cisplatin. Selectivity studies revealed that compounds 2b, 2c, 2f, and 2m showed a superior preference for cancer cells over healthy cells. Mechanistic assays indicated that apoptosis induction occurred predominantly through mitochondrial pathways, with compound 2m exhibiting the highest apoptotic effect. Additionally, compound 2f showed notable inhibitory activity against MMP-9, supported by docking and molecular dynamics analyses. Overall, these findings highlight the promise of this thiazole-pyridine series for further development and poster presentation at the IMMUNO-model symposium.

Subject area: In vitro/ 3D

P11. A DUAL-ENGINEERING STRATEGY TARGETING HLA-E IMMUNE EVASION WITH A/C SWITCH RECEPTOR AND NKG2A KNOCKOUT IN CYTOTOXIC LYMPHOCYTES.

Torralba-Raga, Lamberto[1]; Martin, Karen E[1]; Christensen, Emil[2]; Melchers, Kasper[1]; Krokeide, Silje[1]; Malmberg, Karl-Johan[1].
[1]Department of Cancer Immunology, Oslo University Hospital; [2] Department of Clinical Immunology, University of Southern Denmark.

HLA-E is frequently upregulated across solid tumors, where it functions as a dominant immune checkpoint by engaging the inhibitory receptor NKG2A on NK and $CD8^+$ T cells. To overcome this barrier, we developed the A/C Switch, a synthetic receptor combining the HLA-E binding domain of NKG2A with the activating signaling domain of NKG2C. In $CD8^+$ T cells, the A/C Switch induced potent cytotoxicity against HLA-E^+ leukemia and glioblastoma in vitro and in vivo. We subsequently translated this platform to primary human NK cells, whose endogenous NKG2A expression limits receptor performance. By combining CRISPR/Cas9-mediated knockout of NKG2A with retroviral A/C Switch delivery, we generated >60% dual-edited NK cells within one week while preserving phenotype and expansion. These NKG2A-KO, A/C $Switch^+$ NK cells displayed enhanced cytokine production, superior cytotoxicity against HLA-E-high tumors, and sustained tumor control in vivo, counteracting HLA-E immune evasion.

Subject area: In vitro/ 3D
Keywords: IMMUNE EVASION, IN VITRO, IN VIVO, SOLID TUMORS, NK CELLS, ENGINEERED RECEPTORS, SYNTHETIC RECEPTORS

P12. NOVEL CAR CONSTRUCTS BASED ON NK CELL RECEPTORS AND ANTIBODY SYNERGY FOR TRANSLATIONAL CAR-T THERAPY IN PEDIATRIC CNS TUMORS .

De La Hoz, Marta; Ibáñez, Marta; de Santisteban, María Octavia; Clares, Laura; Mañas, Adriana; Pérez-Martínez, Antonio; Fernández, Lucía.

CNIO.

Central nervous system tumors (CNS-T) are the leading cause of cancer death in pediatrics[1]. The lack of personalized treatment creates an urgent need for safer and more effective therapies.

Immunotherapy with CAR-T cells is a promising alternative, but its development in pediatric solid tumors is limited[2]. We propose an innovative strategy: T cells equipped with CARs derived from NK cell key activating receptors (NKG2D, CD16 or both) in combination with therapeutic antibodies. These "NK-like-CAR-Ts" enable anti-tumor cytotoxicity by either recognizing NKG2D ligands[3] or antibody-coated target cells, mediating Antibody Dependent Cell Cytotoxicity[4].

Our data suggests: “NK-like-CAR-Ts" had low exhaustion marker expression; *in vitro*, dual and CD16-CAR-Ts combined with Dinutuximab-β were the most effective against SJ-GBM2 (glioblastoma) and Daoy (medulloblastoma) cell lines, respectively. Additionally, NKG2D-CAR-Ts infiltrated Daoy 3D-spheroids causing target cell apoptosis.

In sum, our preliminary findings support the potential of “NK-like-CAR-Ts" as a promising and translatable treatment of pediatric CNS-T.

References

[1] Global Cancer Observatory. (2022). Cancer Today: Central nervous systemTumours data [Online database]. International Agency for Research on Cancer. Retrieved December 18, 2025, from https://gco.iarc.fr/today/en/dataviz/pie?mode=cancer&group_populations=1&types=1&age_end=2

[2] Facing CAR T Cell Challenges on the Deadliest Paediatric Brain Tumours - PMC [Internet]. [citado 25 de marzo de 2025]. Disponible en: https://pmc.ncbi.nlm.nih.gov/articles/PMC8616287/. PDMI: 34831165

[3] Haberthur K, Brennan K, Hoglund V, Balcaitis S, Chinn H, Davis A, et al. NKG2D ligand expression in pediatric brain tumors. Cancer Biol Ther. diciembre de 2016;17(12):1253-65. PDMI: 27834580

[4] Stefańczyk SA, Hagelstein I, Lutz MS, Müller S, Holzmayer SJ, Jarjour G, et al. Induction of NK cell reactivity 19 against acute myeloid leukemia by Fc-optimized CD276 (B7-H3) antibody. Blood Cancer J. 18 de abril de 2024;14(1):67. PDMI: 38637557

Subject area: In vitro/ 3D

Keywords: Pediatric CNS tumors, NK-like CAR-T cells, CAR-T cell therapy, NKG2D / CD16, Antibody-dependent cell cytotoxicity (ADCC)

P13. DISSECTING THE MECHANISMS OF CAF-MEDIATED NK CELL IMMUNOSUPPRESSION IN COLORECTAL CANCER.

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University of Galway.

Consensus Molecular Subtype 4 colorectal cancer (CMS4-CRC) is associated with poor prognosis and therapy resistance, driven by an inflamed but immunosuppressive tumor microenvironment (iTME) rich in cancer-associated fibroblasts (CAFs). We investigated how TNF-α–induced tumor secretome (TCS) reprograms CAFs to influence NK-cell antitumour activity. TNF-α TCS–conditioned CAFs were analysed by flow cytometry, and tri-cultures of HCT116 cells, CAFs and NK cells were assessed using IncuCyte live imaging. NK phenotype and HCT116 susceptibility to NK killing were evaluated, and the impact of de-sialylation with sialidase (E-610) and Nectin-2 blockade was tested. CAFs and tumour cells expressed CD155, whereas only CAFs had strong Nectin-2 expression, which was further induced by TNF-α TCS. TNF-α TCS also upregulated IL-6 and COX-2 in CAFs. In tri-cultures, CAFs were more sensitive to NK cytotoxicity than tumour cells; however, NK cells exhibited reduced NKG2D and DNAM-1 along with increased CD96, indicating functional suppression. TNF-α TCS–conditioned CAFs impaired NK activity, which was restored by Nectin-2 blockade and by de-sialylation of conditioned stromal cells. Combined Nectin-2 inhibition and desialylation significantly enhanced NK-mediated cytotoxicity, driven largely by desialylation. These findings show that iTME-modulated CAFs suppress NK function through Nectin-2 and sialylation pathways, highlighting actionable stromal targets for NK-based immunotherapy in CRC.

Subject area: In vitro/ 3D

Keywords: Colorectal Cancer CAFs Stroma NK cells Nectin-2 Sialylation

P14. CYTOKINE-INDUCED MEMORY-LIKE (CIML) NK CELLS WITH RESIDENCY POTENTIAL.

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Natural Killer (NK) cells are innate lymphocytes involved in tumor defense and can acquire memory-like properties after short stimulation with IL-12, IL-15, and IL-18. Following 16–18 hours of cytokine preactivation and a subsequent 7-day resting period, these cells are termed Cytokine-Induced Memory-Like (CIML) NK cells. Although CIML NK cells display enhanced anti-tumor activity, their efficacy in solid tumors remains limited. Given the high plasticity of NK cells, we investigated whether CIML NK cells can acquire tissue-residency markers to improve their ability to infiltrate solid tumors. Peripheral blood NK cells were preactivated with cytokines, with or without transforming growth factor-β (TGF-β), and cultured for seven days. Flow cytometry revealed that TGF-β induced tissue-residency markers CD9, CD49a, and CD103 in CIML NK cells. Functional assays in 2D and 3D A549 tumor models showed preserved degranulation and cytokine production. Multi-omics analyses are ongoing to further characterize these cells.

Subject area: In vitro/ 3D

Keywords: CIML NK cells, TGF-β, plasticity, immunotherapy

P15. PRE-TREATMENT WITH FERROPTOSIS-INDUCERS ENHANCES NK CELL IMMUNOTHERAPY INFILTRATION AND CYTOTOXICITY IN HIGH-RISK NEUROBLASTOMA.

de Santisteban Tara, María Octavia; Mañas, Adriana ; Pérez, Antonio; Suanzes, Claudia; Sánchez, Lucía.

IdiPAZ-CNIO, Clinical Research Unit, Pediatric Oncohematology Group.

Cell-based immunotherapies have transformed hematologic cancer treatment, yet solid tumors like neuroblastoma (NB) remain refractory due to their immunosuppressive microenvironment and low mutational burden. We previously identified ferroptosis, an iron-dependent immunogenic cell death pathway, as a vulnerability in NB. Here, we investigated whether ferroptosis induction can potentiate natural killer (NK) cell-therapy. In two NB patient-derived xenograft models, NK cells only induced moderate tumor growth delay because infiltration remained very limited. Using matched patient-derived organoids, we found that pre-treatment with low-dose ferroptosis inducers markedly enhanced NK92MI cell cytotoxicity and infiltration, promoting changes in activating/inhibitory signal expression as well as damage-associated molecular pattern release. These data suggest ferroptosis induction can rewire the tumor to favor NK cell activity. Given that some of these compounds are clinically approved for other conditions (e.g. Sorafenib, Artesunate), combining ferroptosis-inducing agents with NK cell-therapy offers a clinically actionable approach to overcome immune resistance in NB.

Subject area: In vitro/ 3D

Keywords: Neuroblastoma, Ferroptosis, PDX, Natural killer cells.

P16. CISPLATIN SENSITIVITY IN HEAD AND NECK CANCER: INSIGHT FROM TESTS ON 2D AND 3D MODELS.

Larios, Lorena.
University of Bergen , Pathology , Clinical medicine K1

The predictive accuracy of preclinical drug testing depends on how effectively in vitro models replicate in vivo tumor physiology. 3D models better reflect the structural and functional complexity of the tumor microenvironment than conventional 2D cultures. In this study, the response of head and neck squamous cell carcinoma to cisplatin was evaluated using the LUC4 oral cancer cell line co-cultured with normal and cancer-associated oral fibroblasts in 2D and 3D.

Cell viability assays showed that IC_{50} values in 3D cultures were approximately two-fold higher than in 2D, indicating increased resistance to cisplatin. Apoptosis analysis supported this observation, as 2D cultures displayed higher levels of late apoptosis and reduced viability, while 3D spheroids and organotypic models maintained greater survival. No significant differences were observed between spheroids containing normal versus cancer-associated fibroblasts. These findings highlight the importance of 3D models for improving the predictive value of preclinical cancer drug testing.

Subject area: In vitro/ 3D

P17. UNDERSTANDING BIOLOGICAL DETERMINANTS OF BCG-PRIMED NK CELL ACTIVATION TOWARD CLINICAL TRANSLATION.

Muniesa-Martínez , Inés; Felgueres, María-José; Morales, Lucía ; Martínez G., Víctor; Córdoba-García, Laura ; Suárez-Cabrera, Cristian ; Turón, Martina ; López-Collazo, Eduardo; Del Fresno Sánchez, Carlos; Paramio M., Jesús; Valés- Gómez, Mar.
National Centre for Biotechnology (CNB-CSIC).

Using a Bacillus Calmette-Guérin (BCG)–based priming strategy, we have generated potent anti-tumour NK cells from peripheral blood mononuclear cells using low-dose IL-12, IL-15, and IL-21. This system supports robust NK cell expansion without cell sorting and maintains functionality when initiated from cryopreserved material. BCG-primed NK (BIL-NK) cells display strong cytotoxic activity in patient-derived organoid models and demonstrate efficacy in murine solid-tumours. Here, we evaluated the mechanisms that determine BIL-NK cell activation and effector function. Characterization of initial lymphoid populations reveals parameters that influence NK cell expansion efficiency and functional output. These mechanistic insights provide a framework for rational donor and patient selection, enabling more predictable manufacturing outcomes and informed clinical application. Together, this work links biological mechanism to translational decision-making in NK cell–based immunotherapy.

Subject area: In vitro/ 3D

P18. EPIGENETIC MODULATION UNLEASHES PROSTATE CANCER TARGETING BY NK CELLS.

dos Reis, Filipa D.; da Costa, Mariana L. ; Lobo, João; Carneiro, Isa ; Brandão, Andreia ; Freitas, Rui ; Stojanovic, Ana ; Henrique, Rui ; Jerónimo, Carmen; Correia, Margareta P.

IPO Porto Research Center.

Prostate cancer (PCa) lacks therapeutic strategies for advanced forms of disease. Epigenetic mechanisms, particularly the histone methyltransferase EZH2 and its repressive H3K27me3 mark, regulate PCa development. However, their role on evasion to Natural Killer (NK) cell cytotoxicity is largely unknown. Herein, we employed epigenomic and transcriptomic analyses to evaluate EZH2-dependent mechanisms involved in the impairment of NK cell-mediated antitumor responses. Whole-transcriptome analysis of EZH2 inhibitor (EZH2i)-treated patient tissues revealed a global reprograming towards NK cell-related activation signaling pathways, with *ULBP2* being among the top enriched transcripts, as well as several activation and cytotoxicity markers. CUT&RUN revealed H3K27me3 enrichment at the *ULBP2* loci, which was reduced upon EZH2i treatment. Analysis of patient ATAC-seq and ChIP-seq datasets confirmed low chromatin accessibility and high H3K27me3 deposition.

Our results support the hypothesis of an EZH2i-driven epigenetic reprogramming in PCa towards an increased NK cell recognition.

Subject area: In vitro/ 3D

P19. DISCOVERY AND TRANSLATIONAL VALIDATION OF IMMUNOTHERAPY TARGETS IN PEDIATRIC POSTERIOR FOSSA EPENDYMOMA.

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Vall d'Hebron Institut de Recerca (VHIR) in the Childhood Cancer and Blood Disorders Group, Neural Tumors Laboratory.

Pediatric posterior fossa ependymomas, particularly the PFA subgroup, are aggressive tumors with high relapse rates and limited therapeutic options. Current treatments involve surgery and radiotherapy and are associated with long-term neurotoxicity, underscoring the need for safer and more targeted approaches.

This project integrates transcriptomic profiling with patient-derived tumor models to identify actionable immunotherapy targets for PFA ependymomas, focusing on cell-surface antigens suitable for NK cell–based and CAR-engineered therapies. Differential gene expression analyses of public datasets comparing ependymoma subtypes with normal brain tissue were performed, prioritizing tumor-specific targets with minimal healthy tissue expression. A systematic literature review identified surface antigens targeted in CAR-based therapies for central nervous system tumors and evaluated their relevance in PFA ependymoma.

Patient-derived in vitro spheroid cultures and in vivo orthotopic xenograft models are being developed to validate candidate targets and to assess adoptive immunotherapy using unmodified NK cells by evaluating cytotoxic activity against PFA tumors.

Subject area: Other(Please specify your area in the comments section)

P20. HLA-A*11 AND ITS PROTECTIVE ROLE IN BLADDER CANCER TREATED WITH BGC IMMUNOTHERAPY.

Hita Ruiz, Alicia; Rosique Aznar, Claudia ; Ruiz Lorente, Inmaculada ; Gimeno Arias, Lourdes; López-Abad, Alicia; López Cubillana, Pedro; Campillo Marquina, Jose Antonio ; Galindo, Francisco; Martínez Sanchez, María Victoria; Martínez Hernández, María Dolores; Minguela Puras, Alfredo.

Virgen de la Arrixaca University Clinical Hospital, Murcia.

Introduction: Bacille Calmette-Guerin (BCG) is the immunotherapy of choice for high-risk non-muscle invasive bladder cancer (BC), although recurrence occurs in 50% of patients and 20% progress to advanced stages. **Methods:** Predictive value of HLA class-I allotype was evaluated in 325 BC patients treated with BCG. Proliferation, cytotoxicity, production of cytokines and intracellular nitric oxide were assessed in peripheral blood mononuclear cells after stimulation. **Results:** HLA-A*11 was associated with favorable outcomes after BCG therapy (longer progression-free and overall survival (OS)). However, while the OS was initially 100%, it dropped sharply 5 years after starting BCG therapy, with an unfavorable evolution thereafter. In contrast, HLA-A*11 was associated with unfavorable outcome in patients with muscle invasive BC no treated with BCG. **Conclusion:** The benefits of extending BCG treatment or applying it to muscle invasive BC in patients with favorable HLA biomarkers (HLA-A*11) should be confirmed in well-designed multicenter clinical trials.

Subject area: Other(Please specify your area in the comments section)

P21. SANKOMA: PHASE I/II OPEN-LABEL CLINICAL TRIAL OF ACTIVATED AND EXPANDED NK CELL THERAPY IN CHILDREN, ADOLESCENTS, AND YOUNG ADULTS WITH SARCOMAS.

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Pediatric sarcomas are aggressive tumors with limited therapies, especially for metastatic or refractory disease.The lack of new drug approvals underscores the need for novel treatments. Adoptive cell therapy using natural killer cells activated and expanded with feeder cells (NKAEs) shows promise.Our preclinical studies showed NKAEs effectively target sarcoma cells.The SANKOMA trial (NCT05952310) is a phase I/II study evaluating safety of haploidentical NKAEs plus IL-2 after chemotherapy and low-dose radiotherapy in pediatric and young adult patients with high-risk or refractory sarcomas.

Six of ten planned patients have been enrolled, all males averaging 17.7 years with diverse sarcoma subtypes. One patient achieved complete response, three had stable disease, and two showed progression at day 30 post-first infusion. NK cell infusions were safe and feasible, with no severe adverse events or treatment-related deaths. The trial also studies biomarkers to optimize NK therapies, supporting further development of NKAEs for pediatric sarcoma treatment.

References

[1] Shimasaki, Noriko, et al. NK cells for cancer immunotherapy. Nature Reviews Drug Discovery, vol. 19, no. 3, 2020, pp. 200–218,https://doi.org/10.1038/s41573-019-0052-1.

[2] Vela M, et al. Anti-CXCR4 antibody combined with activated and expanded Natural Killer Cells for sarcoma immunotherapy. Frontiers in Immunology, vol. 10, 2019, https://doi.org/10.3389/fimmu.2019.01814.

[3] Pérez-Martínez A, et al. A phase I/II trial of interleukin-15-stimulated natural killer cell infusion after haplo-identical stem cell transplantation for pediatric refractory solid tumors. Cytotherapy. 2015;17(11):1594–603. Fernández L, et al., Activated and expanded natural killer cells target osteosarcoma tumor initiating cells in an NKG2D–NKG2DL dependent manner, Cancer Letters (2015), doi: 10.1016/j.canlet.2015.07.042.

[4] Fernández L, et al. Memory T cells expressing an NKG2D-car efficiently target osteosarcoma cells." Clinical Cancer Research, vol. 23, no. 19, 2017, pp. 5824– 5835, https://doi.org/10.1158/1078-0432.ccr-17-0075.

[5] Fernández L, et al., Activated and expanded natural killer cells target osteosarcoma tumor initiating cells in an NKG2D–NKG2DL dependent manner, Cancer Letters (2015), doi: 10.1016/j.canlet.2015.07.042.

Subject area: Clinical Trial

Keywords: Pediatric sarcomas, metastatic, adoptive cellular therapy, Natural Killer cells activated and expanded, stable disease, progression.