SAIC VIII LECTURE *Friday, November 18, 9-10 hs*
Chair: Dr. Hernán Farina

DISSEMINATED CANCER CELL DORMANCY: A HOMEOSTATIC SEED AND SOIL PARTNERSHIP

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Increasing evidence shows that cancer cells can disseminate from early-evolved primary lesions much sooner than the classical metastasis models predicted. Here we reveal at a single-cell resolution that mesenchymal- and pluripotency-like programs coordinate dissemination and a long-lived dormancy program of early disseminated cancer cells (early DCCs). Using various in vitro and in vivo genetically engineered mouse models of metastasis, single-cell RNA sequencing, and human sample analysis, we reveal how in early breast cancer lesions and early DCCs the transcription factor ZFP281 induces a permissive state for heterogeneous mesenchymal-like (M-like) transcriptional programs. This program is further sustained by signals derived from tissue resident macrophages in the lung. These programs also carry a dormancy signature and are absent in proliferative primary tumors and metastasis. Importantly, the absence of the M-like signatures in human breast tumors correlates with high-risk recurrence. FGF2 and TWIST1 induce ZFP281 expression, and the latter transcription factors cooperate to induce the M-like state. ZFP281 not only controls the early spread of cancer cells but also locks early DCCs in a dormant state by preventing the acquisition of an epithelial-like proliferative program and consequent metastasis outgrowth, which is associated with the downregulation of CDH11 and upregulation of CDH1. We identify ZFP281 and the M-like dormancy program as drivers of early dissemination and barriers that early DCCs must overcome to initiate metastatic outgrowth. This dormancy program is further reinforced by homeostatic tissue resident macrophages that suppress metastatic reactivation.

SAI IV LECTURE *Friday, November 18, 19 hs*
Chair: Dr. Emilio Malchiodi

HISTORICAL REVIEW IN THE CELEBRATION OF 50 YEARS OF ARGENTINIAN SOCIETY OF IMMUNOLOGY (SAI) 1972-2022

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The Argentine Society of Immunology (SAI) was created in 1972 and its first president was Dr Alois E. Bachmann, a physician and Professor of Microbiology and Bacteriology at the Faculty of Medical Sciences of the University of Buenos Aires, and its vice-president was Dr Christiane Dosne-Pasqualini a Doctor in Experimental Medicine graduated from McGill University in Montreal, Canada who was a CONICET researcher at that time. The subsequent year, Dr Pasqualini was appointed president of the Argentine Society of Immunology. At the moment of its foundation, our society had only 71 members. Today the Argentinean Society of Immmunology gathers more than 500 members from 65 research institutes and 16 hospitals throughout the country, having close ties with different public universities in our country and abroad. Perhaps anticipating this growth, Dr Bachmann called this foundational milestone an “immunological hatching”. At that time, the meetings of immunologists were held in the context of the Immunology Club. Among those present were the Argentinian Clinical Research Society members such as Dr Pasqualini, Dr María Marta Elizalde, Dr Marta Braun, Dr Clelia Riera, Dr Elsa Vottero de Cima, Dr Alicia Mazzoli, and Dr Bachman, Dr Londner, Dr Morini, Dr Manni, and Dr Ricardo Margni, along with youngest researchers such as Alberto Fossati, Silvia Hajos, Martín Isturiz, and Leonardo Fainboim.

Thus, in 1972, the First Argentinian Congress of Immunology was held, and the Latin American Association of Immunology (ALAI) was created. In the 1980s, the SAI members were internationally recognized as part of international societies such as the Latin American Immunology Association (ALAI, currently ALACI due to the incorporation of Caribbean Immunology Societies) and IUIS (International Union of Immunological Societies).

The words of one of the pioneers Dr Alberto Fossati summarize the role of the SAI in our country: *“The scientific activity carried out by the SAI throughout this half-century of life has certainly been intense. It always required a great effort from its leaders and partners who had to face critical situations -especially in the economic or political sphere- that were solved while always protecting our society. This commitment and devotion allowed for the continued growth and quality of Immunology in science and technology in our country. Over the years, our*

society has become a forum for exchanging knowledge and far-reaching collaborative work that fills us with satisfaction".

Currently, the SAI has an outstanding responsibility in the dissemination and debate of scientific knowledge through numerous courses, sponsorships, seminars, webinars, and conferences, as well as participating in the spread of articles in different media. The broad representation of women among its members and on its board of directors is also noteworthy. SAI's contribution to the society is unquestionable and aims to democratize knowledge, creating bridges between researchers and health care professionals by answering the questions raised concerning clinical cases involving immunology. This 50-year tour of the Argentine Society of Immunology prepares us to face new challenges that involve other scenarios in which the immune system will be a key player.

The commemoration lectureship of the 50th anniversary of the Argentinian Society of Immunology will be presented by Dr Gabriel A. Rabinovich. Gabriel is an active, outstanding, and generous member of our society with a solid commitment to scientific progress that widely embrace SAI's spirit. His distinguished career has been devoted to immunology and glycobiology, contributing enormously to our society in several aspects. During his career, Gabriel has been recognized worldwide as a pioneer in glycoimmunology, making relevant discoveries on galectin-glycan interactions and their impact in the regulation of immune responses. His findings, reflected in more than 300 publications in leading journals, provide novel mechanistic insights and therapeutic targets in a broad range of pathophysiologic settings including cancer, autoimmune inflammation, and infection.

Text by: Laura Cervi, Griselda Moreno, and Mariana Salatino

A SWEET ADVENTURE FROM AN UNEXPECTED DISCOVERY TOWERS THE DESIGN OF NOVEL THERAPEUTIC AGENTS IN AUTOIMMUNITY, INFECTION AND CANCER

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SAFIS II LECTURE *Friday, November 18, 18-19 hs*
Chair: Graciela Cremaschi.

OBESITY-STRESS INTERRELATIONSHIP. ASSOCIATED COGNITIVE AND METABOLIC IMMUNE DISORDERS

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Chronic exposure to stressful situations and consumption of hypercaloric diets are common conditions in modern society and have been identified as predisposing factors for different disorders. Moreover, it has been suggested that an adverse intrauterine environment may result in deleterious effects on the offspring "per se" or after exposure to a challenge later in life. In this context, we study whether exposure to prenatal stress (PS) or adult stress could lead to the development of obesity and associated metabolic, behavioral, and immune disorders. Also, we search for peripheral markers as predictors of these disorders. Taking into account the relevance of the inclusion of sex as a biological variable in research, our investigations were carried out in both males and females. We studied the effect of chronic stress (CS) in the adulthood in C57Bl/6J mice that were feed with control or high fat diet (HFD) after weaning. Results indicate that males are more susceptible than the females in modulating metabolic and cognitive functions under HFD and CS. In both sexes HFD induced weight gain, fat accumulation, insulin resistance, high cholesterol; but only males exposed to CS showed: i) impaired glucose tolerance with higher glucose levels, ii) increased IFNgamma mRNA expression in hippocampus, suggesting a greater neuroinflammatory response, iii) poorer cognitive performance related to a decrease in hippocampal and spleen BDNF mRNA expression. In addition, we analyzed the impact of PS exposure in cognitive performance and the development of obesity and metabolic alterations. In BALB/c mice, we found that PS females but not males exhibited an impairment in spatial memory in parallel with a decrease in BDNF, an increase in glucocorticoid receptors and an alteration of Th1/Th2 in the hippocampus and peripheral lymph nodes as well. Moreover, PS females were more resilient to PS metabolic consequences; but under a HFD, an increase in glucose and insulin levels and higher visceral adipose tissue mRNA expression of leptin, resistin and IL-1beta was found, suggesting a pro-inflammatory profile. In addition, they also presented an increase in body weight and adiposity and a rise in cholesterol levels. The emerging results of this research could promote the identification of new therapeutic interventions to prevent the progression and/or heritability of these disorders.