A new approach using memory cells opens possibilities in the fight against drug-resistant bacterial infections

- **A study from the Institute of Biomedicine of Seville (IBiS) develops an innovative approach based on the adoptive transfer of memory cells to combat infections caused by multidrug-resistant Acinetobacter baumannii, a global priority pathogen according to the WHO.**

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Antibiotic resistance is one of the most serious challenges in modern medicine. Among the most feared pathogens is Acinetobacter baumannii, a highly resistant bacterium responsible for severe infections, particularly in intensive care unit patients. In May 2024, the World Health Organization (WHO) once again included A. baumannii on its list of priority multidrug-resistant bacteria, emphasizing the urgency of developing new treatments against this pathogen. The research group **"Bacterial Resistance and Antimicrobials"** at the **Institute of Biomedicine of Seville (IBiS)**, led by **Dr. José Miguel Cisneros** and **Dr. María Eugenia Pachón Ibáñez**, has tackled this issue with a pioneering approach based on the adoptive transfer of memory lymphocytes, potentially changing the way infections caused by this type of bacteria are treated.

The emergence and persistence of infections by multidrug-resistant bacteria (MDR), such as *A. baumannii*, pose a significant global public health challenge. This bacterium, particularly common in nosocomial (hospital-acquired) infections, can acquire and transfer resistance genes, severely limiting therapeutic options. Additionally, these infections primarily affect vulnerable patients, such as those in intensive care units, and are associated with an extremely high mortality rate.

Since the WHO first classified *A. baumannii* as a critical pathogen in 2017, no significant advances have been made in the introduction of new effective drugs to treat the infections it causes. Despite global efforts in research, development, and innovation (R&D&I), the situation persists, underscoring the urgency of finding alternative and effective solutions.

A promising alternative

This study, led by the IBiS group and published in the *International Journal of Molecular Sciences*, proposes an innovative approach based on the adoptive transfer of memory lymphocytes as an alternative to conventional antibiotic treatment. This method involves using memory B cells and CD4+ T cells, which are specialized immune cells that "remember" how to combat previous infections. “The goal is for these cells to recognize and eliminate the bacterium more effectively and durably,” explains **Dr. María Eugenia Pachón-Ibáñez.**

The experiments were conducted in a mouse pneumonia model caused by *A. baumannii* strains with different susceptibility phenotypes: one sensitive and another resistant to colistin, one of the few antibiotics still used as a last resort. The study's results showed that a single dose of memory cells (B or CD4+ T) was as effective as a three-day treatment with sulbactam, a clinically used antibiotic, in reducing bacterial loads in the lungs and blood.

In the case of the MDR and colistin-resistant strain, the adoptive transfer of memory cells was also effective, significantly reducing the number of bacteria in the lungs and improving bacterial clearance from the blood compared to other treatments, such as tigecycline, which is commonly used for these infections. Furthermore, the memory cell treatment increased mouse **survival** rates similarly to antibiotics, suggesting it could be a viable alternative for human patients.

These results are promising and suggest that the adoptive transfer of memory cells could become an effective therapeutic strategy against infections caused by multidrug-resistant *A. baumannii*. As infections caused by multidrug-resistant pathogens continue to rise, finding new therapeutic approaches is crucial. The advantage of memory cell transfer is that it could potentially eliminate the need for high doses of antibiotics, reducing side effects in patients and the risk of further antibiotic resistance development.

“A single dose of memory B or CD4+ T cells was as effective as a three-day treatment with sulbactam in eliminating bacterial loads,” comments Dr. Pachón-Ibáñez.

Although these preclinical results are encouraging, further research is needed to evaluate the potential of this therapy in combination with antibiotics. The hypothesis is that combining both treatments could further enhance efficacy, decrease mortality, and reduce bacterial loads more quickly and efficiently.

Next steps: clinical trials

The next step will be to test this approach in controlled clinical trials to determine whether the adoptive transfer of memory cells can be equally effective in humans. “These promising results will be further investigated, requiring additional studies to assess the potential of combining memory cell and antibiotic therapies to enhance antibiotic efficacy,” adds **Dr. Pachón**. “If this hypothesis is confirmed, the next step

would be to conduct randomized controlled clinical trials to determine whether this new approach could improve outcomes for infections caused by MDR *A. baumannii* strains."

The research team will also explore whether this treatment can be effective against other multidrug-resistant bacteria, such as *Klebsiella pneumoniae* or *Pseudomonas aeruginosa*, which are also classified as critical threats by the WHO. This could open new treatment avenues for a significant diversity of nosocomial pathogens.

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Image 1 – From left to right: Soraya Herrera Espejo and María Eugenia Pachón Ibáñez

***Reference**: Could the adoptive transfer of memory lymphocytes be an alternative treatment for Acinetobacter baumannii infections? https://doi.org/10.3390/ijms251910550*

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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