significativamente a sobrevida livre de eventos e as respostas ao tratamento de malignidades hematológicas em comparação ao tratamento padrão (Locke, 2021; Ecklund, 2024), com uma redução de risco notável, além do custo-benefício do tratamento (Perales, 2022). No entanto, a alta incidência de eventos adversos graves, incluindo síndrome de liberação de citocinas e eventos neurológicos, representa um desafio significativo e destaca a necessidade de um monitoramento rigoroso e estratégias eficazes de manejo (Ali, 2024; Sanderson, 2024). **Conclusão:** A terapia CAR-T Cell tem revolucionado o tratamento de doenças onco-hematológicas oferecendo uma nova perspectiva para os pacientes. Os avanços na área da engenharia genética e da imunoterapia têm permitido o desenvolvimento de células T modificadas para atacar células cancerígenas específicas, aumentando a eficácia do tratamento e reduzindo os efeitos colaterais. Embora ainda existam desafios a serem superados, como a necessidade de melhorar a eficácia e a segurança da terapia, os avanços na terapia CAR-T são promissores, e com pesquisa contínua, espera-se maior acessibilidade e eficácia, reforçando a luta contra o câncer.

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TARGETING PRC2 ENHANCES THE ANTITUMOR CYTOTOXIC CAPACITY OF ANTI-CD19 CAR-T CELLS AGAINST HEMATOLOGICAL MALIGNANCIES

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Chimeric Antigen Receptor (CAR) T cell therapy was adopted as a clinical modality for patients with relapsed/refractory hematological malignancies. Despite the clinical efficacy of CAR-T cell therapy, a considerable fraction of patients still relapses during the first months following CAR-T cell infusion. The limited CAR-T cell efficiency is thought to relate to epigenetic mechanisms involved in T-cell suppression and dysfunction. Here, screening of multiple epigenetic inhibitors revealed that targeting PRC2 consistently enhanced the cytotoxic/effector phenotype of CD8 T-cells. Notably, PRC2 inhibition promoted the differentiation of GZMB+ effector memory 19BBζ CAR-T cells and enhanced their antitumor activity both in vitro and in vivo. Consistent with their long-lasting antitumor activity, PRC2-inhibited 19BBζ CAR-T cells did not exhibit any signs of dysfunctionality/exhaustion. Furthermore, TCR restimulation along with PRC2 inhibition of patient-derived anti-CD19 CAR-T cells also induced the development of GZMB + effector memory cells and elicited potent antitumor responses against CD19+ Daudi cells. In line with this, the-gene signature derived from in-house PRC2-inhibited 19BBζ CAR-T cells was enriched in tisagenlecleucel (tisa-cel) BBζCAR-T cell therapy responders with large B-cell lymphoma. Collectively, our results demonstrated that targeting PRC2 may be a promising approach to enhance a functional effector program in CAR-T cells against hematological malignancies.

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FATAL CASE OF DENGUE HEMORRHAGIC FEVER DURING AUTOLOGOUS HEMATOPOIETIC STEM CELL TRANSPLANTATION

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Introduction: Dengue is a viral disease caused by an arbovirus transmitted by mosquitoes,the Aedes aegypti, which proliferates in tropical climates. Factors such as urbanization, population growth, international travel, and climate change contribute to its rapid spread. It can progress with severe complications such as hemorrhage, liver failure, and shock. In the transplant population, fever, headache, muscle, and joint pain are less common, while the chance of developing ascites and pleural effusion is higher. Transplant patients have a higher incidence of severe dengue cases and a higher mortality. Its presentation and evolution in hematologic patients, especially in those undergoing bone marrow transplant, have not been well characterized in the literature, with few reports available to date. **Objective:** Describe a case of dengue hemorrhagic fever during autologous stem cell transplantation. Method: Review of medical records and literature. **Result:** A 58-year-old woman from São Paulo, Brazil, with hypertension and diabetes, was diagnosed in January 2023 with Anaplastic Large Cell Lymphoma ALK-negative. Received first-line treatment with 6 cycles of CHOEP and achieved complete response after 4 cycles, being referred for Autologous Hematopoietic Stem Cell Transplantation. Stem cell mobilization was done with GCSF, and hematopoietic progenitor cells were collected at 3.22×10e6/Kg.ECOG:0, was asymptomatic, and started conditioning with BuCyE. On day -5, she had an isolated fever spike without neutropenia or other symptoms.On day -2, she developed headache, abdominal pain, nausea, and diarrhea, with a positive NS1 antigen result, intravenous fluid therapy was initiated, and close monitoring for alarming symptoms of dengue fever commenced. Another fever episode on day -1, with lower back pain, abdominal pain, and elevated transaminases. On day 0, received hematopoietic progenitor cell infusion without complications, but maintained nausea, diarrhea, and abdominal pain. On day +1, she had another fever episode, gastrointestinal symptoms, and complained of arthralgia. Cefepime was started for febrile neutropenia, and cultures were collected. On day +2, due to worsening abdominal pain, an abdominal CT scan was performed, showing diverticulitis. She was transferred to the ICU due to hematuria and hematochezia.