Emilio Luis Malchiodi

Emilio Luis Malchiodi is scientist and immunologist from Argentina (Emilio Malchiodi | LinkedIn). He holds the position of Professor Titular in Immunology at the Faculty of Pharmacy and Biochemistry (FFyB), University of Buenos Aires (UBA). He also is Superior Researcher at the National Research Council of Argentina (CONICET). His research contributions extend to various areas, including Chagas disease, leishmaniasis, and structural immunology. Emilio has recently received the prestigious "Cesar Milstein Prize" for Research in Biotechnology with impact in Health from Pablo Cassará Foundation-CONICET. Emilio is also a Professor of Immunology in the International Master in Biomedical Sciences (IMBS) program of the UBA and the Albert Ludwigs University, Freiburg, Germany.

Emilio is the President of the Latin American and Caribbean Association for Immunology (ALACI), the regional association of the IUIS. He has been spearheading the 14th ALACI meeting which will take place 4-8 November 2024 in Buenos Aires, Argentina.

What motivated you to focus on the development of vaccines against Chagas disease and Leishmaniasis?

At the beginning of my career, I was driven by the health challenges faced by people in underserved regions. Chagas disease is a neglected tropical infectious disease in Latin America where ~10,000,000 individuals are infected (56,000 new infections/year). Chagas disease is currently endemic to 21 Latin-American countries and has become a global concern because of globalization and mass migration of chronically infected individuals. Thus, Chagas disease is now reported in 19 non-endemic countries (*e.g*. 120,000 and 1,200,000 infected people are living in Europe and the United States, respectively). In Argentina, chronic Chagas disease remains a significant concern, with approximately 1.3 million individuals infected and an estimated 1,000 newborns affected annually through vertical transmission. In many Latin American countries, endemic regions for both Chagas disease and leishmaniasis overlap, which made accurate differential diagnosis a major challenge during my PhD studies. My work with different diagnostic antigens ultimately led me to explore potential vaccine candidates focusing on recombinant antigens combined with novel adjuvants, DNA delivery systems such as bacteria, viruses, virus-like particles (VLPs) and nanoparticles, and, lately, mRNA-based vaccines. CRUZIVAX, the vaccine prototype we have been working on, is currently being validated up to first-in-human studies (www.cruzivax.eu). We are also evaluating vaccine candidates for Leishmaniasis, a parasitic disease causing mucosal and visceral damage with strong impact in Latin America but also in other tropical and subtropical regions of the world; and Yellow and Zika fevers, two mosquito-transmitted viral diseases, which cause death and congenital malformations.

Could you share any recent breakthroughs or challenges in this area?

Chagas disease is a neglected tropical disease transmitted by

blood-sucking insects, and almost every mammal can serve as a reservoir for the causative parasite, *Trypanosoma cruzi*. Acute Chagas infection is often mild, with symptoms that can be easily mistaken for other infections. However, the parasite persists, leading to a chronic phase that can affect the heart and cause conditions such as megavisceras. When treated during the acute stage, the drugs Nifurtimox and Benznidazole—discovered over 60 years ago—are effective, but their efficacy is significantly reduced in the chronic phase. These drugs require administration for 60 to 90 days and are associated with numerous adverse effects, often leading to treatment discontinuation. To date, no vaccine candidate has been tested in humans.

We are currently leading the CRUZIVAX Project (Horizon2020 #815418), aimed at the preclinical and clinical validation of a needle-free, intranasal prophylactic and therapeutic vaccine against Chagas disease. The vaccine is based on a chimeric trivalent antigen and the novel adjuvant cyclic-di-AMP. A consortium of 12 laboratories, including the LAVAX and LIME labs at UBA, Argentina, and 10 other laboratories across Europe, is collaborating on this effort. The project involves GLP and GMP production of vaccine components, preclinical validation in various animal models, toxicology studies, preparation, and execution of a Phase I clinical trial, as well as health economics and demand assessment studies.

Could you briefly explain your work around the Major Histocompatibility Complex class I and II molecules?

During and after my postdoctoral studies at the Center for Advanced Research in Biotechnology, University of Maryland, USA, I have conducted detailed structural and biophysical studies on Natural Killer cell receptors and its ligand MHC class I molecules, as well as on bacterial superantigens (SAgs) and their interactions with TCR and MHC-II molecules. Superantigens are bacterial exotoxins capable of triggering a massive release of interleukins, leading to Toxic Shock

Syndrome and potentially death. SAgs have the capacity to induce apoptosis or necrosis in antigen-presenting cells by binding to MHC class II molecules. Several research groups are investigating these toxins as potential immunotherapies for cancer treatment. Our studies have evaluated the ability of modified bacterial SAgs to inhibit the proliferation of both Hodgkin and non-Hodgkin B cell lymphomas. Our results have shown that SAgs significantly decreased cell viability compared to the basal control, and this effect was synergistic with vincristine treatment, allowing for a three-order reduction in the required vincristine treatment dose. In addition to their profound impact on cells of the adaptive immune system, we are now investigating how bacterial superantigens interact with cells of the innate immune system, such as macrophages, neutrophils, and eosinophils.

The mouse NK cell receptors Ly49 play a crucial role in detecting virus-infected and cancerous cells, leading to their elimination. NK cells use Ly49 receptors to interact with MHC-I molecules on target cells to determine whether they are infected or transformed. For the first time, we crystallized and determined the three-dimensional structure of the stalk region of a Ly49 receptor and analysed its interaction with MHC-I molecules.

Can you describe your role in the development of new technologies or innovations in your field?

I have developed a platform based on Surface Plasmon Resonance (SPR) to analyse molecular interactions, a key requirement for approving therapeutic biosimilars for human use. Reducing the cost of immunotherapy is essential for low-income countries, and biosimilars play a crucial role in making these treatments more affordable. We collaborate with pharmaceutical companies in the development and implementation of biosimilar immunotherapeutic drugs by assessing the interaction between these drugs and their target molecules or cells using SPR (Biacore). Our contributions include the development of

biosimilars such as TNF-alpha inhibitors (e.g., Etanercept) for treating rheumatic diseases like moderate to severe rheumatoid arthritis and psoriatic arthritis, colony-stimulating factors (e.g., Pegfilgrastim) for neutropenia, IFN-β for relapsing forms of multiple sclerosis, and human parathormone (e.g., Teriparatide) for osteoporosis. Additionally, we are developing a microfluidic Lab-on-a-Chip platform based on the Biacore system for process testing and monitoring in medical diagnostics and pharmaceuticals.

What role do you play as the Director of the Institute of Humoral Immunology (IDEHU)?

I have been (2014-2024) the Director of the Instituto de Estudios de la Inmunidad Humoral (IDEHU), a research Institute focalizing in several Immunology specialties including Vaccinology, Cellular and molecular immunology, Host-pathogen interactions, Innate immunity and Inflammation, Reproductive Immunology, Diagnosis, and Diabetes. IDEHU colocalized with the Immunology Chair, where I hold the position of Full Professor since 2008. We teach Immunology to Biochemistry and Pharmacy students, and in three other undergraduate courses every year in the Faculty of Pharmacy and Biochemistry (~5,000 students) at the University of Buenos Aires (300,000 students). Additionally, I teach in three specialized postgraduate courses and one International Master Program, in collaboration with the Albert Ludwig University in Freiburg, Germany, oriented towards biologists, medical doctors, biochemists, pharmacists, biotechnologists, and related professionals. The incorporation of students, graduates, and postdoctoral researchers in IDEHU laboratories is highly active, supported by a robust PhD program. Over the years, our PhD program has led to the graduation of more than 60 PhD students in Immunology.

Congratulations on the ALACI Presidency! What do you aim to achieve during your term?

I have several goals and objectives including disseminate Immunology in our region as part of the IUIS vision to achieve "Immunology without Borders"; organize the triennial Congress in Buenos Aires 4-8 November; organize and fund regional courses; promote teaching of Immunology through undergraduate and postgraduate courses and training of students and young researchers; and contribute to improving health in the region through the transdisciplinary and preventive nature of Immunology and participation in public campaigns.

From 2022 to 2024, in collaboration with the Argentinian Immunology Society and the ALACI Executive Committee, my key activities included the launch of a new ALACI website (https://alaci.org) and the activation of social media channels. I also played a central role in organizing the 14th Latin American and Caribbean Immunology Congress (Buenos Aires, 4-8 November 2024), which will feature three pre-congress courses and a Workshop on Abstract Writing and Oral Communication Skills. Additionally, I organized activities for the International Day of Immunology (29 April 2024), which led Argentina to win the 1st prize awarded by the IUIS. Furthermore, we co-organized and participated in graduate courses in Immunology in Chile (2023), Mexico (2024), and Argentina (FOCIS-ALACI 2024), and contributed to organizing and participating in the ALACI Symposium at the FOCIS 2024 Meeting in San Francisco (June 2024).

The 14th ALACI meeting is soon. Could you share the main themes of the meeting?

I am confident that the ALACI Congress will be a great success, with more than 100 top tier invited speakers from around the world. Notable names include Miriam Merad, Rino Rappuoli, Rita Carsetti, Adriana Gruppi, Gabriel Nuñez, Alberto Mantovani, Ana María Lennon-Duménil, Elene Piaggio, Andrea Carfi, Alexis Kalergis, Diane Mathis, Ricardo Gazzinelli, Maria L. Alegre, Juan C. Zuñiga-Pflücker,

Christophe Benoist, Rudolf Valenta, Sebastian Amigorena, Federica Sallusto, Laura McKay, and Gabriel Rabinovich, to name just the keynote speakers. All the invited speakers have demonstrated a strong commitment to attending the event in Buenos Aires, generously covering their own travel expenses.

Best of luck for November! What challenges have you faced as the President of the ALACI meeting?

Organizing a congress is always a complex task, and much of the responsibility falls on the Executive Committee. However, the greatest challenge we faced was securing the necessary funding to cover the Congress expenses. In Latin America, organizing an international congress of this scale requires over $200,000, and it has been particularly difficult to find sponsors willing to commit the needed funds, due to Argentina's challenging economic situation. Despite this, the Executive Committee worked tirelessly to explore various funding avenues, navigating the complexities of the financial environment.

Thankfully, the IUIS Executive Committee has been incredibly supportive, providing generous assistance at a critical moment. Moreover, the commitment of our invited speakers has been invaluable; many of them agreed to attend with minimal financial support from the Organizing Committee, demonstrating their dedication to the success of the event. This collective effort has been instrumental in overcoming the financial hurdles.

Interview by Bonamy (Bon) Holtak