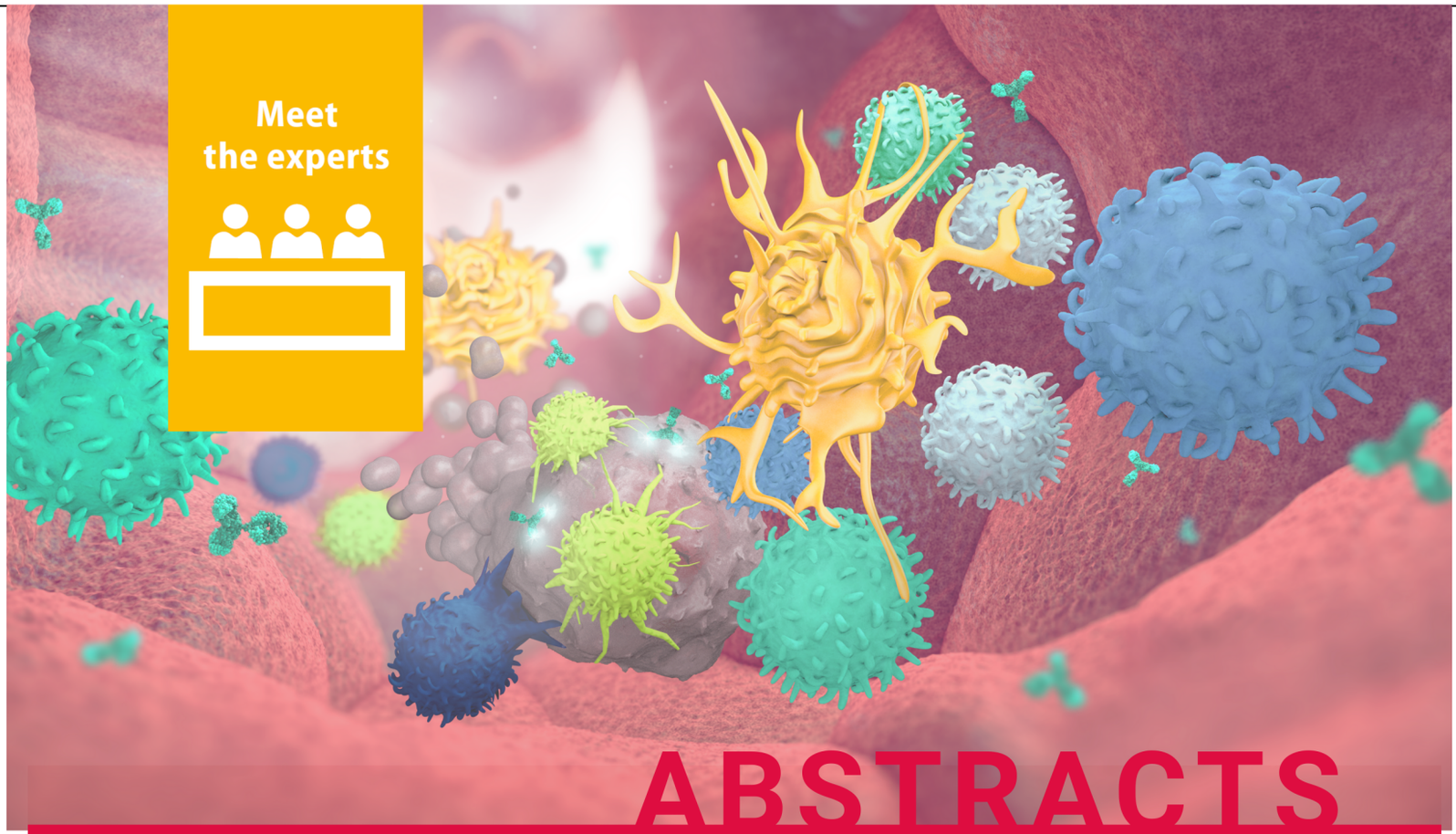

ABSTRACTS

MACS® Immuno-Oncology Days

CNIC Inflammation and Immunity Day

Friday, September 30, 2022

CNIC Auditorium

C/ Melchor Fernández Almagro, 3, 28029 Madrid

Organizing committee: David Sancho, Andrés Hidalgo

GOBIERNO DE ESPAÑA
MINISTERIO DE CIENCIA E INNOVACIÓN
Instituto de Salud Carlos III
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Miltenyi Biotec

PROGRAM

Agenda

Morning session

Chair **Gillian Dunphy** CNIC, Madrid Spain

09:00 a.m. **Registration**

09:30 a.m. ***Lipid droplets and the host–pathogen dynamic: FATal attraction?***
Albert Pol
Hospital Clínic, Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), Barcelona, Spain

10:20 a.m. ***Epigenetic licensing of tumor-promoting inflammation in pancreatic cancer***
Direna Alonso-Curbelo
Institute for Research in Biomedicine (IRB), Barcelona, Spain

11:10 a.m. ***The impact of inflammation(s) on cancer immunotherapy***
Álvaro Teijeira Sánchez
CIMA, Universidad de Navarra, Spain

12:00 p.m. **Lunch**

Afternoon session

Chair **Iván Ballesteros** CNIC, Madrid, Spain

01:20 p.m. ***Stroma-macrophage interactions***
Marc Bajénoff
CNRS, INSERM, Centre d'immunologie de Marseille-Luminy (CIML), Marseille, France

02:10 p.m. ***Aging of hematopoietic stem cells: epigenetic drift and remodeling of the niche***
Carolina Florian
Bellvitge Biomedical Research Institute (IDIBELL), Barcelona, Spain
Program for advancing the Clinical Translation of Regenerative Medicine of Catalonia, P-CMR[C], Barcelona, Spain.

03:00 p.m. ***Tissue Macrophage Heterogeneity***
Florent Ginhoux
A*STAR, Singapore
Gustave Roussy Institute, Villejuif, France

03:50 p.m. **Concluding remarks**

CNIC is the scientific organizer of this event and Miltenyi Biotec the unique sponsor.

CHAIRS

Gillian Dunphy CNIC, Madrid Spain

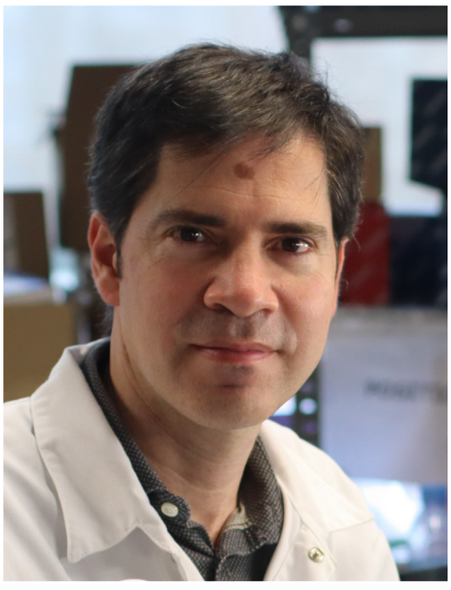
She is interested in innate immune signalling, especially in response to viral infection. This interest began with her PhD work in the University of Dundee investigating how the STING pathway is activated in response to DNA damage and viral ligands. She then moved to the Centro Nacional de Investigaciones Cardiovasculares (CNIC) where she has been working for the past 3 years, continuing to explore her favourite signalling pathways. She is currently a Marie-Curie research fellow in the lab of Dr. David Sancho, investigating the link between innate immune signalling and cellular metabolism in dendritic cells and macrophages.

Iván Ballesteros CNIC, Madrid, Spain

He has a particular interest on understanding how the functional organization of the innate immune system works. He studied biology and obtained his PhD in Pharmacology in 2012 at the Universidad Complutense de Madrid, where he characterized how the presence of immune diversity critically determines the outcome of stroke. Later, during his first postdoctoral period in Memorial Sloan Kettering Cancer Centre, he characterized the genetic programs that emerge during development and that instruct macrophage heterogeneity in tissues. For the past five years, he has worked as a postdoctoral researcher at the Centro Nacional de Investigaciones Cardiovasculares (CNIC), where he has led studies exploring the diversity of neutrophils in steady state, and discovered that tissues co-opt neutrophils fates to induce transcriptional programs. He is currently a Ramón y Cajal fellow at CNIC and continue to explore the architecture of the innate immune system to generate novel therapeutic strategies to fight disease and to develop new diagnostic or prognostic tool.

ORGANIZING COMMITTEE

Andrés Hidalgo Alonso
Goup Leader
Cell & Developmental Biology
Fundación Centro Nacional de Investigaciones Cardiovasculares Carlos III (CNIC)
Madrid, Spain



David Sancho Madrid
Group Leader
Immunobiology laboratory
Fundación Centro Nacional de Investigaciones Cardiovasculares Carlos III (CNIC)
Madrid, Spain

INTRODUCTION

These are exciting times for immunologists! In addition to the established role of immunity and inflammation in diseases such as infectious diseases, autoimmunity, allergy, immunodeficiencies, or transplant rejection, other diseases like metabolic syndrome, cardiovascular and neurological diseases or cancer are now considered immune-related disorders. The CNIC Inflammation & Immunity Day 2022 is held every two years at the Spanish National Center for Cardiovascular Research (CNIC) with the support of Miltenyi Biotec. It aims to explore different aspects of regulation, mechanisms, and consequences of immune cells in disease. This year, the symposium will focus on Immuno-oncology and Inflammation, with great speakers that cover a broad range of topics within this field.

We hope that you will enjoy the multidisciplinary program and panel discussions on the described topics, which will be led by our panel of excellent speakers!

SPEAKERS

Speakers include:

Dr. Albert Pol (Barcelona), Dr. Direna Alonso-Curbelo (Barcelona), Dr. Álvaro Teijeira Sánchez (Navarra), Dr. Marc Bajénoff (Marseille), Dr. Carolina Florian (Barcelona) and Dr. Florent Ginhoux (Singapore, Villejuif).

Let´s know them better!

Dr. Albert Pol holds a PhD from the Biochemistry and the Cell Biology Department of the Medical School from University of Barcelona (Spain). He then completed a postdoctoral stay in the laboratory of Professor Robert G Parton at IMB-UQ (Australia). He started his independent research career in 2001 through different grant awards and since 2007 he is an ICREA research professor and founded the Lipid Trafficking and Disease Team at IDIBAPS (Spain). His research focuses on lipid biology and more specifically on understanding how cells solve an intriguing dilemma: store large amounts of nutrients while reducing lipotoxicity. Since 2001 we have studied the cell biology and physiology of lipid droplets (organelles designed for eukaryotic cells to achieve this key adaptative advantage) in the context of obesity, liver regeneration, cancer, and immunity. He has authored more than 30 publications, and many in top tier journals. For his outstanding career, he is also recipient of numerous awards such as “City of Barcelona”. He combines research with teaching biology courses at the University of Barcelona.

SPEAKER

Lipid droplets and the host–pathogen dynamic: FATal attraction?

Albert Pol, Hospital Clínic, Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), Barcelona, Spain

The research by Dr. Albert Pol focuses on the cell biology and physiology of lipid droplets (LDs). Long ago considered as inert and often detrimental cytosolic fat inclusions or even defined as ectopic fat accumulation, LDs are only recently recognized as bona fide intracellular organelles with crucial functions that go beyond the storage of lipids. The research group of Dr. Pol has significantly contributed to this recognition: From the pioneering description that integral plasma membrane proteins, such as caveolins, dynamically traffic through LDs (J Cell Biol 2001), the demonstration that LDs are essential for liver regeneration (Science 2006), to the recent discovery that LDs are innate immunity hubs (Science 2020). This paradigm-shifting study revealed that LDs attract and kill intracellular bacteria.

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Dr. Alonso-Curbelo studied Pharmacy at the Universidad Complutense de Madrid and did her PhD studies, focused on melanoma, in Dr. Marisol Soengas' laboratory at the Spanish National Cancer Research Centre (Madrid, Spain). From the end of 2013 until autumn 2021, she worked as a postdoctoral researcher in Dr. Scott W. Lowe's laboratory at Memorial Sloan Kettering Cancer Center (New York, USA), where she combined innovative mouse models and functional genomics methods to study the interplay between tumor cells and their co-evolving microenvironment. One of her most impactful publications described how cancer-driver mutations and tissue damage cooperate to promote pancreatic tumorigenesis, uncovering early epigenetic alterations that contribute to this process. Since 2022, she leads the "Inflammation, Tissue Plasticity & Cancer" group the IRB Barcelona, focused on understanding the molecular and cellular basis of neoplastic transformation and tumor immune evasion in pancreatic and liver cancers. Her work to date has received several national and international recognitions, including the AACR Scholar-In-Training Award and the Blavatnik Regional Award for Young Scientists. In addition to her scientific production, Dr. Alonso-Curbelo is also an active player in bringing science closer to society and promoting diversity in Research.

SPEAKER

Epigenetic licensing of tumor-promoting inflammation in pancreatic cancer

Direna Alonso Curbelo, Institute for Research in Biomedicine (IRB), Barcelona, Spain

Cancer results from a complex interaction between genetic mutations and environmental insults that triggers changes in cell identity and tissue state. These changes are highly reminiscent of wound healing processes yet, paradoxically, contribute to cancer development and metastatic progression. To understand how physiological plasticity goes awry during tumor development, we integrated single-cell profiling methods and functional genomics tools to characterize and perturb molecular and cellular networks defining normal, inflamed, pre-malignant and malignant tissues in autochthonous models of pancreatic cancer. We uncover aberrant chromatin states in the pancreatic epithelium uniquely induced by the cooperative action of tissue damage and cancer-predisposing mutations (oncogenic Kras), that distinguish neoplastic transformation from normal regeneration and are selected for during tumor evolution. These early epigenomic alterations endow discrete epithelial cells with an enhanced capacity to drive and sense inflammation, and establish feedback loops with their environment that define and direct tumorigenesis. We propose that a better understanding of the interplay between genetic mutations, environmental context and cell identity programs will expose specific vulnerabilities that may be exploited for cancer interception.

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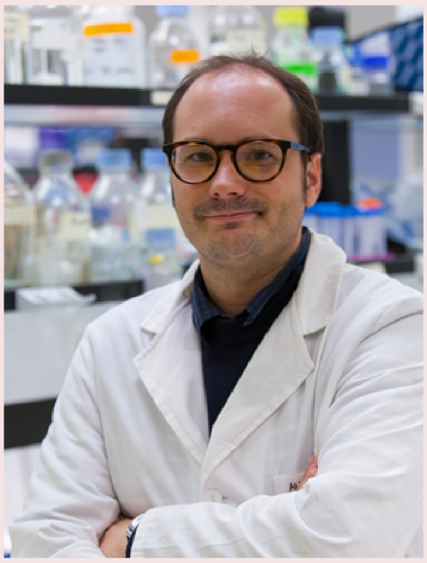

Dr. Álvaro Teijeira Sánchez obtained his PhD in the lab of Dr Rouzaut in CIMA Universidad de Navarra studying the mechanisms that drive dendritic cell migration through lymphatic vessels. Then he joined Cornelia Halin's lab in ETH Zürich to continue studying the mechanisms directing immune cell migration via lymphatic vessels where, using intravital microscopy, he identified novel mechanisms facilitating effective migration to LNs of both T cells and dendritic cells. He then joined Dr Melero's lab back in Pamplona for a second Postdoc with the aim to apply live imaging settings to the study of cancer immunotherapy. Alvaro Teijeira has received prestigious postdoctoral fellowship as the Swiss Excellence scholarship for postdoctoral studies, a Juan de la Cierva contract and a La Caixa junior leader fellowship and is now starting his own independent research group as a Ramon y Cajal Fellow in CIMA, Universidad de Navarra. During these years his research has been focused in the study of the mechanism of action of different immunostimulatory agents as CD137 agonists and IL-12 and the study of the role of dendritic cells and neutrophil in anti-tumor immunity, mainly applying live and intravital microscopy approaches. He has co authored more than 60 papers in prestigious cancer and immunology journals (Cancer Cell, Immunity, Cancer Discovery,...).

SPEAKER

The impact of inflammation(s) on cancer immunotherapy

Álvaro Teijeira Sánchez, CIMA, Universidad de Navarra

Despite its great success in several malignancies immune checkpoint blockade is a cancer immunotherapy that still does not provide any clinical benefit in a number of patients. Thanks to a number studies performed in clinical series of tumor tissue we know that the nature and composition of the immune infiltrate is one of the key features that defines patients that can benefit from cancer immunotherapy. These means that although all the immune cells are part of an inflammatory response not all types of inflammation allow a good antitumor response or facilitate the success of these therapies. We aim to present here two different inflammatory axis that mainly impair the success of cancer immunotherapy or support their action. We first show that IL-8 is induced by TNF alpha and IL-1 Beta in the tumor microenvironment as part of an inflammatory axis that limits the success of immune checkpoint blockade. One of the mechanisms of action such chemokine is to induce NETosis that can also be detrimental to immune checkpoint blockade by limiting immune cell contacts with target cells. cDC1 dendritic cell infiltration, however, strongly correlates with clinical success of immune checkpoint blockade and mice constitutively deficient in such population are unresponsive to such immunotherapies. We have made use of a DTR mouse model in which cDC1 cells can be depleted at will to identify that cDC1 cells are needed at the onset of several immunotherapies to maintain effective anti-tumor CD8 T cell responses, but their presence is not needed once the immunotherapy has already started. Overall, we will focus on two types of inflammation in the cancer setting that help or limit anti-tumor immune responses and that can be therapeutically actionable to increase the success of cancer immunotherapy in the cancer setting.

Notes

Dr. Marc Bajénoff joined the Centre d'Immunologie de Marseille Luminy (CIML) in 1998 and performed his doctoral training under the supervision of Dr S. Guerder. He then joined the laboratory of Prof Glaichenhaus (Valbonne, France) and Prof R. Germain at the Lymphocyte Biology Section, National Institutes of Health for his post-doctoral studies. He developed the first applications of the 2-photon methods for intravital imaging to an extensive analysis of the function of stromal elements within lymphoid tissues. In 2010, he established the "Immunobiology of stromal cells" group at CIML and in 2015, he was awarded an ERC consolidator grant to study the dynamics of lymphoid stromal cells.
His general research interests are in understanding the immunobiology of stromal cells and how these versatile cells control the immune system at multiple levels. More recently, his laboratory has developed a strong interest in studying the crosstalk between stromal cells and macrophages across tissues.

SPEAKER

Stroma-macrophage interactions

Marc Bajénoff, CNRS, INSERM, Centre d'immunologie de Marseille-Luminy (CIML), Marseille, France

The concept of the macrophage niche stipulates that the homeostasis of myeloid cells is locally regulated by nurturing "niches" such as fibroblasts. While this concept probably applies to most immotile tissue resident macrophages, we questionned its validity for blood circulating monocytes. Here, I will present results suggesting that the concept of the macrophage niche is also valid for blood circulating monocytes.

Notes

Dr. Carolina Florian holds a PhD from the University of Milano (Italy). She pursued postdoctoral training at the Institute of Molecular Medicine in Ulm University (Germany) from 2009 to 2015. In 2016, she was awarded an Emmy Noether Grant from the German Research Foundation (DFG) dedicated to outstanding early-career researchers. In 2018, she was appointed as group leader at CMRB (Spain). Her research in the past 5 years strongly challenged the concept that aging is an irreversible process and showed that it is possible to pharmacologically target the aged-dependent alteration of stem cell epigenetic polarity and functionally rejuvenate aged HSCs in vivo. Somatic stem cells are central for tissue homeostasis and regeneration. Their age-dependent functional decline constitutes a hallmark of tissue attrition upon aging, eventually limiting health-span and lifespan. Dr. Florian's work is committed to further grow the understanding of alterations affecting aged somatic stem cells and she is investigating changes of the epigenetic architecture that drive stem cell aging, to improve tissue attrition with age or even to prevent aging-associated diseases.

SPEAKER

Aging of hematopoietic stem cells: epigenetic drift and remodeling of the niche

Stem Cell Aging Group, Regenerative Medicine Program, Institut d'Investigació Biomèdica de Bellvitge - IDIBELL, L'Hospitalet de Llobregat, Barcelona, Spain
Program for advancing the Clinical Translation of Regenerative Medicine of Catalonia, P-CMR[C], L'Hospitalet de Llobregat, Barcelona, Spain.

With ageing, intrinsic hematopoietic stem cell (HSC) activity decreases, resulting in impaired tissue homeostasis, reduced engraftment following transplantation and increased susceptibility to diseases. Indeed, aged stem cells experience a process called "epigenetic drift" that is described as the erosion affecting to the epigenome and the chromatin architecture. We have shown that the loss of H4K16ac epi-polarity upon aging is accompanied by specific changes in chromatin architecture, like alterations in chromosome compartmentalization and increase in chromatin accessibility.
Moreover, we have also characterized some of the effects of aging on the HSC niche, which is a specialized microenvironment, where a complex and dynamic network of interactions across multiple cell types regulates HSC function.
By using in-vivo long-term label retention assays we demonstrated that aged labelling retaining HSCs, which are in the old mice the most quiescent HSC subpopulation with the highest regenerative capacity and cellular and epigenetic polarity, reside predominantly in perisinusoidal niches. We demonstrated that sinusoidal niches are uniquely preserved in shape, morphology and number upon ageing. Finally, we showed that myeloablative chemotherapy can selectively disrupt aged sinusoidal niches long term, which is linked to to the lack of recovery of endothelial Jag2 at sinusoids. Overall, we have characterized the functional alterations of the aged HSC niche and unveiled that perisinusoidal niches are uniquely preserved and protect HSCs from ageing.

Notes

Dr. Florent Ginhoux graduated in Biochemistry from the University Pierre et Marie CURIE (UPMC), Paris VI, obtained a Masters degree in Immunology from the Pasteur Institute in 2000 and his PhD in 2004 from UPMC, Paris VI. As a postdoctoral fellow, he joined the Laboratory of Miriam Merad in the Mount Sinai School of Medicine (MSSM), New York, where he studied the ontogeny and the homeostasis of cutaneous dendritic cell populations, with a strong focus on Langerhans cells and Microglia. In 2008, he became an Assistant Professor in the Department of Gene and Cell Medicine, MSSM and member of the Immunology Institute of MSSM. He joined the Singapore Immunology Network (SIgN), A*STAR in May 2009 as a Junior Principal Investigator and became Senior Principal Investigator in 2014. He joined the EMBO Young Investigator (YIP) program in 2013 and is a Web of Science Highly Cited Researcher since 2016. He is also an Adjunct Visiting Associate Professor in the Shanghai Immunology Institute, Jiao Tong University, in Shanghai, China since 2015 and Adjunct Associate Professor in the Translational Immunology Institute, SingHealth and Duke NUS, Singapore since 2016. He is now a Laboratory Director in Gustave Roussy focusing on pediatric cancers and the role of myeloid cells in tumor progression and became an EMBO member in 2022.

SPEAKER

Tissue Macrophage Heterogeneity

Florent Ginhoux, A*STAR, Singapore. Gustave Roussy Institute, Villejuif, France

Resident tissue macrophages (RTMs) have a broad spectrum of immune- and non-immune-related tissue-supporting activities. The roots of this heterogeneity and versatility are only beginning to be understood. Here, we propose a conceptual framework for considering the RTM heterogeneity that organizes the factors shaping RTM identity within four cardinal points: (1) ontogeny and the view that adult RTM populations comprise a defined mixture of cells that arise from either embryonic precursors or adult monocytes; (2) local factors unique to the niche of residence, evolving during development and aging; (3) inflammation status; and (4) the cumulative effect of time spent in a specific tissue that contributes to the resilient adaptation of macrophages to their dynamic environment.

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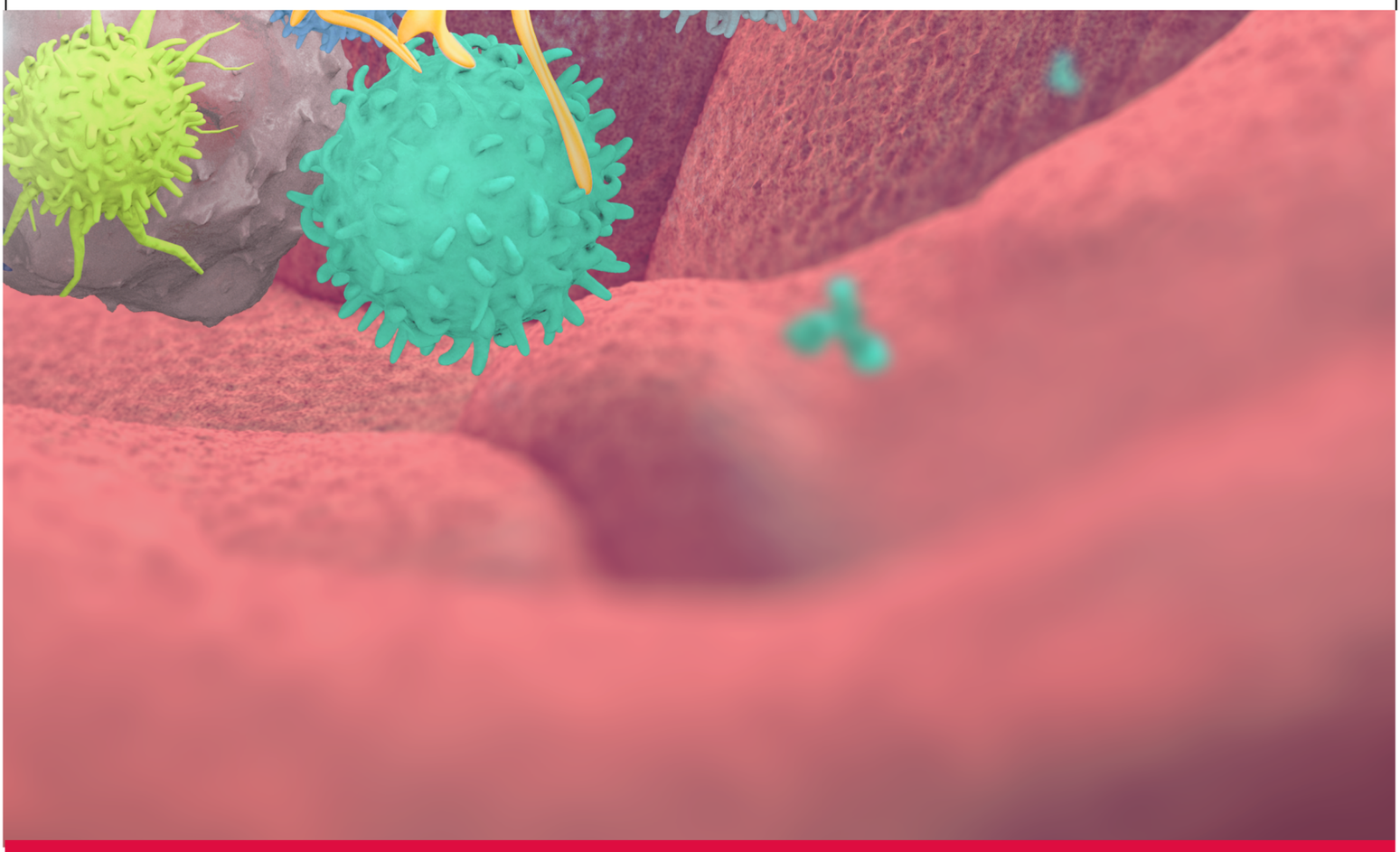

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Miltenyi Biotec S.L. | C/Luis Buñuel 2 | Ciudad de la Imagen | 28223 Pozuelo de Alarcón (Madrid) | Spain |
Phone +34 91 512 12 90 | Fax +34 91 512 12 91
macses@miltenyi.com | www.miltenyibiotec.com

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