A study from IBiS develops a more effective CAR-T therapy for the treatment of multiple myeloma

- **This study focuses on developing an improved version of CAR-T cell therapy, called CARTemis-1, specifically designed to more efficiently target a key protein in multiple myeloma cells known as BCMA.**

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The "**Cellular Therapy and New Therapeutic Targets in Onco-Hematology**" research team at the **Institute of Biomedicine of Seville (IBiS),** led by **Dr. José Antonio Pérez Simón** in collaboration with other international centers, has conducted a study centered on developing an improved version of CAR-T cell therapy, called CARTemis-1. This therapy is specifically designed to more efficiently target a key protein in multiple myeloma cells, known as BCMA.

Although current treatments have shown good results, many patients relapse, and the presence of soluble BCMA in the blood can weaken the therapy's effectiveness. To address this, CARTemis-1 was optimized to resist the effects of this soluble BCMA protein, allowing it to maintain its tumor-killing ability even in the presence of high concentrations of the protein.

The study, published in the scientific journal *Cellular Oncology*, not only improves the resistance of CARTemis-1 but also optimizes its design to enhance its ability to attack tumor cells. According to **Belén Sierro Martínez**, the study's lead author and a researcher in **IBiS**'s "**Cellular Therapy and New Therapeutic Targets in Onco-Hematology"** group, "CARTemis-1 incorporates a more flexible structure that enables CAR-T cells to access myeloma cells more easily and destroy them more efficiently." This improved approach resulted in increased production of anti-tumor cytokines and a more potent cytotoxic effect.

What is CAR-T therapy, and why is this advancement important?

CAR-T cell therapy is one of the groundbreaking innovations in cancer immunotherapy. It involves the genetic modification of a patient's T cells (a type of immune cell) to enable them to recognize and destroy tumor cells. In the case of multiple myeloma, CAR-T cells are designed to target a specific protein, **BCMA**, present on the surface of myeloma cells.

However, while CAR-T therapy has shown promising results in patients with advanced multiple myeloma, the treatment is not without limitations. One of the main challenges is relapse, which occurs in many patients due to a decrease in the therapy's efficacy over time. Additionally, the presence of a soluble form of the BCMA protein in the blood can reduce CAR-T cells' ability to attack tumor cells.

To overcome these limitations, the IBiS research team developed CARTemis-1, an optimized version of CAR-T cells specifically targeting the BCMA protein. CARTemis-1 was designed to resist the effects of soluble BCMA, allowing it to maintain its tumor-killing capacity even in the presence of high concentrations of this protein in the blood.

Furthermore, CARTemis-1 incorporates a more flexible design, improving its ability to access myeloma cells and destroy them more efficiently. This enhanced flexibility not only facilitates the binding of CAR-T cells to tumor cells but also results in increased production of anti-tumor cytokines—key proteins in the immune system's fight against cancer—and a more potent cytotoxic effect. As a result, CARTemis-1 has demonstrated significantly greater effectiveness in preclinical studies compared to previous CAR-T cell versions.

Improved manufacturing process: keys to a more efficient product

One of the significant challenges in developing CAR-T therapies is the manufacturing process. The team succeeded in incorporating a series of improvements into the production process, enhancing the quality of CAR-T cells by generating more memory cells, which are essential for a long-lasting immune response, and reducing exhaustion markers that typically affect the performance of these cells.

The production of CARTemis-1, under Good Manufacturing Practice (GMP) conditions, meets all regulatory requirements, paving the way for its use in clinical trials. "Thanks to its optimized design and its ability to resist soluble BCMA, CARTemis-1 has great potential to provide a more effective and durable treatment option for patients with multiple myeloma. This revolutionary therapy, developed by our research group, has already been approved by the Spanish Medicines Agency. A Phase I/II clinical trial using this new version of enhanced CAR cells will begin in early 2025 at the **Virgen del Rocío University Hospital in Seville**," explains **Dr. Estefanía García Guerrero**, Program Leader for CAR Therapy within **IBiS**'s "**Cellular Therapy and New Therapeutic Targets in Onco-Hematology**" group.

The development of CARTemis-1 represents a significant advancement in the field of immunotherapy for multiple myeloma. By improving both the design of CAR-T cells and the manufacturing process, the therapy not only becomes more effective in attacking tumor cells but is also more resilient to barriers limiting the efficacy of current treatments.

The study was funded by the Carlos III Health Institute (ISCIII) and the Ministry of Science and Innovation, with its clinical translation carried out in collaboration with the Andalusian Network for the Design and Translation of Advanced Therapies.

Reference: *Next-generation BCMA-targeted chimeric antigen receptor CARTemis-1: the impact of manufacturing procedure on CAR T-cell features*

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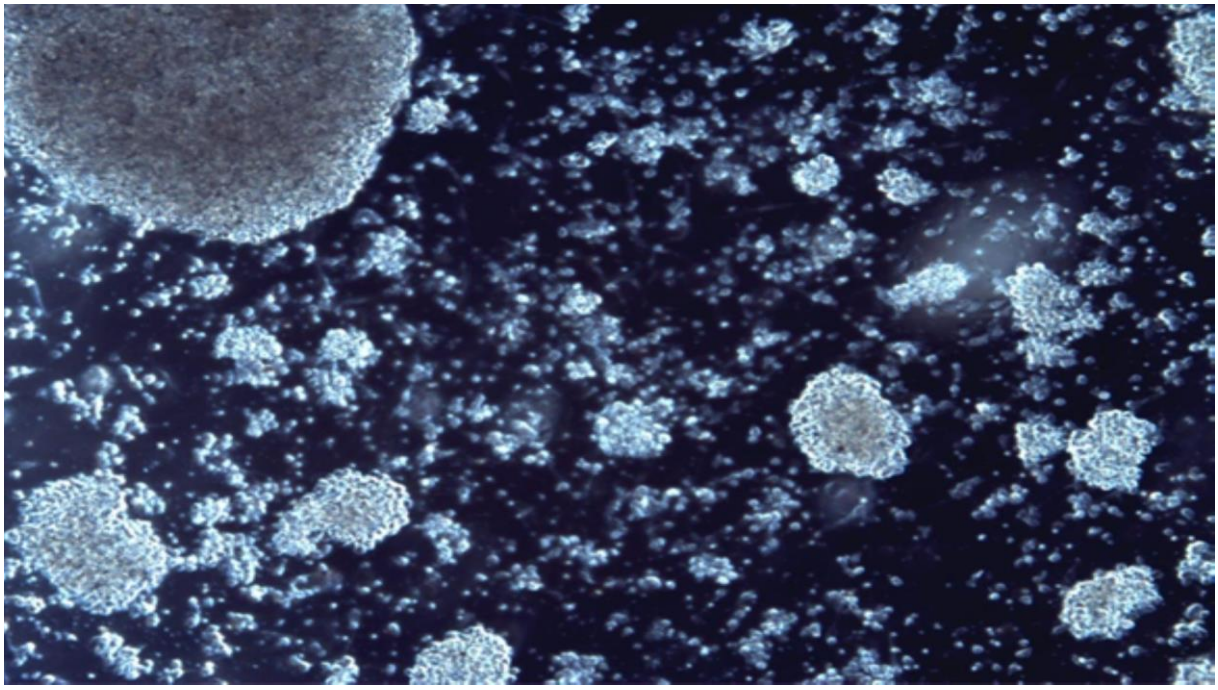

Image 1 *- CAR T cells generated from a patient's blood under GMP standards.*

About IBiS

The Institute of Biomedicine of Seville (**IBiS**) is a multidisciplinary center focused on carrying out fundamental research on the causes and mechanisms of the most prevalent pathologies in the population and the development of new methods to diagnose and to treat diseases.

IBiS is made up of 41 consolidated groups and 39 affiliated groups led by researchers from the University of Seville, the Spanish National Research Council (CSIC) and the Virgen del Rocío and Virgen Macarena University Hospitals and Valme, organized around five thematic areas: Infectious Diseases and Immune System,

Neurosciences, Onco-hematology and Genetics, Cardiovascular Pathology, Respiratory / Other Systemic Pathologies and Liver, Digestive and Inflammatory Diseases.

IBiS depends institutionally on the Department (Consejería) of Health and Consumption of the Junta de Andalucía; the Andalusian Health Service (SAS); the Department (Consejería) of University, Research and Innovation; the University of Seville and the Spanish National Research Council (CSIC). It is managed by the Foundation for the Management of Health Research in Seville (FISEVI).

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