L'Acadèmia
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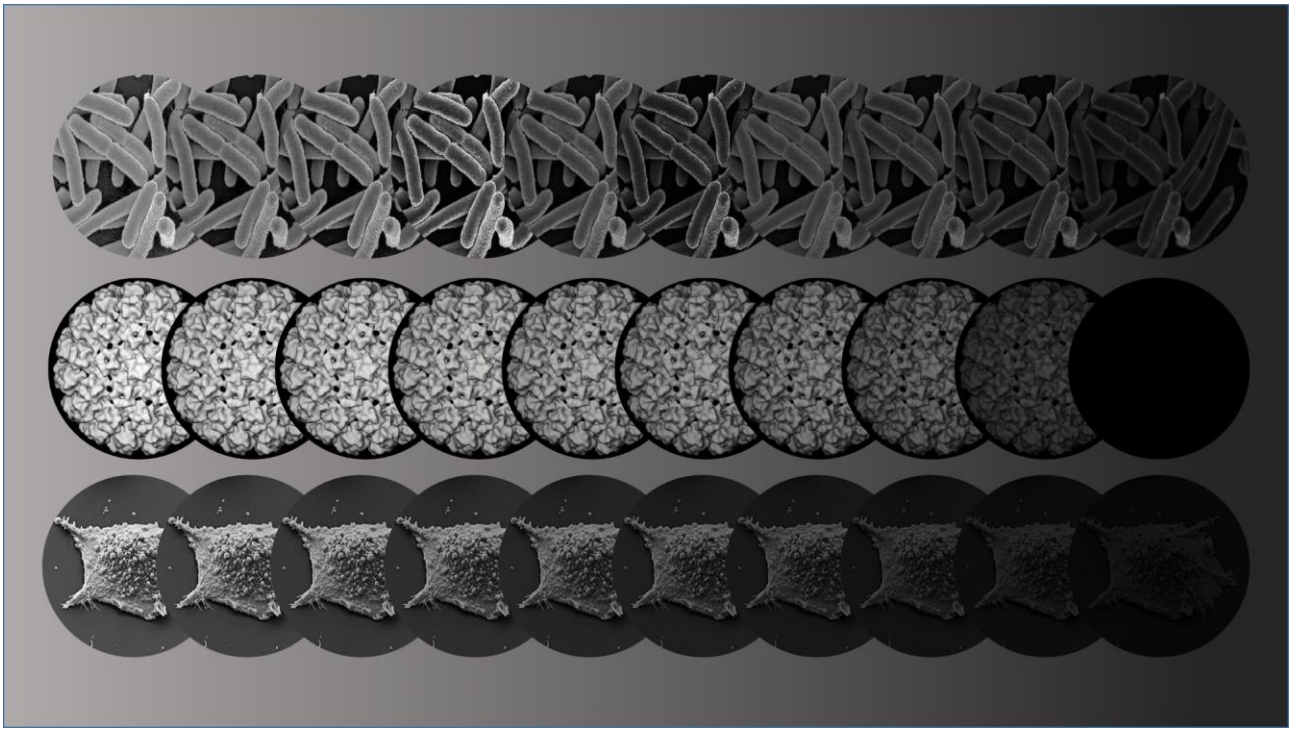
SCI
SOCIETAT CATALANA D'IMMUNOLOGIA

XIII CONGRÉS

Societat Catalana d'Immunologia (SCI)

Programa Final

Barcelona, 14 i 15 de Novembre de 2019
Auditori de l'Acadèmia de Ciències Mèdiques i de la Salut de Catalunya i de Balears



Evasió del Sistema Immunitari per patògens i tumors

Immune evasion by pathogens and tumors

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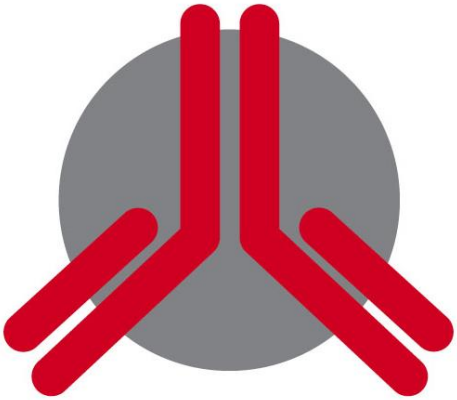

Congress Office:
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Welcome to the Congress,

On behalf of the organising committee, we would like warmly welcome you to the XIIIth Societat Catalana d'Immunologia Congress (SCI congress). We make every effort to ensure the excellence of the scientific content and that young researchers will have the opportunity to present and discuss their data.

Dr. Ricardo Pujol-Borrell
SCI President

XIIIth Congress of the Catalan Society of Immunology: Immune evasion by pathogens and tumors has been accredited by the Catalan Lifelong Learning Board of the Healthcare Professions with 0,5 credits (Record: 09/026139-MD).

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Content

Awards to the best communication and to the best poster at the XIII Congress SCI 2019, sponsored by SCI

This year SCI sponsors the awards for the best communication (200 €) and for the best poster (100 €) of this congress. The Chairpersons of the different sessions of the congress and the board members of the SCI will select the best oral communications presented, taking into account its scientific value and the aspects related to the presentation. The poster awarded will be chosen by the congress attendees activating the electronic vote inside the electronic panels of the posters. The results will be announced at the end of the congress.

Scheme first day

Thursday, November 14th	
15:30 16:00	Arrival, Registration and Documentation delivery
16:00 16:05	**Welcome to the XIIIth CONGRESS of the SCI** Dr. Ricardo Pujol-Borrell (President of SCI)
16:05 17:00	**Opening Lecture – In Memoriam Dra. Teresa Gallart** Chair: Dra. Odette Vinyes (HCB-IDIBAPS) Speaker: Dra. Montse Plana (HCB-IDIBAPS) Speaker: Dr. Felipe García-Prado (HCB, UB) ***HIV. Immunopathology and immunotherapy***
17:00 17:30	Poster viewing – Coffee Break *Posters can be viewed on the 4 electronic panels located in the Hall*
17:30 18:30	Chair: Dra. Aura Muntasell (UPF) Speaker**: Dra. PILAR NAVARRO** (Instituto de Investigaciones Biomédicas de Barcelona-CSIC, Spain) ***Tumor immune escape in pancreatic cancer: a key role for Galectin-1***
18:30 19:00	Poster viewing – Coffee Break *Posters can be viewed on the 4 electronic panels located in the Hall*
19:00 20:00	Parallel Session I - **Oral communications on Basic Immunology** Chair: Dr. Pablo Engel (UB) 19:00h An enveloped Virus-Like Particle (VLP) platform with high-density antigen display induces a strong humoral immune response. **F. Tarrés-Freixas** et al. (oral presentation 1). 19:20h Characterization of the specificity of the intermediate proteasome β5i. **E. Scholz** et al. (oral presentation 2). 19:40h Repertoire analysis of B-cells from mice with Sjögren's Syndrome reveals a high number of auto/polyreactive B cell clones. **M. Sáez-Moya** et al. (oral presentation 3). Parallel Session II - **Oral communications on Clinical Immunology** Chair: Dr. Ricardo Pujol (VHIR; UAB) 19:00h Epstein-Barr Virus+ B Cells in the Breast Cancer Immune Response: A Case Report. **A. Aran** et al. (oral presentation 1bis). 19:20h Novel compound identified by drug repositioning ameliorates experimental autoimmune diabetes. **A. Villalba** et al. (oral presentation 2bis). 19:40h PD1 and PD-L1 in Graves' disease: new clues for pathogenesis. **D. Álvarez-Sierra** et al. (oral presentation 3bis).
20:00	**End of session**

Scheme second day

Friday, November 15th	
08:30 09:00	Arrival, Registration and Documentation delivery
09:00 10:00	Chair: Dr. Andreas Meyerhans (UPF). **Dra. JULIA GARCÍA-PARDO** (The IrsiCaixa AIDS Research Institute, Badalona) ***HIV-1 infection:Going under the radar of immunity***
10:00 11:00	Session III - **Oral Communications on Innate immunity** Chair: Dr. Francisco Lozano (HCB, UB) 10:00h DNA polymerase µ protects macrophages from double-strand DNA breaks produced during pro-inflammatory activation. **A. Celada** et al. (oral presentation 4). 10:12h Deficient expression of the lymphocyte scavenger receptor cd6 confers increased susceptibility to sepsis induced by polymicrobial peritonitis. **C. Català** et al. (oral presentation 5). 10:24h Predictive value of tumor-associated and circulating NK cells for neoadjuvant therapy response in primary HER2-positive breast cancer patients. **A. Muntasell** et al. (oral presentation 6). 10:36h Interaction between mucosal and cutaneous immune responses to *Streptococcus pyogenes* in psoriasis: a role for antigen specific Igs and CLA+ T cells. **C. de Jesús** et al. (oral presentation 7). 10:48h Cytomegalovirus restricts ICOSL expression on APCs to limit T cell costimulation and promote viral immune escape. **G. Angulo** et al. (oral presentation 8).
11:00 11:30	Poster viewing – Coffee Break *Posters can be viewed on the 4 electronic panels located in the Hall*
11:30 12:30	Chair: Dr. Pablo Engel (UB) **Dr. SEPPO MERI** (University of Helsinki, Finland) ***How do microbes and tumor cells escape killing by the complement system?***
12:30 13:30	**Ordinary General Meeting / Junta General Ordinària** **SOCIETAT CATALANA d'IMMUNOLOGIA (SCI)** (12:30h – First Call) *Us hi esperem a tots: els socis i no-socis!!*
13:30 15:00	Poster viewing – LUNCH Social event on terrace *Posters can be viewed on the 4 electronic panels located in the Hall*

15:00 16:30	Session IV - **Oral Communications on Immunology and disease** Chair: Dra. Eva Martínez-Cáceres (HUGTiP) and Dra. Silvia Vidal (HUSCSP) 15:00h Differential expression of TSHR isoforms in thyroid and thymus may contribute to TSHR Tolerance Failure in Graves' Disease Patients Via Two Distinct Mechanisms. **Ana Marín** et al. (oral presentation 9). 15:13h Identifying changes in peripheral lymphocyte subpopulations at the onset of adult type 1 diabetes and their long-term evolution. **Aina Teniente-Serra** et al. (oral presentation 10). 15.27h Expanding the Clinical and Genetic Spectra of Primary Immunodeficiency-Related Disorders with Clinical Exome Sequencing: Expected and Unexpected Findings. **Clara Franco-Jarava** et al. (oral presentation 11). 15:39h Characterization of the immune response in autoimmune chronic urticaria patients and the effect of anti-IgE treatment. **Cristina Alejandra López** et al. (oral presentation 12). 15:52h Molecular and functional characterization of a novel mutation in a late-onset ADA deficient patient. **Ana Toribio** et al (oral presentation 13). 16:05h High production of house dust mite-induced IL-31 in atopic dermatitis patients with specific IgE levels. **Lídia Sans-de San Nicolás** et al. (oral presentation 14). 16:18 Molecular basis of primary hemophagocytic lymphohistiocytosis: Presentation of the HLH database. **Laura Viñas-Giménez** et al. (oral presentation 15).
16:30 17:00	Poster viewing – Coffee Break *Posters can be viewed on the 4 electronic panels located in the Hall*
17:00 18:00	Chair: Dr. Jorge Carrillo (IrsiCaixa AIDS Research Institute, Badalona) **Dra. ANA ANGULO** (Universitat de Barcelona) ***Viral host homologs as a strategy of immune evasion***
18:00 18:15	Prize to the best communication and poster. Dr. Ricardo Pujol-Borrell (President of SCI).
18:15 18:30	Closing of the Congress Ricardo Pujol-Borrell (President of SCI). End of Congress

Corporative Abbreviations

BST	Banc de Sang i Teixits
CDB	Centrede Diagnòstic Biomèdic
CIBER-BBN	Centro de Investigación Biomédica en Red de Bioingeniería, Biomateriales y Nanomedicina
CIBERDEM	Centro de Investigación Biomédica en Red de Diabetes y Enfermedades Metabólicas Asociadas
CIBER-ER	Centro de Investigación Biomédica en Red de Enfermedades Raras
CIBERES	Centro de Investigación Biomédica en Red de Enfermedades Respiratorias
CIBERONC	Centro de Investigación Biomédica en Red de Oncología
CIMA	Centro de Investigación Médica Aplicada
CLILAB	Consorci del Laboratori Intercomarcal
CSIC	Consejo Superior de Investigaciones Científicas
HCB	Hospital Clínic de Barcelona
HSCSP	Hospital de la Santa Creu i Sant Pau
HSJD	Hospital Sant Joan de Déu
HUBell	Hospital Universitari de Bellvitge
HUGTiP	Hospital Universitari Germans Trias i Pujol
HUSCSP	Hospital Universitari de la Santa Creu i Sant Pau
HUVH	Hospital Universitari Vall d'Hebron
IBB	Institut de Biotecnologia i Biomedicina
ICMD	Institut Clínic de Medicina i Dermatologia
ICREA	Institució Catalana de Recerca i Estudis Avançats
IDIBAPS	Institut d'Investigacions Biomèdiques August Pi i Sunyer
IDIBELL	Institut d'Investigació Biomèdica de Bellvitge
IGTP	Institut d'Investigació en Ciències de la Salut Germans Trias i Pujol**¡Error! Marcador no definid**
IIB Sant Pau	Institut Investigació Biomèdica Sant Pau
IIBB	Institut d'Investigacions Biomèdiques de Barcelona-
IMIM	Institut Hospital del Mar d'Investigacions Mèdiques
INSA-UB	Institut de Recerca en Nutrició i Seguretat Alimentària, Universitat de Barcelona
IRB Lleida	Institut de Recerca Biomèdica Lleida
IRHUSCSP	Institut de Recerca Hospital Universitari de la Santa Creu i Sant Pau
IRSJD	Institut de Recerca Sant Joan de Déu
ISCIII	Instituto de Salud Carlos III
LCMN	Laboratori Clínic de la Metropolitana Nord
SCI	Societat Catalana d'Immunologia
UAB	Universitat Autònoma de Barcelona
UB	Universitat de Barcelona
UCC	Universiatat Central de Catalunya
UPF	Universitat Pompeu Fabra
UPIIP	Unitat Pediatrica de Malalties Infeccioses i Immunodeficiències Primaries
UVIC	Universitat de Vic
VHIO	Vall d'Hebron Institut d'Oncologia
VHIR	Vall d'Hebron Institut de Recerca

Abstracts
Oral Communications — Session I
Basic Immunology 1 - 3

1 An enveloped Virus-Like Particle (VLP) platform with high-density antigen display induces a strong humoral immune response

Ferran Tarrés-Freixas[1]; Carmen Aguilar-Gurrieri[1]; Luis M. Molinos-Albert[1]; Ismael Varela[1]; Raquel Ortiz[1]; Maria Luisa Rodríguez de la Concepción[1]; Benjamin Trinité[1]; Silvia Marfil[1]; Carlos Ávila[1]; Laura Cervera[2]; Sònia Gutiérrez-Granados[2]; María Mercedes Segura[2]; Francesc Gòdia[2]; Bonaventura Clotet[1,3]; Jorge Carrillo[1]; Julià Blanco[1,3].

[1]IrsiCaixa Aids Research Institute; [2]Universitat Autònoma de Barcelona; [3]Universitat de Vic-UCC

Human Immunodeficiency Virus-Like Particles (HIV-VLPs) are non-infectious, non-replicative and highly immunogenic Gag-based enveloped structures that mimic the virus' morphology. The HIV envelope glycoprotein (Env) is the main target of protective neutralising antibodies, but the poor incorporation of Env into virions is an obstacle to induce potent humoral responses against the virus. The aim of the present work is to develop HIV-derived VLPs with a high density of Env-derived immunogens on their surface. To do so, HIV-1 p55Gag was fused with a gp41-derived protein (Min).

Gag (control) and MinGag VLPs were collected 48 hours after transient transfection of HEK293F cells. VLPs were purified by crossflow filtration and HPLC. Protein expression was verified by flow cytometry, ELISA and western blot. VLP immunogenicity was assessed in C57bl/6 mice following two approaches: a) four doses of purified VLPs (VVVV; 90ng of p24/dose in PBS) and b) two doses of DNA (20µg of DNA in PBS) followed by two additional doses of purified VLPs (DDVV). DNA vaccination was performed in vivo by muscle electroporation. All immunisations were performed at 3-week intervals.

Immunogenicity results showed that MinGag-VLPs induced a robust antibody response in the VVVV group, reaching plateau after one immunisation. Interestingly, a 10-fold increase in anti-gag and anti-gp41 antibodies was achieved in the prime-boost regimen (DDVV). Non-neutralising activity was detected; however, anti-Min response was characterised by a strong bias to IgG2c, a Th1-like IgG subclass. In contrast, anti-gag response was more heterogeneous including IgG1, IgG2b and IgG2c antibodies.

Altogether, these results demonstrate that our new HIV-based VLP platform induces a strong antigenspecific Th1-like humoral immune response. In addition, the DNA-VLP prime-boost immunization strategyshowed a better performance compared with the use of only VLPs. Further studies will assess the potential of these VLPs to generate an effector antibody-dependent protective response against HIV.

2 Characterization of the specificity of the intermediate proteasome β5i

Erika Scholz[1]; Anna Mestre-Ferrer[1]; Adrián Tirado[1]; Montserrat Carrascal[2]; Françesc Canals[3]; Iñaki Álvarez[1]

[1]Institut de Biotecnologia i Biomedicina. Universitat Autònoma de Barcelona; [2]CSIC/UAB Proteomics Laboratory, IIBB-CSIC/Institut d'Investigacions Biomèdiques August Pi i Sunyer; [3]Vall d'Hebron University Hospital Research Institute Proteomics Laboratory.

The proteasome is a multicatalytic complex responsible for most of the cytosolic protein degradation. In addition to the standard proteasome (containing the catalytic subunits β1, β2 and β5) and the immunoproteasome (β1i, β2i and β5i), intermediate proteasomes are present in normal tissues and, in a higher percentage, in dendritic and tumoral cells. Two intermediate proteasomes have been described: one containing β5i with the components of the standard proteasome β1 and β2, and other containing the components of the immunoproteasome β1i and β5i with β2. Their relevance has been demonstrated as some HLA-I ligands derived from tumors are generated specifically by intermediate proteasomes. The activity of intermediate proteasomes have been studied through digestions with purified 20S proteasome of fluorogenic substrates or HLA-I ligand peptide precursors. In this work, we studied the specificity of the constitutive proteasome and the intermediate proteasome β5i by in vitro digestions of peptide precursors with purified 20S proteasomes. An exhaustive analysis of the proteasome specificity showed that the intermediate proteasome β5i presents an increased trypsin-like activity.

3 Repertoire analysis of B-cells from mice with Sjögren's Syndrome reveals a high number of auto/polyreactive B cell clones

Manuel Sáez-Moya[1]; Rebeca Gutiérrez-Cózar[1]; Joan Puñet-Ortiz[1]; Julià Blanco[3,4]; Jorge Carrillo[3]; Pablo Engel[1,2]

[1]Department of Biomedical Sciences, Medical School. University of Barcelona, Barcelona, Spain; [2]Institut d'Investigacions Biomèdiques August Pi i Sunyer, Barcelona, Spain.; [3]AIDS Research Institute IrsiCaixa, IGTP, Hospital Universitari Germans Trias i Pujol, Badalona,Spain; [4]Universitat de Vic-Central de Catalunya, UVIC-UCC, Vic, Spain.

In genetically prone individuals, chronic immune activation may lead to expansion of autoreactive lymphocyte clones that can induce organ damage developing autoimmune disorders. Sjögren's Syndrome (SjS) is one of the most common systemic chronic autoimmune diseases that primarily affects exocrine glands with progressive dryness of mouth and eyes. B-cell maturation checkpoints that regulate selftolerance appear to be altered in autoimmune diseases such as SjS. Despite the accumulated evidences of profound B-cell alterations of humoral immunity, the repertoire and onset of B-cell autoreactivity in SjS remains to be determined.

We hypothesize that SjS mice will have an increased frequency of self-reactive B cells with a progressive evolution to antigen-driven oligoclonality.

Here, we study the B cell repertoire of NOD.H-2h4 mice, a mouse model of spontaneous autoimmunity mimicking SjS without developing diabetes. All female mice presented salivary gland infiltrates and autoantibodies such as anti-dsDNA and anti-Ro52, both characteristic of SjS, at the age of 24 weeks. We created a library of 456 hybridomas from NOD.H-2h4 female mice splenocytes at three different time points: 28, 47 and 66 weeks old. The presence of mono or polyreactive autoantibodies against dsDNA, Ro52, LPS, insulin, histones and OVA was evaluated by ELISA and their cellular staining patterns by IFA and FACS. We observed a high percentatge of autoreactivity among clones from NOD.H-2h4 mice. IgM antibodies autoreactivity was maintained, while autoreactive IgG antibodies increased with mice age, which was notoriously evident for anti-Ro52 autoantibodies. Interestingly, all anti-Ro52 autoantibodies were polyreactive.

Our results indicate that in the NOD.H-2h4 mouse model of SjS, IgG+ B cells are mainly polyreactive and might be expanded following an unknown antigen-driven positive selection process.

1bis Epstein-Barr Virus+ B Cells in the Breast Cancer Immune Response: A Case Report

Andrea Aran[1]; Cristina Bernadó[2]; Vicente Peg[3]; Rosa Maria Rabanal[4]; Esther Zamora[2]; Mireia Bernuz[1]; Elisa Molina[1]; Yago A. Arribas[1]; Joaquín Arribas[2]; Montserrat Carrascal[5]; Javier Cortés[2,6]

[1]Institut de Biotecnologia i Biomedicina, Universitat Autònoma de Barcelona; [2]Vall d'Hebron Institute of Oncology; [3]Vall d'Hebron Institut de Recerca; [4]Departament de Medicina i Cirurgia Animals, Universitat Autònoma de Barcelona; [5]Laboratori de Proteòmica CSIC, Universitat Autònoma de Barcelona; [6]Instituto Oncológico Baselga, Hospital Quirón.

Tumor-Infiltrating Lymphocytes (TILs) are composed by several immune subpopulations including NK, NKT, Tαβ, Tγδ and B cells. Although some of these cells can have antitumoral activities, there is also a large number of cells which are not tumor-specific, known as bystander cells. These cells may not have a direct role in the antitumoral response but could lead to a modulation of the immune response after time. Recent studies have described fatal encephalitis and myocarditis in cancer patients after immune checkpoint therapies, in which Epstein-Barr Virus (EBV)-specific T cells may be involved. Since EBV is able to infect B cells and epithelial cells, both present in the tumor site, the first events of these fatal responses could start in the tumor microenvironment due to the presence of EBV-infected cells, although this has not been deeply studied.

Thus, the main objectives of this project are (i) to use EBV-transformed B cells from the tumor site as a model to study the tumor-infiltrating EBV+ B cells and (ii) to use these EBV-transformed B cells to study their relationship with autologous T cells isolated from the tumor site.

TILs have been isolated from a triple negative breast cancer (TNBC) patient before neoadjuvancy. T cells have been expanded directly from the biopsy and EBV-transformed B cells (autoEBV-LCLs) were obtained from an EBV-derived lymphocytic tumor in a Patient-Derived Xenograft (PDX). AutoEBV-LCLs have been used as antigen presenting cells to expand T cells from TILs. Expansions of specific T cells have been monitored by T Cell Receptor (TCR) high-throughput sequencing. Furthermore, peptides presented by HLA have been eluted from autoEBV-LCLs, followed by MS analysis. Specific T cells have been obtained, suggesting that the presence of EBV+ B cells in the tumor microenvironment could be a modulating factor of the immune system.

2bis Novel compound identified by drug repositioning ameliorates experimental autoimmune diabetes

Adrian Villalba[1]; Silvia Rodríguez-Fernández[1]; David Perna-Barrull[1]; Rosa Maria Ampudia[1]; Federico Vázquez[2]; Laia Gómez-Muñoz[1]; Eva Aguilera[2]; Daniel Maspoch[3,4]; Joan Verdaguer[5,6]; Marta Vives-Pi[1,6]

[1]Immunology Section, Germans Trias i Pujol Hospital, UAB, Badalona; [2]Endocrinology Section, Germans Trias i Pujol Hospital, UAB, Badalona; [3]Catalan Institute of Nanoscience and Nanotechnology, Bellaterra; [4]ICREA, Barcelona; [5]Department of Experimental Medicine, University of Lleida IRB Lleida; [6]CIBERDEM, ISCIII, Barcelona; Spain.

To reverse type 1 diabetes (T1D), the arrest of selective autoimmune destruction must be combined with a β-cell regenerative strategy. Hence, immunotherapies could be optimized by using compounds able to improve β-cell fitness.

The aim of this study was todevelop a new combined therapy by coupling a previouslydescribed nano-immunotherapy based on liposomes with new β-cell regenerative compounds.

A drug repurposing analysis was performed to screen already-available compounds that could putatively promote β-cell regeneration by neogenesis, transdifferentiation of α-cells or replication of pre-existing β-cells. One drug was identified based on its predicted efficacy value and was named *AVI1* (protected by intellectual property issues). The therapeutic effect of *AVI1* was tested both in NOD (the spontaneous model of T1D) and NOD-*Scid* IL2rg$^{-/-}$ mice (NSG) rendered diabetic. Daily administration of *AVI1* during 30 days ameliorated hyperglycaemia in diabetic NGS. Intra-Peritoneal Glucose Tolerance Test showed that diabetic NSG mice treated with *AVI1* recovered normoglycaemia after 210min, whereas diabetic non-treated mica remained hyperglycaemic. Histological analysis of the pancreas revealed the appearance of insulin and glucagon bihormonal cells at 48h of treatment but not at 2 weeks or after withdrawal, correlating well with an increase in the expression of insulin and glucagon in islets co-cultured with *AVI1* for 48h. A partial and transient increase in the β-cell mass after 2 weeks of daily treatment was observed due to a boost in the β-cell number. Neo-islets were found emerging from the ducts and formed by CK19^{+}insulin^{+} double positive cells, both at 2 weeks of *AVI1* administration and after its removal. Finally, delivery of liposomes combined with *AVI1* reversed hyperglycaemia in 50% of diabetic NOD mice during the first 2 weeks of treatment.

Despite further research is needed, a combined therapy consisting of immunomodulation and β-cell replacement suggests a therapeutic potential in T1D.

3bis PD1 and PD-L1 in Graves' disease: new clues for pathogenesis

Daniel Álvarez-Sierra[1,2,9]; Ana Marín-Sánchez[1,2]; Paloma Ruiz-Blázquez[1,9]; Carmela Iglesias-Felip[1,4,5]; Óscar González[1,6]; Anna Casteras[7]; Roser Ferrer Costa[8]; Paolo Nuciforo[3]; Roger Colobran[1,2,9]; Carmen de Jesús Gil[1,9]; Ricardo Pujol-Borrell[1,2,9]

[1]Vall d'Hebron Research Institute (VHIR); [2]Immunology Division Hospital Universitari Vall d'Hebron; [3]Vall d'Hebron Institute of Oncology (VHIO); [4]Department of Pathology, Autonomous University of Barcelona; [5]Histopathology Division, Hospital Universitari Vall d'Hebron; [6]Surgery Department, Hospital Universitari Vall d'Hebron; [7]Endocrinology Division, Hospital Universitari Vall d'Hebron; [8]Clinical Biochemestry Division, Hospital Universitari Vall d'Hebron; [9]Department of Cell Biology, Physiology and Immunology.

Previously we reported expression of PD-L1 by human thyroid follicular cells (TFCs) in glands from patients with autoimmune thyroid diseases (AITDs): Hashimoto thyroiditis (HT) and Graves' disease (GD). We have further investigated PD-1 expression in PBMCs and intrathyroidal lymphocytes (ITLs) from AITD patients as well as the relationship of TFC PD-L1 expression with IFNs.

Thyroid frozen tissue blocks were cut into 5µm sections and PD-L1 expression was studied by indirect immunofluorescence. Total RNA was extracted from matched frozen tissue, and IFNA1, IFNA4, IFNB and IFNG relative gene expression was measured by qPCR. PD-1 expression was assessed by flow cytometry in CD4 and CD8 T lymphocytes memory subsets in PBMCs of 10 healthy controls (HC) and 10 GD patients, and 10 paired ITLs samples of GD patients.

Proportion of PD-1$^+$ CD4 T cells, but not CD8+, was moderately increased in peripheral CD4 T cells from GD patients compared to HC (16.9±5.4 vs.9.8±5.4, $p<0.05$). Interestingly, in IFL stained cryostat sections from 9 GD and 5 HT thyroid glands we found that 58.2% and 59.1% of CD4 and CD8 respectively, expressed PD-1. Of them, approximately one third were PD1 bright. Flow cytometry confirmed that PD-1$^+$ T cells corresponded mainly to central (CD45RA-CCR7$^+$) and effector (CD45RA-CCR7$^-$) memory subpopulations. On the other hand, we further assessed PD-L1 expression by TFCs and found that it correlated with IFNG gene expression by qPCR, but not with IFNA1, IFNA4 nor IFNB1.

The finding that of PDL1$^+$ TFC and PD1$^+$ T cells coexist in close proximity in AITD thyroid glands suggests that autoreactive T cells may be actively inhibited by PD-L1$^+$ TFCs. This could be a physiological mechanism to maintain tolerance in inflamed tissue. Once the autoimmune disease is established, it mayslow its progression and, in the case of AITD, explain its very protracted clinical course.

4 DNA polymerase μ protects macrophages from double-strand DNA breaks produced during pro-inflammatory activation

Antonio Celada[1]; Tania Vico[1]; Carlos Sebastián[1]; Selma Pereira-Lopes[1]; Juan A. Calatayud-Subias[1]; Juan Tur[1]; Maria Serra[1]; Antonio Bernad[2]; Jorge Lloberas[1]

[1]Grup of Biology of Macrophage, Department of Cellular Biology, Physiology and Immunology, Universitat de Barcelona; [2]Department of Cardiovascular Development and Repair, Fundación Centro Nacional de Investigaciones Cardiología.

DNA polymerase μ (Polμ) is a partner for the non-homologous end-joining (NHEJ) DNA repair pathway for double-strand breaks (DSBs), and its deficiency causes reduced DNA repair

We examined the role of Polμ in macrophage functional activity because their activation produces large amounts of reactive oxygen species that can cause DNA lesions.

Polμ is preferentially expressed in macrophages and pro-inflammatory stimuli that induce ROS, such as activators of TLR, led to increased Polμ levels. Inhibition of ROS production blocks Polμ induction. The analysis of macrophages derived from Polμ$^{-/-}$ mice show no defects in maturation, activation or in proliferation. However, while control macrophages recover quickly after etoposide treatment, a DSBs-causing agent, Polμ$^{-/-}$ macrophages showed reduced proliferation and enhanced apoptosis. This demonstrates that Polμ in macrophages is involved in DSBs repair. Pro-inflammatory activation causes DSBs in macrophages that are increased in the ones of Polμ$^{-/-}$ accompanied by an increase of apoptosis. Further, using an *in vivo* model of inflammation in the muscle and a model of infection, we demonstrated that Polμ is crucial for macrophage survival and for normal inflammatory responses.

Our findings show that Polμ is required for DSBs repair of inflammation-induced DNA damage in macrophages to balance the production of ROS.

5 Deficient expression of the lymphocyte scavenger receptor CD6 confers increased susceptibility to sepsis induced by polymicrobial peritonitis

Cristina Català[1]; María Velasco-de Andrés[1]; Sergi Casadó-Llombart[1]; Mario Martínez-Florensa[1]; Fernando Aranda[1]; Marta Consuegra-Fernández[1]; Francisco Lozano[1,2,3]

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The innate immune response to bacterial pathogens relies on the recognition of Microbial-Associated Molecular Patterns (MAMPs) by the so called Pattern Recognition Receptors (PPRs) - a relatively small group of non-polymorphic, non-clonally distributed and germline-encoded receptors belonging to diferent structural families. In this context, CD6 is a lymphocyte-specific surface PRR belonging to the ancient and highly conserved Scavenger Receptor Cysteine-Rich Superfamily (SRCR-SF) and known to interact with PAMPs from Gram-negative (LPS) and Gram-positive (LTA, PGN) bacteria. Accordingly, the whole soluble CD6 ectodomain or short peptide sequences from it have shown preventive and therapeutic effects in experimental mouse sepsis, either alone or in combination with antibiotics. Although the properties of these soluble forms have been broadly studied, less is known regarding the role of the membrane-bound CD6 in bacterial infection and sepsis. To address this issue, the cecal ligation and puncture (CLP) experimental sepsis model was carried out in CD6-deficient (*cd6*$^{-/-}$) C57BL/6 mice. The present work shows reduced survival rates of cd6-/-mice compared to wild type (WT) controls. Indeed, *cd6*$^{-/-}$ mice also showed higher levels of pro-inflammatory cytokines in serum and higher bacterial load in blood, spleen and peritoneal lavage 24h after CLP. These results indicate that CD6-deficient mice are less able to control the infection progression and sepsis. Moreover, *cd6*$^{-/-}$ splenocytes exposed to both alive and fixed Gramnegative and -positive bacteria ex vivo produced higher levels of pro-inflammatory cytokines in comparison with those from WT mice. Taken together, these results suggest that the lymphocyte surface receptor CD6 plays a critical role in bacterial sepsis-induced inflammation by still to unveil mechanisms**.**

6 Predictive value of tumor-associated and circulating NK cells for neoadjuvant therapy response in primary HER2-positive breast cancer patients

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We investigated the value of distinct NK cell-related variables for predicting pathological complete response (pCR) in primary HER2$^+$ breast cancer patients undergoing anti-HER2 antibody-based neoadjuvant treatment.

Tumor-infiltrating NK cell numbers (TI-NK) were assessed by double immunohistochemistry (CD56$^+$CD3$^-$) in pretreatment tumor biopsies from two cohorts of patients with HER2-positive breast cancer [discovery (n = 42) and validation (n = 71)]. Tumor-infiltrating lymphocytes (TIL) were scored according to international guidelines. In both cohorts, TILs and TI-NK cells were significantly associated with pCR, independently of clinicopathologic factors, and TI-NK cells appeared as well associated with prolonged disease-free survival. GSVEA evidenced a positive correlation between NK cell, activated dendritic cell and CD8 T cell gene signatures in HER2+ breast carcinomas from the Cancer Genome Atlas (n = 190), supporting the value of NK cells as surrogates of effective antitumor immunity.

On the other hand, immunophenotypic analysis of circulating NK cells in prospectively recruited patients (n=66), evidenced an inverse correlation between baseline CD57$^+$ NK cells and pCR, independently of age, conventional clinicopathological factors and CD16A 158F/V genotype. This association was also uncoupled from the presence of HCMV-induced NKG2C$^+$ adaptive NK cells. Remarkably, CD57$^+$ NK cells were reduced in breast tumor-associated infiltrates as compared to paired peripheral blood samples, suggesting their deficient homing, proliferation and/or survival in the tumor niche. Indeed, patients with high circulating CD57$^+$ NK cell numbers lacked tumor-infiltrating NK cells; perhaps explaining CD57$^+$NK cell association with resistance to anti-HER2 antibody-based treatment.

Overall, baseline tumor-infiltrating and circulating CD57$^+$ NK cell numbers predicted pCR to anti-HER2 antibody-based neoadjuvant treatment in primary breast cancer patients, pointing to the putative influence of tumor-infiltrating and the differentiation profile of circulating NK cells on the efficacy of anti-HER2$^+$antibodies.

7 Interaction between mucosal and cutaneous immune responses to *Streptococcus pyogenes* in psoriasis: a role for antigen specific Igs and CLA+ T cells

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Although mucosal and cutaneous tissues are closely involved in psoriasis pathology, the interaction between their specific immune responses *Streptococcus pyogenes* infection is well-known to trigger and exacerbate psoriasis lesions in both guttate and plaque forms of the disease. In our study, plasma from untreated psoriasis patients (n=50) and healthy controls (HC, n=21) were analyzed for the presence of IgG and IgA against S. pyogenes extract (SE), as well as CLA+/- T cells response to SE when cocultured with autologous epidermal cells. Interestingly, plaque psoriasis patients (PPP), despite being negative for ASO (Anti-Streptolysin O) antibody titter, present increased levels of IgA anti-SE compared to controls ($p<.05$), but not IgG. Based on healthy controls' specific IgA/G anti-SE plasma levels, patients were classified in two groups: low or high. Importantly, PPP with high plasma IgA anti-SE levels (38,1%) have stronger SE dependent in vitro induction of IL17 by CLA^+T cells, but not CLA-T cells, when compared to those with low IgA anti-SE or HC.
Non association is observed between anti-SE IgG levels and cytokine response in vitro. However, guttate psoriasis patients (GPP) with higher anti-SE IgG (90,9%) and IgA (18,2%) levels presented stronger IL17A and IL17F response mediated by CLA^+ T cells than those with lower Igs levels and HC. The combined analysis of humoral and CLA^+ T cell response to the same antigen in psoriasis constitute a relevant tool to understand how microbial exposure mucosa influence psoriasis trigger and development. Microbe specific IgA could be relevant for better understanding patients' heterogeneity.

8 Cytomegalovirus restricts ICOSL expression on APCs to limit T cell costimulation and promote viral immune escape

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Cytomegaloviruses (CMVs) employ multiple mechanisms to modulate immunity and promote persistent infections, including the manipulation of the phenotype and functions of antigen presenting cells (APCs). APCs play a main role triggering different arms of the adaptive immunity against pathogens. Indeed, induction of optimal T-cell responses depends on the interaction of T-cell costimulatory receptors with their ligands expressed on APCs. One important costimulatory receptor-ligand pair is ICOS-ICOSL.

Here, we report that ICOSL is targeted during murine CMV (MCMV) infection of APCs. The use of a set of MCMV deletion mutants led to the identification of a unique viral gene responsible for the loss of this molecule at the cell surface. We show that this viral protein interacts with ICOSL, preventing its trafficking to the cell membrane and redirecting it to lysosomal degradation. In vitro functional experiments revealed that the viral product is capable to dampen the ability of infected APCs to stimulate CD8+ T cell responses during antigen presentation. Furthermore, *in vivo* assays administering an anti-ICOSL antibody to infected mice led to a significant decrease in both T follicular helper cells and germinal center B cells, impairing the generation of MCMV-specific antibodies. Notably, a reduction of neutralizing antibodies was also observed.

These results demonstrate that ICOSL-dependent costimulation is critical for the antiviral immune response to MCMV infection. Finally, our findings indicating that human CMV and other human herpesviruses have also evolved strategies to efficiently target ICOSL suggest that the blockade of the ICOSL:ICOS axis is a broader immune evasion tactic crucial in the maintenance of life-long viral persistence.

9 Differential expression of TSHR isoforms in thyroid and thymus may contribute to TSHR Tolerance Failure in Graves' Disease Patients Via Two Distinct Mechanisms

Ana Marín-Sánchez[2,5]; Alicia Sellés Sánchez[2]; Francesc Rudilla[3,4]; Daniel Álvarez de la Sierra[2,5]; Roger Colobran[1,2,5]; Dolores Jaraquemada[5]; Ricardo Pujol-Borrell[1,2,5]

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Failure of tolerance to the thyrotropin receptor (TSHR) is crucial in Graves' disease (GD) pathogenesis. Noncoding SNPs, rs179247 and rs12101255 of TSHR intron 1 carry the stronger association to GD after the HLA-DR3 allele. To explain their effect, two non-mutually excluding mechanisms have been proposed: differential regulation of TSHR soluble isoform expression or modulation of TSHR expression in the thymus leading to peripheral and central tolerance failure, respectively. To discern among these two mechanisms, we investigated the effect of the intronic SNPs, rs179247 and rs12101255, on the expression of TSHR and its isoforms in both thymus and thyroid tissue.

The expression of the full-length transcripts (flTSHR) and short transcripts (ST4 and ST5) was assessed by qPCR using Taqman probes in 39 thymus and 49 thyroid glands, all previously genotyped for of rs179247 and rs12101255. There was no significant effect of GD-associated SNPs on TSHR isoform expression in thymus or in thyroid. Interestingly, the expression level of flTSHR and ST4 in thymus was higher than predicted, being approximately 20% of the expression in thyroid.

SNP-defined allele-specific TSHR expression was measured simultaneously by massive parallel sequencing (NGS) in gDNA and cDNA from rs179247 heterozygous donors (19 thymus and 8 thyroid samples). These results confirmed the preferential transcription of TSHR protective G allele in thymus but not in thyroid (Colobran 2011).

These findings argue against the effect of these TSHR alleles in the production of soluble TSHR isoforms by thyroid cells, but confirm their effect on thymic expression. The unexpected finding of abundant short isoforms of TSHR in the thymus, and more precisely, in DP thymocytes rather than in thymic epithelial cells, suggests new mechanisms by which tolerance to TSHR may be particularly fragile. Comparative analysis of DR3-associated T cell epitopes on the different isoforms may help to underpin this proposal.

10 Identifying changes in peripheral lymphocyte subpopulations at the onset of adult type 1 diabetes and their long-term evolution

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T- and B-lymphocytes play an important role in the pathogenesis of type 1 diabetes (T1D). Flow cytometry allows their characterization in peripheral blood, letting to investigate changes in cellular subpopulations that can provide insights in T1D pathophysiology.

With this purpose, $CD4^+$ and $CD8^+$ T cells (including naïve, central memory, effector memory and terminally differentiated effector (TEMRA), Th17 and Tregs) and B cells subsets (naïve, unswitched memory, switched memory and transitional B cells) were analysed in peripheral blood of adult T1D patients at onset (n=35) and after ≥2 years (n=11) using multiparametric flow cytometry. Sex and age matched HD (n=40) were used as controls.

Here we report a decrease in the percentage of early and late effector memory CD4+ and $CD8^+$ T cells ($TCD4^+$: $p<0.001$ and $p<0.001$, $TCD8^+$: $p=0.027$ and $p<0.001$). In contrast, the percentage and the absolute numbers of naïve $CD4^+$ and $CD8^+$ T cells ($CD4^+$: $p=0.008$ and $p=0.0241$, $TCD8^+$: $p=0.002$ and $p<0.001$) were increased in peripheral blood compared with HD. Moreover, an increase in the percentage of total B cells and transitional B cells was found at onset compared with HD ($p=0.009$ and $p<0.001$, respectively). Regarding Tregs, we observed a decrease in the percentage of memory and activated Treg subsets ($p<0.001$ in both subsets).No changes were detected in Th17 subpopulations.

After 2 years follow-up this profile was maintained with the exception of an increase in the percentage of IgM memory B cells ($p=0.003$) compared with baseline was found.

In conclusion, the observed changes in the percentage and/or absolute number of lymphocyte subpopulations of adult T1D patients support the hypothesis that effector cells migrate to the pancreas and this autoimmune process perseveres along the disease.

11 Expanding the clinical and genetic spectra of primary immunodeficiency-related disorders with clinical exome sequencing: expected and unexpected findings

Clara Franco-Jarava[3,4]; Francesc Rudilla[1,2]; Mónica Martínez-Gallo[3,4]; Marina García-Prat[4,5]; Andrea Martín-Nalda[4,5]; Jacques Rivière[4,5]; Aina Aguiló-Cucurull[3,4]; Ricardo Pujol-Borrell[3,4]; Pere Soler-Palacín[4,5]; Roger Colobran[3,4,6]

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Primary immunodeficiencies (PIDs) refer to a clinically, immunologically, and genetically heterogeneous group of over 350 disorders affecting development or function of the immune system. The increasing use of next-generation sequencing (NGS) technology has greatly facilitated identification of genetic defects in PID patients in daily clinical practice. Several NGS approaches are available, from the unbiased whole exome sequencing (WES) to specific gene panels.

Here, we report on a 3-year experience with clinical exome sequencing (CES) for genetic diagnosis of PIDs.

We used the TruSight One sequencing panel, which includes 4813 disease-associated genes, in 61 unrelated patients (pediatric and adults). The analysis was done in 2 steps: first, we focused on a virtual PID panel and then, we expanded the analysis to the remaining genes. A molecular diagnosis was achieved in 19 (31%) patients: 12 (20%) with mutations in genes included in the virtual PID panel and 7 (11%) with mutations in other genes. These latter cases provided interesting and somewhat unexpected findings that expand the clinical and genetic spectra of PID-related disorders, and are useful to consider in the differential diagnosis. We also discuss 5 patients (8%) with incomplete genotypes or variants of uncertain significance. Finally, we address the limitations of CES exemplified by 7 patients (11%) with negative results on CES who were later diagnosed by other approaches (more specific PID panels, WES, and comparative genomic hybridization array). In summary, the genetic diagnosis rate using CES was 31% (including a description of 12 novel mutations), which rose to 42% after including diagnoses achieved by later use of other techniques.

The description of patients with mutations in genes not included in the PID classification illustrates the heterogeneity and complexity of PID-related disorders.

12 Characterization of the immune response in autoimmune chronic urticarial patients and the effect of anti-IgE treatment

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Introduction

The pathogenic mechanisms involved in chronic urticaria (CU) are complex. It is known that in approximately 40% of the patients, an autoimmune pathogenesis IgG mediated is involved, as well an association with autoimmune thyroid disease was reported. Anti-IgE treatment with omalizumab is used to treat CU patients leading to clinical improvement. However, the relationship between omalizumab and the immune response involved in the disease is still unknown.

Aim

To characterize the immune response of patients with CU and associated autoimmunity.

Methods

An observational study of 49 patients diagnosed of CU, 22 in treatment with omalizumab and 27 with nonimmunomodulatory drugs (NID) was conducted. We performed flow cytometry immunophenotyping of T cell subpopulations and indirect Basophil Activation Test (BAT; to detect IgG autoantibodies anti-IgE). Serum levels of total IgE and anti-thyroid antibodies were measured.

Results

Only 8 patients (18%) gave a positive result in indirect BAT test, 3 of them under omalizumab treatment. None of the healthy donors tested (n=10) was positive. The immunophenotype analysis found that patients with positive BAT had higher levels of activated $CD4^+$ T lymphocytes than those with a negative result in BAT test. Moreover, patients with anti-thyroid antibodies showed a higher percentage of effector memory $CD8^+$ T cells than patients without anti-thyroid antibodies. Regarding the effect of omalizumab in T cell subsets, patients under treatment showed a lower percentage of activated $CD4^+$ T lymphocytes but a higher percentage of central and effector memory Th1 and Th2 subpopulations compared with HD (n=50) and NID patients.

Conclusions

In this preliminary study, distinct patterns of T cell subsets were found in patients with autoantibodies anti-IgE and anti-thyroid. Furthermore, relevant changes in memory T cell subpopulations had been observed in patients under omalizumab. Further investigation is needed to correlate these changes with treatment response.

13 Molecular and functional characterization of a novel mutation in a late onset ADA deficient patient

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Adenosine deaminase (ADA) is a housekeeping enzyme that participates in the metabolism of purines, catalyzing the hydrolysis of adenosine to inosine, and it has an important function in the development and maintenance of the immune system. ADA is expressed both intracellularly and on the cell surface as an ectoenzyme regulating the levels of extracellular (deoxy) adenosine. Cell-surface ADA also has an extra-enzymic function via its interaction with CD26 (ADA binding protein) which can have a co-stimulatory effect in Tcell activation. The deficiency of ADA causes approximately 15-20% of Severe Combined Immunodeficiency (SCID) that arises from profound defects of immune system development and function, and affected individuals are susceptible to severe and recurrent infections. ADA deficiency is a very heterogenous metabolic disorder. Here, we report a case of late-onset ADA deficiency with a compound heterozygous mutation in ADA gene (p.L107P/p.M1V) in a 18-year-old patient of non-consanguineous parents who was admitted with recurrent infections after EBV-related Hodgkin lymphoma and splenomegaly at the age of 8y.o. Despite normal complete blood count and immunoglobulin levels, the patient presented B and NK cell lymphopenia. Low levels of erythrocyte ADA were confirmed twice whereas adenosine and 2-deoxiadenosine levels in urine were normal. On the one hand, we identified a described null mutation p.L107P that negatively affects the ADA protein. On the other hand, we found a novel mutation affecting the start codon (p.M1V). In this work, we characterized the novel mutation p.M1V measuring ADA expression, molecular localization and enzymatic activity in transfected cells and PBMCs. Our results suggest that the p.M1V mutation allows the weakly translation of the protein with enzymatic activity.Therefore, these compound heterozygous mutations (p.M1V/p.L107P) in ADA gene result in a milder phenotype due to the residual ADA activity corresponding to the p.M1V allele.

14 High production of house dust mite-induced IL-31 in atopic dermatitis patients with specific IgE levels

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Atopic dermatitis (AD) is a chronic Th1/Th2/Th17/Th22-driven inflammatory skin disease affecting both adults and children worldwide. Type 2 memory cutaneous lymphocyte-associated antigen (CLA)+ T cells(Th2) produce, among other cytokines, interleukine-31 (IL-31), that has been described to induce pruritus through its receptor located in the skin sensory neurons. In the present study, we evaluate the production of relevant AD T-cell derived mediators using an ex vivo model induced by AD allergens.

Purified memory CLA+/- T cells from severe non-treated AD patients (n=15) were cultured with autologous antigen presenting cells (APCs) with or without House Dust Mite (HDM) extract stimulation for five days. IL-4, IL-13, IL-17A, IL-31 and IFN-γ were quantitatively measured in culture supernatants. HDM preferentially activates circulating CLA+ T cells and APCs with simultaneous production of Th2 cytokines IL-4, IL-13 and IL-31 and Th17 cytokine IL-17A, but not Th1 cells. Of note, samples from patients with specific IgE for *D.pteronyssinus* and *D.farinae* > 100 kU/L (allergen sensitized) showed significantly higher production of IL-13, IL-4 and IL-31 than those with lower levels of specific IgE. Also, there was consistent correlation of IL-31 production with IL-4 and IL-13. The production of IL-31 in allergen sensitized-derived cultures was induced in an inflammatory context dominated by IL-13.

Our findings suggest that IL-31 may play a relevant role in pruritus when is induced in allergen sensitized AD patients and those patients eventually being more responders to IL-31 blockade strategies.

15 Molecular basis of primary hemophagocytic lymphohistiocytosis: Presentation of the HLH database

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Background

Primary immunodeficiencies (PIDs) are a collection of heterogeneous clinical entities and the lack of comprehensive disease-specific mutation databases may difficult or delay the classification of the genetic variants found in genetic tests. This is especially true for hemophagocytic lymphohistiocytosis (HLH), a life-threatening PID classically considered as autosomal recessive but with an increasingly demonstrated genetic heterogeneity.

Objective: The objective of this study was to build an open-access repository to collect detailed information of known genetic mutations underlying HLH.

Methods

We manually reviewed more than 120 papers to collect all published mutations related to HLH. We retrieved relevant information about allelic status, number of patients with the same mutation, and whether functional assays have been done. We stored all data it in a PostgreSQL database and then built a website on top of it, using the Django framework.

Results

The HLHdb (https://www.biotoclin.org/HLHdb) gathers information of published mutations in the 4 genes identified in primary HLH (PRF1, UNC13D, STXBP2, STX11). It comprises 240 missense, 69 frameshift, 51 nonsense, 51 splicing, 10 in-frame indel, 7 deep intronic and 5 large rearrangements variants along with their allelic status, carrier(s) information and functional evidence. Additionally, we integrate information from other relevant databases, like clinical evidence from ClinVar and UniProt, population allele frequency from ExAC and gnomAD and pathogenicity predictions from well-known tools (PolyPhen-2, SIFT, etc). Finally, we show the location of the variant relative to the gene exon and protein domain structures.

Conclusion

The HLHdb covers a broad range of data about the reported mutations in primary HLH genes. This free access and easy-to-use resource will facilitate the molecular testing of HLH patients and emphasizes the need of this type of disease-specific database for other PIDs.

e-poster List
Posters Clinical Immunology 1 - 7

The authors will attend the poster on **14/11/2019**: 17:00-17:30h, 18:30-19:00h Panel 4

1 Study of the transcriptome of the Dorsal Root Ganglia in NOD mice, a model ofr autoimmune diabetes

Marta Corral-Pujol[1]; Berta Arpa-Puigdemont[1]; Estela Rosell-Masses[1]; Leire Egia-Mendikute[1]; Celia Vived-Maza[1]; Julia Luna Salinas[1]; Concepción Mora Giral[1]; Alex Sánchez[2]; Dídac Mauricio[3,4]; Thomas Stratmann[4]; Marta Vives-Pi[4,5]; Joan Verdaguer[1],[4]

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La diabetis tipus 1 (DT1) és una malaltia autoimmunitària caracteritzada per la destrucció selectiva de les cèl·lules β-pancreàtiques. Estudis previs demostren que, al mateix temps, existeix una respostaautoimmunitària contra el sistema nerviós perifèric (SNP) que regula l'activitat dels illots pancreàtics. Les neurones sensorials que innerven el pàncrees tenen els cossos cel·lulars en els ganglis dorsals raquidis (GDR). Alteracions funcionals en aquestes s'han relacionat amb el desenvolupament de DT1.

La hipòtesi d'aquest estudi és que la DT1 s'origina a causa d'un procés neurodegeneratiu que induiria un alliberament anormal d'autoantígens. Aquests desencadenarien una la resposta contra el SNP però també contra les cèl·lules β, donant lloc a l'aparició de la DT1.

Hem realitzat anàlisis d'expressió per determinar la causa i/o molècules implicades en aquest possible procés neurodegeneratiu. Els resultats suggereixen que l'estrès de reticle endoplasmàtic no és només un problema existent en les cèl·lules β, sinó que també està present en les cèl·lules del SNP, l'altra diana coneguda de la DT1. Els resultats també indiquen que existeix un defecte degeneratiu en les cèl·lules del GDR. Aquesta disfunció del SNP pot predisposar-lo a ser diana del sistema immunitari, donant lloc a DT1. Si la nostra hipòtesi és correcta, les cèl·lules del GDR d'individus susceptibles a diabetis també presentarien alteracions en la transcripció d'una amplia gamma de gens. Alguns dels gens candidats que, segons els nostres resultats en ratolins NOD, presenten diferències en els nivells de transcripció són Scg5 i Vcp. Això es dona tant en cèl·lules del GDR, com en cèl·lules blanques de la sang. Com que no és possible accedir in vivo als GDR, l'anàlisi d'expressió gènica d'aquests gens en sang podria ser una manera fàcil per detectar individus amb susceptibilitat a desenvolupar DT1 abans de l'inici de la malaltia.

Posters
Clinical Immunology 1 - 7

The authors will attend the poster on **14/11/2019**: 17:00-17:30h, 18:30-19:00h Panel 4

2 Validation of Cyclin D3 as a master regulator of apoptosis of pancreatic beta cells in autoinmune diabetes (T1D)

Julia Luna Salinas[1]; Celia Vived-Maza[1]; Baldo Oliva[3,4]; Concepción Mora Giral[1,21]

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Type 1 diabetes (T1D) is an autoimmune condition caused by the lymphocyte-mediated destruction of the insulin-producing β cells in pancreatic islets. Despite the increasing global prevalence of T1D, there is a poor understanding of the molecular mechanisms that lead to pancreatic β cells apoptosis. Moreover, there is no cure for the disease. Currently, the standard treatment consists of life-long exogenous insulin administration combined with a tight monitoring of glucose levels.

In an effort to better understanding of the molecular changes occurring in beta cells because of the autoimmune assault we performed a mRNA expression analysis and identified CyclinD3 as a final molecular entity causally related to β cell viability. More specifically, we found that protein CyclinD3 expression levels were inversely related to the lymphocyte-infiltration levels without impairing beta cell proliferation activity.nTo identify the antiapoptotic pathway modulated by CyclinD3 in pancreatic beta cells during T1D onset we performed a protein-protein interaction screening using the *Matchmaker yeast two hybrid (Y2H) (Clontech)* technique.

Our first approach was to identify potential protein interaction partners to CyclinD3 using a Normalized Universal cDNA Mouse Library (*Genescript*). From these first screening we obtained several potential interaction partners, one of them directly related to redox metabolism. We also validated these interactions with the full-length cDNA of each protein.

Then, we predicted these potentially interactive sequences using bioinformatics servers *(i-loops, i-frag)* that identify common minimum protein sequences and domains with two know interacting proteins.

Currently, we are working on the *Matchmaker Y2H* of CyclinD3 mutants, which has totally deleted the potential interaction region, with each one of our protein candidates.

In order to narrow down the interaction crucial sequence, next step to follow will be the obtention of single point mutations that only affect our interaction of interest without impair total CyclinD3 structure and function.

Posters
Clinical Immunology 1 - 7

The authors will attend the poster on **14/11/2019**: 17:00-17:30h, 18:30-19:00h Panel 4

3 Prevention of rotavirus infection by the administration of a postbiotic in a suckling rat model

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Human milk is composed of micronutrients and macronutrients, including many biologically active compounds. Among them, there are some with direct immune protective role as well as those contributing to the newborn immune maturation, such as microbial modulators (microbiota, oligosaccharides, etc.). Infant formulas try to include also these types of bioactive components.

Rotaviruses (RVs) are the main cause of severe and acute diarrhoea in children. It is well known that microbial modulators from the human milk have an important role in intestinal homeostasis and immunedevelopment, for this reason, we hypothesize that postbiotics - inactivated fragments or bacteria metabolitescan provide a beneficial effect on the incidence and severity of the RV gastroenteritis.

Thus, the aim of this study is to analyse the effects of a particular postbiotic product on RV infection in suckling rats.

In order to achieve this purpose, 9 litters of neonatal suckling rats (N=8 each) were intragastrically administered daily with the vehicle or the postbiotic from day 2 to the end of the study and with the RV (or vehicle) on day 5. Different variables such as the body weight, clinical indexes and faecal data were evaluated from day 3 to day 16. Immunological parameters such as viral elimination and total and specific plasma anti-RV immunoglobulins (Ig) were also measured.

The postbiotic treatment positively modulated the body weight and, the incidence and severity of diarrhoea was also statistically reduced. Although the viral elimination was enhanced by the postbiotic intervention, no changes in total or specific anti-RV immunoglobulins in plasma were found.

We can conclude that the administration of the postbiotic during suckling has a beneficial impact on incidence and severity of the diarrhoea caused by the RV, thus suggesting the interest of adding these type of compounds to infant formulas.

Posters
Clinical Immunology 1 - 7

The authors will attend the poster on **14/11/2019**: 17:00-17:30h, 18:30-19:00h Panel 4

4 Immunological profiling of chronic obstructive airways disease and idiopathic pulmonary fibrosis

Núria Mendoza Barco[1]; Sandra Casas-Recasens[2]; Fernanda Hernández[1,3]; Nuria Albacar[1,3]; Guillaume Noell[1]; Alvar Agustí[1,2,3]; Jacobo Sellares[1,2,3]; Rosa Faner[1,2]

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Respiratory diseases, as Chronic Obstructive Pulmonary Disease (COPD) and Idiopathic Pulmonary Fibrosis (IPF), are heterogeneous and complex conditions, which in some individuals coexist. The etiology of both conditions is largely unknown and even considered opposite, but to some extend both have been associated with the presence of an abnormal immune response which is still not fully understood.

The aim of this work was tocharacterize the similarities and differences of the lung and blood immune cell profile in IPF and COPD vs. normal lung function controls.

To infer the lung infiltrate composition we used an immune cell deconvolution method in the microarray gene expression data from the 582 subjects of the Lung Tissue Research Consortium: 160 IPF, 220 COPD and 108 controls. The whole dataset was split in two to have a test and a validation cohort. We compared the differences in distribution of the immune cell signatures across diseases. Key genes were validated by qPCR and we finally assessed if any of these changes could be detected in blood by flow cytometry.

In lung, B-cell related signatureswere up-regulated both in IPF and severe COPD. IPF was also characterized by an up-regulation of activated CD4 and CD8 cells signatures. In contrast, in severe COPD we observed an increase in CD8, Th1, Th17, macrophages, monocytes and dendritic signatures. Thesefindings were replicated in the second dataset and validated by qPCR.

In blood of IPF we observed a significant decrease in $CD8^+$ naïve T cells and a trend toward lower levels of $CD8^+CD28^+$ cells in both IPF and COPD.

We conclude that IPF and COPD have both shared and distinct immune profile abnormalities in the lung and blood, which might be underlying the shared co-occurrence and the specific disease pathology. The association of these immune profiles with clinical endpoints is under evaluation.

Posters
Clinical Immunology 1 - 7

The authors will attend the poster on **15/11/2019**: 11:00-11:30h, 16:30-17:00h Panel 4

5 Rare triple rodent tissue pattern in a post-transplanted patient with progressive familial intrahepatic cholestasis type 2

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Introduction

Progressive familial intrahepatic cholestasis type 2 (PFIC2) is a rare disease caused by mutations on the BCB11 gene, which encodes the bile salt export pump (BSEP) expressed in the canalicular membrane of hepatocytes. This disease typically manifests during early childhood and eventually leads to liver cirrhosis, often requiring liver transplantation (LTX). It is estimated that the prevalence of recurrence after LTX in these patients is 8% due to de novo appearance of anti-BSEP antibodies. Here, we report a clinical case of a post-transplanted PFIC2 patient in whom anti-BSEP-like antibodies were found.

Materials and methods

Anti-smooth-muscle, anti-liver-kidney-microsomal, and anti-mitochondrial antibodies were assessed by indirect immunofluorescence (IIF) on triple rodent tissue (TRT) as part of the analytical follow-up of the patient. IIF patterns were tested at serum screening dilutions of 1:40. Titers were determined by 2-fold endpoint titration.

Results

The patient is a 12 years old boy who was diagnosed of PFIC2 based on negative BSEP canalicular immunostaining on liver biopsy and received a LTX in his first year of life. In the last years, he has not presented any significant complications. TRT showed a strong canalicular staining pattern at a titer of 1:320. Considering the clinical history of the patient, and the fact that rat Bsep is highly homologous to human BSEP, presence of anti-BSEP-like antibodies was informed. A more specific assay is needed to confirm the specificity of the found antibodies. At this time, the patient did not present any clinical worsening.

Conclusions

During routine TRT screening of post-transplanted PFIC2 patients canalicular staining should be evaluated to discard the appearance of anti-BSEP antibodies. Currently there is no clear therapeutic strategy in the case of detecting anti-BSEP antibodies before clinical worsening of the patient. However, since anti-BSEP antibodies have been proved as pathogenic, the patient should be followed-up more exhaustively.

Posters
Clinical Immunology 1 - 7

The authors will attend the poster on **15/11/2019**: 11:00-11:30h, 16:30-17:00h Panel 4

6 Identification of a dominant activating RAC2 mutation in a patient with atypical epidermodysplasia verruciformis

Janire Perurena-Prieto[1]; Ingrid López-Lerma[2]; Patricia Bassas-Freixas[2]; Sandra Salgado-Perandrés[1]; Clara Franco-Jarava[1]; Roger Colobran-Oriol[1]; Vicente García-Patos[2]; Mónica Martínez-Gallo[1]

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Background and aims

Epidermodysplasia verruciformis (EV) is characterized by susceptibility to human β-papillomavirus (β-HPV) infection and is strongly associated with skin carcinomas. Typical EV is caused by mutations in two proteins involved in the keratinocyte-intrinsic immunity, EVER1 and EVER2. However, clinical symptoms of EV has been associated with a variety of mutations causative of T cell defects. The aim of this study was to identify a possible primary immunodeficiency in a patient with a severe atypical EV.

Clinical data and methods

A 32-year-old woman presented with multiple superinfected ulcers. She was diagnosed of EV on her infancy due to her skin lesions. She developed multiple squamous-cell carcinoma since she was 20. A stable circulating monoclonal CD4+/CD8+ T-cell population was demonstratedaccounting 10% of total lymphocytes. A hypocellular bone marrow was detected on a biopsy. A high-risk HPV was found on a cervical cytology. Lymphocyte subpopulations were analyzed by an extensive flow cytometry panel. A targeted NGS panel focused in genes causing primary immunodeficiencies was performed to achieve the genetic diagnosis.

Results

General lymphopenia was detected, with severely diminished B cells. IgG levels were slightly low. $CD4^+$ T cells showed an effector-memory phenotype, mainly Th1-T17. CD8+ T cell showed a terminally differentiated (CCR7lowCD45RAhigh) phenotype. A recently described dominant activating mutation (c.101C>A/p.P34H) was found in *RAC2* gene coding the small GTPase, RAC2.

Conclusions

This is the first case with activating mutation in *RAC2* gene presenting atypical EV. Additional *in vitro* studies are underway to reverse this activating function.

Posters
Clinical Immunology 1 - 7

The authors will attend the poster on **15/11/2019**: 11:00-11:30h, 16:30-17:00h Panel 4

7 Immunological study of a human acellular dermal matrix graft in an animal model for use in pelvic reconstructive surgery

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Introduction

Mesh reinforced repair is a standard procedure in pelvic reconstructive surgery. However, synthetic mesh materials are associated with a risk of severe complications such as fibrosis and inflammation causing erosion and pain. Therefore, there is a growing interest in finding better materials that help to improve outcomes.

A human acellular dermal matrix (hADM) has been developed by Barcelona Tissue Bank, obtained from human cadaveric skin that undergoes a descellularitation process in order to remove the cellular components of the tissue leaving the extracellular matrix intact.

Aim

To characterize the local immunological response produced by a hADM-graft and by a synthetic polypropylene (PP) mesh implanted in an animal model and to determine its correlation with the clinical complications observed.

Material and methods

Twenty NZ rabbits were randomized into two groups: 10 received hADM-grafts and 10 were implanted with PP-mesh. Each rabbit had 2 segments implanted into the abdomen and 2 into the vagina, in the submucosal layer. The grafts were removed 180 days later and included in paraffin. The study was approved by the Animal Experimentation Ethics Committee and by government authorities (FUE-2017-00561151, Project number-9669) Inflammatory infiltration area and cell markers (CD3, CD79a, RAM11) were measured with haematoxylin staining and immunohistochemistry.

Results

Clinical complications(wound infection, extrusion) and abnormal surgical findings(erosion, fibrosis) associated with the grafts were more common in the PP mesh group (70% vs 20%) and (60% vs 10%), respectively. The presence of infiltrates with $CD3^+$, $CD79a^+$ and $RAM11^+$ cells were more prevalent in hADM group than in PP-mesh group (9/10 rabbits vs 2/10 rabbits).

Conclusions

hADM shows good tissue integration with few clinical complications. The greater number of infiltrates observed in the hADM group in this study in a rabbit model is probably due to an allogeneic response against the graft as it derives from human cadaveric skin.

Posters
Diagnostic Immunology 8 - 13

The authors will attend the poster on **15/11/2019**: 11:00-11:30h, 16:30-17:00h Panel 1

8 Diagnostic value of serum KL-6 in Interstitial Lung Disease: results from a Spanish cohort

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Introduction

Interstitial Lung disease (ILD) is a group of pulmonary disorders with similar pattern of inflammation and fibrosis in the lung interstitium. One of them include ILD associated to connective tissue disorders (CTD-ILD). KL-6 is a mucin-like glycoprotein the elevation of which in serum is related to regenerating epithelial cells and the presence of fibrotic lung lesions. KL-6 has been widely studied as an ILD diagnostic and prognostic biomarker in Japan. However, there is scarce data about its value in other populations.

Objective

To investigate the diagnostic value of serum KL-6 levels to detect ILD in a Spanish cohort.

Methods

ILD patients referred to our specialized unit and controls were prospectively included. Cases were stratified in four groups: patients with ILD without CTD, patients with CTD without ILD, patients with CTD-ILD and controls. At diagnosis, KL-6 serum levels were determined using the chemiluminescence reagent “Lumipulse KL-6” (Fujirebio). KL-6 serum levels of the four groups were compared, and specificity and sensitivity to discriminate ILD were stablished. ROC analysis was performed to determine the optimal cut-off value.

Results

A total of 101 subjects were included: 19 control individuals, 33 ILD without CTD, 24 CTD without ILD and 25 with CTD-ILD. Mean of KL-6U/mL (±SD) was 333.3±51.9 in controls, 1040±351 in ILD without CTD, 281.6±46.8 in CTD without ILD and 1195±315.6 in CTD-ILD. The higher specificity (93%) and sensibility (83%) to discriminate ILD was achieved with levels of KL-6 >450U/ml.

Conclusions

Our data show that values of serum KL-6 greater than 450 U/mL have excellent sensitivity and specificity to detect ILD, being a useful biomarker also in Spanish populations. KL-6 elevated levels are due to ILD in both autoimmune and non-autoimmune disorders. Therefore, serum KL-6 levels could be a useful biomarker to predict pulmonary involvement in patients with CTDs.

Posters
Diagnostic Immunology 8 - 13

The authors will attend the poster on **15/11/2019**: 11:00-11:30h, 16:30-17:00h Panel 1

9 Anti-centromere antibodies detection by IFI and its correlation with anti-CENP-A and anti-CENP-B by Immunoblotting

T. Franco-Leyva[1]; L. Alserawan[1]; E. Moltó[1]; Y. Álvaro[1]; V. Calahorro[1]; A. Baucells[1]; C. Juárez[1]; L. Martínez-Martínez[1]; A. Mariscal[1]

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Introduction

Anti-centromere antibodies (ACA) are associated with Systemic sclerosis (SSc). Although not being exclusive of SSc, they are present on 20-40%of patients and are related to defined clinicalcharacteristics. ACA are directed against multiple centromere proteins (CENP), most frequently CENP-A and CENP-B. Presence of ACA can be detected by indirect immunofluorescence (IFI), immunoblotting (IB) or ELISA.

Objective

To compare the concordance between IFI and IB in ACA detection, to correlate the CENP specificity (A or B) with the IFI titer and to evaluate the need of a confirmatory method (IB) on the laboratory daily routine.

Material and methods

Retrospective observational study involving 118 samples from our hospital that were analyzed both by IFI (Hep-2 INOVA), and IB (Euroimmun) and were ACA positive by either method.

Results

106(89,8%) samples were ACA+ by IFI: 87(82%) were anti-CENP-A+ and B+, 8(7,5%) were A+/B-, 5(4,7%) were A-/B+, and 6(5,7%) were A-/B- by IB. The remaining 12(10,2%) samples had other ANA patterns by IFI, mostly speckled; 3(25%) were A+/B+, 4(33,3%) were A+/B- and 5(41,7%) were A-/B+ by IB. From the 90 samples with an IFI centromeric titer ≥1/640, 83(92.2%) were both anti-CENPA+ and anti-CENP-B+ by IB. From 16 samples with an IFI centromeric titer <1/640 only 4(25%) were both anti-CENP-A+ and anti-CENP-B+ by IB.

Conclusions

High centromeric titers correlated mostly (92,2%) to both CENP-A and CENP-B antibodies while only 25% of lower titers did. Therefore, we propose that the detection of ACA by IFI needs to be verified by IB only in low titers (<1/640). However, 12 (10,2%) samples were positive by IB but weren't ACA positive by IFI. This could be due to concealment of the centromeric pattern. Therefore, samples should be tested by IB in the absence of centromeric IFI pattern if clinical suspicion is high.

Posters
Diagnostic Immunology 8 - 13

The authors will attend the poster on **15/11/2019**: 11:00-11:30h, 16:30-17:00h Panel 1

10 Determination of anti-TIF1 and autoantibodies through commercial *vs* home-made immunoblot: a comparison with clinical relevance

Anaís Mariscal Rodríguez[1]; Ana Milena Millán Arciniegas[1]; Andrés Baucells de la Peña[1]; Leticia Alserawan de Lamo[1]; Teresa Franco-Leyva[1]; Esther Moga Naranjo[1]; Laura Martínez-Martínez[1]; Cándido Juárez Rubio[1]; Ángeles Martínez Carretero[1]; Iván Castellví Barranco[1]; Albert Selva O'Callahan[2].

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Introduction

Anti-TIF1γ autoantibody is specific for dermatomyositis (DM) and a marker of cancer in the context of this disease. Since 2011, we analyze anti-TIF1γ by home-made immunoblot (hIB) with recombinant human protein (OriGene) after having demonstrated excellent agreement(κ=0.88) between our IB and the reference standard technique: immunoprecipitation. At 2014, TIF1γ was included in the Euroline Autoimmune Inflammatory Myopathies (Euroimmun). However, no studies have been carried out to evaluate the agreement between the commercial (cIB) and home-made (hIB) IB.

Aims

To compare commercial and home-made IB results and its clinical relevance.

Methods

Patients with anti-TIF1γ determination were selected from two tertiary-level hospitals since 2014. Patients were grouped according to diagnosis: 35 DM(22 without cancer and 13 with cancer-associated myositis(CAM)), 6 Systemic Autoimmune Diseases(EAS) non-DM and 19 with other diagnoses.

Results

60 patients were evaluated (73.3% women).

- 17/60 negatives for both techniques
- 6/60 positives for hIB.
- 21/60 positives for the cIB.
- 16/60 positives for both techniques.

cIB and hIB concurred in 33 patients(55%), yielding a kappa(κ) coefficient of 0.1527(p=0.18). Of the 43 patients positive for one of the techniques:

- 21/43 were positive for cIB: 2/21 DM, 2/21 EAS non-DM and 17/21 with other diagnoses.
- 6/43 were positive for hIB: 4/6 DM and 2/6 EAS non-DM.
- 16/43 were positive for both techniques: 14/16 DM, 1/16 EAS non-DM and 1/16 with other diagnoses.

The sensitivity and specificity of both techniques to detect anti-TIF1γ in the context of DM was 45.7% and 16% for cIB and 51.4% and 84% for hIB.

Conclusions

The two techniques (cIB vs hIB) were poorly concordant (κ=0.1527). A large number of patients with other pathologies was positive with cIB. So, the specificity of cIB to detect anti-TIF1γ in DM context was lower. As a conclusion, these results support the need to confirm cIB by hIB to avoid false positives of TIF1γ.

Posters
Diagnostic Immunology 8 - 13

The authors will attend the poster on **15/11/2019**: 11:00-11:30h, 16:30-17:00h Panel 2

11 Genetic evaluation with targeted massive parallel sequencing in a large cohort of patients with common variable immunodeficiency (CVID) under immunoglobulin replacement therapy

Marina García Prat[2]; Eva Polverino[3]; Antonio Álvarez Fernández[3]; Patricia Chang Macchiu[3]; Jacques G. Rivière[2]; Andrea Martín Nalda[2]; Mónica Martínez-Gallo[1]; Clara Franco-Jarava[1]; Romina Dieli Crimi[1]; Ricardo Pujol-Borrell[1]; Roger Colobran Oriol[1]; Pere Soler-Palacín[2]

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Introduction

As its name suggests, Common Variable Immunodeficiency (CVID) is the **most frequent** Primary Immunodeficiency (PID) subset and it's **highly variable** regarding clinical presentation, age and severity. For that reason, it has always been suspected that CVID may be caused for more than one genetic mutation (polygenic) rather than a single mutation (monogenic). Due to the need of nonspecific immunoglobulin replacement therapy a rapid diagnosis is essential for these patients in order to start the treatment before developing severe complications.

Objectives

In this study, we want to identify monogenic mutations in CVID patients and compare their evolution from those with a probable polygenic cause. Moreover, we want to offer targeted treatment where possible and at the same time, a genetic and preconceptional counseling for patients and their families.

Patients & Methods

A cohort of pediatric and adult patients with CVID has been established following the diagnostic criteria of *Bonilla et al. 2015.* Epidemiological and clinical characteristics of CVID patients were obtained. DNA was collected and genetic study was performed using a custom NGS panel of 323 PID genes.

Results

To date, 126 patients constitute the cohort. DNA sample of 81 patients has been obtained (64.28%), 34of which have been included in the genetic panel (41.97%), obtaining 14 positive results (41.17%). The most prevalent clinical manifestation is recurrent respiratory infections (92.8%), followed by functional respiratory deterioration (88.9%) and gastrointestinal tract involvement (63.5%). Regarding the 14 positive genetic results, the most prevalent mutated gene was *TACI* (4/14), followed by *PIK3R1* (3/14), *NFKB1* (3/14), *LRBA* (2/14), *CTLA4* (1/14) and *IKZF1* (1/14).

Discussion: This project will allow optimizing the diagnosis and treatment of CVID patients. For all the above we consider this study as an urgent need to improve diagnosis, treatment and prognosis of CVID patients.

Posters
Diagnostic Immunology 8 - 13

The authors will attend the poster on **15/11/2019**: 11:00-11:30h, 16:30-17:00h Panel 2

12 Diagnosis of IgE Multiple Myeloma: exclusion or routine?

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IgE Multiple Myeloma (MM) is a rare disorder, accounting for just 0,1% of all patients with MM. Herein, we report a 76-year-old man who turned to our hospital with critical conditions like fatigue, nausea, lower limbs weakness and anorexia for fifteen days. During his admission in the emergency room a worsening of his chronic renal insufficiency and microcytic anemia were related.

Biochemical and immunological studies aimed at MM diagnosis. These included complete blood count, serum chemistry panel, serum protein capillary zone electrophoresis (CZE; Capillarys Sebia®) and serum immunofixation electrophoresis (IFE; 9 IF, Hydrasys, Sebia®) using anti-IgG, IgA, IgM, kappa (κ) and lambda (λ) antisera. Evaluation of κ and λ free light chains (FLC) concentration was also performed.

CZE showed a monoclonal protein of 26,4 g/L. Moreover, a large monoclonal κ light chain band with no heavy chain associated was identified by IFE. Quantification of κ chain was 3.810 mg/L (3,3-19,4 mg/L). The difference between monoclonal component quantification and κ chains concentration evidenced that monoclonal component wasn't κ chains only. IgD was undetectable (0-15 mg/dL), and IgE levels were between normal ranges, 58,7 KU/L (0-87 KU/L). A second IFE with anti-IgE antisera exhibited a band for IgE and the first κ light chain detected, thus confirming the presence of an IgE- κ isotype monoclonal protein.

In conclusion, it is important to think about IgE or IgD monoclonal proteins when we have a single monoclonal component of light chains and there are discrepancies between monoclonal component quantification and FLC concentration.

Posters
Diagnostic Immunology 8 - 13

The authors will attend the poster on **15/11/2019**: 11:00-11:30h, 16:30-17:00h Panel 2

13 The role of HLA-DR expression on monocytes and Sepsis Index as predictive sepsis biomarkers in critical patients at the Intensive Care Unit

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Introduction

Sepsis is characterized by a simultaneous imbalance of hyperinflammation and immunosuppression. The expression of HLA-DR in monocytes (mHLA-DR) and of CD64 in neutrophils (nCD64) are considered, respectively, predictive and diagnostic biomarkers of infection. The ratio nCD64/mHLA-DR has been described as a prognostic biomarker of sepsis.

Objective

To evaluate the relationship between mHLA-DR expression and ratio nCD64/mHLA-DR in patients admitted to the Intensive Care Unit (ICU) and the development of infection.

Methods

Prospective longitudinal study of 77 no infected patients admitted to the ICU from our hospital (HGTiP) due to stroke or severe traumatic brain injury. The mHLA-DR and nCD64 expression were analyzed in whole blood samples at admission (baseline), +3, +6, +9, +12 and +15 days after admission, using a standardized flow cytometry protocol.

Results

During the follow-up, 71% of patients became infected (infection without sepsis, sepsis or septic shock). Analysing retrospectively, infected patients showed – already after three days of admission- a lower percentage of mHLA-DR$^+$ (85.8 ± 16.22% *vs*. 92.5 ± 12.13%, p <0.001) and a higher ratio nCD64/mHLADR (0.12 ± 0.19 vs. 0.04 ± 0.08, p <0.001) than the non-infected ones.

Conclusion

The immumonitoring of mHLA-DR expression and ratio nCD64/mHLA-DR may help to identify those patients with susceptibility to develop infection and sepsis and to facilitate their management at the ICU.

Posters
Methodology and Techniques 14 - 16

The authors will attend the poster on **15/11/2019**: 11:00-11:30h, 16:30-17:00h Panel 3

14 Animal model of allergic asthma for therapeutic studies

Marta Périz[1,2]; Francisco J. Pérez-Cano[1,2]; Santiago Pastor-Soplin[3]; Margarida Castell[1,2]; Ivan Best[3]; Malen Massot-Cladera[1,2]

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Asthma is a chronic airway inflammation affecting over 300 million individuals of all ages worldwide. To evaluate new therapeutic strategies, we aimed to set up a model of acute allergic asthma in rats.

For this purpose, five-week-old female Brown Norway rats were intraperitoneally (i.p.) sensitized with ovalbumin (OVA) together with aluminum hydroxide (Alum) and with or without *Bordetella pertussis* toxin (Bpt). One week later, rats received a second sensitization (i.p.) without toxin. After three weeks, rats werechallenged with either 5 or 50 mg/mL of OVA by intranasal instillation. Anaphylactic shock was then evaluated by measuring body temperature and motor activity. Twenty-four hours later, blood,bronchoalveolar lavage fluid (BALF) and nasal tissue were collected for leucocyte analyses. Moreover, anti- OVA antibodies were determined in serum.

OVA sensitizations, both with and without Bpt, induced a significant increase in total anti-OVA antibodies. However, the animals receiving Bpt showed higher anti-OVA IgE levels than those that did not receive it. Both doses used in OVA challenge were able to reduce motor activity in the following 15 min up to 90%, but did not significantly modify body temperature. Moreover, OVA challenges decreased the proportion of lymphocytes and increased that of granulocytes in blood. The highest OVA dose used in the challengereduced the proportion of monocytes and increased that of lymphocytes in the BALF. In addition, histological staining of nasal tissue from rats challenged with the highest dose showed leucocyte infiltration.

In conclusion, we have achieved a rat asthma model sensitizing with OVA+Bpt+Alum, which affectation, after inducing an anaphylactic shock, can be objectively evaluated in the systemic, nasal and bronchoalveolar compartments.

This study was funded by the National Fund for Scientific and Technological Innovation (FONDECYT) of Peru (Contract 137-2017).

Posters
Methodology and Techniques 14 - 16

The authors will attend the poster on **15/11/2019**: 11:00-11:30h, 16:30-17:00h Panel 3

15 Anti-neutrophil cytoplasmic antibody testing: laboratory experience

María Teresa Sanz-Martínez[1]; Laura Viñas-Giménez[1]; Janire Perurena Prieto[1]; Anais Bofill Turu[1]; Alejandro Pérez Rodríguez[1]; Yolanda Pérez Rosillo[1]; Ana Zurro Fernández[1]; Manuel Hernández-González[1]

[1]Hospital Universitari Vall d´Hebron.

Introduction

According to international consensus statement issued in 1999, indirect immunofluorescence assay (IFA) is the initial screening method to detect the presence of ANCAs. However, it has questioned whether the two-stage diagnostic strategy currently accepted for ANCA detection, firstly IFA and secondly antigen-specific immunoassays, is the best approach due to the availability of antigen-specific immunoassays highly sensitive and specific.

Objective

To evaluate the ANCA consensus in the clinical laboratory practice from a tertiary referral hospital.

Material and Methods

The results of patients tested for ANCA between January 2014 and December 2018 were retrospectively reviewed. IFA were performed on a composite slide that included: human neutrophils fixed with ethanol, human neutrophils fixed with formalin and HEP2 cells with neutrophils fixed with ethanol. Antibodies against myeloperoxidase (MPO) and proteinase 3 (PR3) were tested by a commercial Chemiluminescent Immuno-Assay (CLIA).

Results

Out of 10281 patients with ANCA tested, 1131 (11%) gave a positive result. Out of these 10281 ANCA analysed, 1738 (16.9%) were ordered from primary care and 8543 (83.1%) were hospital cases. The positivity rate for tests ordered from primary care practices was 6%, whereas it was 11.9% from those ordered from hospital. Atypical pattern (X-ANCA) was the most frequent (64.5%) followed by perinuclear (P-ANCA) (19.3%) and cytoplasmatic (C-ANCA) (15.5%). 51.2% of P-ANCA and 36.2% of C-ANCA were positive for MPOANCA and PR3-ANCA respectively, whereas 98% of X-ANCA tested were negative by CLIA.

Conclusion

IFA is a highly sensitive method that allows to identify X-ANCA, the majority pattern and increasingly related to different diseases such as inflammatory bowel disease. Moreover, this method can detect the high percentage of P-ANCA and C-ANCA positives and MPO and PR3 negatives that it could bespecifics to other granulocyte cytoplasm antigens such as elastase, cathepsin G or lactoferrin.

Posters
Methodology and Techniques 14 - 16

The authors will attend the poster on **15/11/2019**: 11:00-11:30h, 16:30-17:00h Panel 3

16 Antinuclear Autoantibody testing in pediatric population

Laura Viñas-Giménez[1]; María Teresa Sanz-Martínez[1]; Janire Perurena Prieto[1]; Anais Bofill Turu[1]; Alejandro Pérez Rodríguez[1]; Yolanda Pérez Rosillo[1]; Ana Zurro Fernández[1]; Manuel Hernández-González[1]

[1]Hospital Universitari Vall d'Hebron.

Introduction

Antinuclear Autoantibody testing (ANA) forms an important part of diagnostic workup of children with suspected systemic autoimmune rheumatic diseases (SARD). However, it is important to point out that the diagnostic utility is limited since there are healthy children with low-titer positive ANA. It is known that ANA has a high sensitivity yet a very poor positive predictive value due to its overzealous use in low-risk populations. Thus, in clinical laboratory practice positive ANA interpretation is challenging.

Objective

To address the relationship between ANA positivity and confirmatory tests in pediatric population.

Methods

Retrospectively, children (0-17 years) referred at Vall d'Hebron hospital, during the years of 2014-2018, to test ANA have been included. The evaluation included assessment of ANA positivity, serum titers and their immunofluorescence pattern and specificity. ANA test was detected by an indirect immunofluorescence (IIF) method using HEp-2 cells as substrate. Confirmatory test of ANA were chemiluminescence (ENA7-panel) and ELISA (dsDNA)

Results

A total of 2724 patients were analyzed. ANA were positive in 1304 (48%) children (1:40 in 24%, 1:80 in 41%, 1:160 in 19%, 1:320 in 7%, 1:640 in 3% and >1:640 in 2%). Patterns of immunofluorescence staining were nuclear-speckle in 61%, homogeneous in 17%, nucleolar in 8%, and mix patterns in 11%. Patients with confirmed ANA specificity were 11% for ENA7 (3% in 1:40, 7% in 1:80, 9% in 1:160, 17% in 1:320, 20% in 1:640 and 63% in >1:640) and 6% for dsDNA (1% in 1:40, 1% in 1:80, 8% in 1:160, 7% in 1:320, 27% in 1:640 and 31% in >1:640).

Conclusion

These findings suggests that at low titre ENA7 and dsDNA have very low yield. Therefore, in these cases clinical information may be very crucial to determine next step in the search for the specificities and so in the accurate diagnose of children.

Posters
Innate Response 17 - 19

The authors will attend the poster on **14/11/2019**: 17:00-17:30h, 18:30-19:00h Panel 1

17 Enhancement of intestinal epithelial barrier maturation in preterm rats by leptin and epidermal growth factor

Blanca Grases-Pintó[1,2]; Paulina Torres-Castro[1,2]; Lidia Marín-Morote[1,2]; Mar Abril-Gil[1,2]; María José Rodríguez-Lagunas[1,2]; Margarida Castell[1,2]; Francisco José Pérez-Cano[1,2]; Àngels Franch[1,2]

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Preterm newborns have an impaired innate and adaptive immune responses as well as underdeveloped epithelial barrier function. Breastfeeding has a key role promoting the maturation of these systems due to milk's rich composition in bioactive compounds, such as adipokines and growth factors.

The aim of the present study was to establish the effect of the supplementation with leptin or epidermalgrowth factor (EGF) on the intestinal epithelial barrier development in a preclinical model of prematurity.

For this purpose, premature Wistar rats, obtained by caesarean section one day before their physiologicalday of birth, were daily supplemented with leptin or EGF during their first 10 days of life. On day 10, an *in vivo* assay was carried out to evaluate the intestinal permeability. After that, PAS and immunofluorescence stainings were carried out to study the histological architecture and the distribution of tight junction proteins of the small intestine. Moreover, the intestinal RNA expression of some intestinal genes was determined by Real Time-PCR.

Preterm rats showed lower intestinal permeability compared to the term ones and both leptin and EGF supplementations were able to reverse this prematurity state. Regarding the histomorphometric study of the small intestine, the supplementation with leptin and EGF to preterm rats increased goblet cell size to a similar extent to that of term rats. In addition, a delocalization of ZO-1 in preterm animals was observed with respect to term rats, fact that seem to be prevented by the EGF supplementation. Moreover, EGF also increased claudin-2 expression with respect to term rats. With regard to intestinal gene expression, the increase in FcRn observed due to prematurity was counteracted by EGF supplementation. Furthermore,leptin administration increased MUC-3 gene expression.

Overall, these results suggest that leptin and EGF improve the maturation of the intestinal barrier function in preterm rats.

Posters
Innate Response 17 - 19

The authors will attend the poster on **14/11/2019**: 17:00-17:30h, 18:30-19:00h Panel 1

18 Airway FABP4 is decreased in COPD patients with airway bacterial infection

Lídia Perea[1]; Ana Rodrigo-Troyano[2]; Elisabet Cantó[1]; Marisol Domínguez-Álvarez[3]; Jordi Giner[2]; Ferran Sánchez-Reus[4]; Alfons Torrego[2]; Judit Villar-García[3]; Sara Quero[5]; Marian García[5]; Eduard Monsó[5]; Rosa Faner[6]; Alvar Agustí[6]; Silvia Vidal[1]; Oriol Sibila[2]

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Introduction: Airway infection worsens outcomes in COPD. Fatty-acid binding protein 4 (FABP4) is an adipokine released by alveolar macrophages and epithelial cells that may play a role as innate immunity against airway infection. The aim of the study was to determine the relationship between pulmonary FABP4 levels and airway infection in stable COPD patients.

Methods: 52 adult patients with clinically stable COPD (mean age 65.2±7.9, mean FEV1 59.0±15.8 % of predicted) and 29 controls were prospectively enrolled at 5 university centers in Barcelona (Spain). Bronchoalveolar lavage fluid (BAL) and induced sputum were obtained. Bacterial infection was defined by the presence of pathogenic bacteria at ≥103 cfu/ml in BAL. FABP4 levels were measured in BAL and sputum by ELISA. BAL total protein was determined using Qubit fluorometer and BAL FABP4 levels were adjusted by the total protein content.

Results: Airway infection was detected in 10 COPD patients (19%), being *Haemophilus* spp (n=8, 80%) the most common one. COPD patients presented lower FABP4 levels in BAL than controls (p=0.03). Infected patients presented lower sputum FABP4 levels than non-infected patients (p=0.0075). A correlation between sputum and BAL FABP4 was observed (r=0.33, p=0.02). In addition, BAL and sputum FABP4 were positively correlated with FEV1 (r=0.28, p=0.04 and r=0.33, p=0.02).

Conclusions: Airway FABP4 is decreased in COPD patients with airway infection. This finding suggested that FABP4 may be important in the pathogenesis of airway infection in COPD.

**Supported by FIS PI15/02042, Fundació Ramon Pla I Armengol and FIS PI15/00167*

The authors will attend the poster on **14/11/2019**: 17:00-17:30h, 18:30-19:00h Panel 1

19 Analyses of porcine Tumor Necrosis Factor Receptor 2 in endothelium

Kelly Casós[1]; Sebastián G. Kuguel[1]; Mireia Uribe-Herranz[1,2]; Cristina Costa[1]

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TNF plays a wide array of functions that result in immune cell activation and inflammation. Accordingly, a role of TNF has been demonstrated in rejection of xenografted cells and organs. We previously cloned the cDNA of pig TNF-Receptor 2 (pTNFR2) to study its contribution and found four isoforms generated by two alternative splicings. The processing of the ΔE4 splicing shortens the TNF-binding domain compromising this function. We hypothesized that the membrane-bound isoforms display distinct activities and performed structural and expression studies to elucidate their roles in endothelium.

In silico simulation of the binding of TNFR2 to human TNFα allowed identifying four amino acids encoded by exon 4 and preserved for both human and pig TNFR2 (Leu106, Gln109, Arg113 and Leu114) as potentially relevant for TNF binding. Regarding the expression analyses, the relative amount of the alternative splicings was determined by quantitative RT-PCR (TaqMan protocol) in porcine aortic endothelial cells (PAEC) in resting and cytokine-stimulated conditions (24-hour time course). The predominant isoform detected by quantitative RT-PCR was the full receptor. Human IL-1α and TNFα produced both a strong up-regulation of the mRNA expression of all the isoforms, which displayed similar kinetics. However, differential response patterns were found as the transcripts peaked at 4 hours after IL-1α treatment and at 24 hours for TNFα. Notably, the expression of pTNFR2 on the cell surface, as determined by flow cytometry, did not correlate with the mRNA levels. Particularly, pTNFR2 expression decreased after exposure to either IL-1α or TNFα for 24 hours. On the contrary, SLA-I was clearly up-regulated and TNFR1 was slightly increased for both pro-inflammatory cytokines. TGFβ1 displayed a minor effect both at the mRNA and cell-surface expression levels. Thus, we reveal relevant information of pTNFR2 at the molecular and expression levels that provide further insight on the process of xenograft rejection.

Posters
Acquired Response 20 - 25

The authors will attend the poster on **14/11/2019**: 17:00-17:30h, 18:30-19:00h Panel 2

20 CD137 (4-1BB) costimulation counteracts TGF-β1 impairment of antibody-dependent NK cell anti-tumor responses

Mariona Cabo[1]; Sara Santana[1]; Marcel Costa-García[2]; Roberto Lozano-Rodríguez[1]; Michelle Ataya[1]; Mª Carmen Ochoa[3]; Pedro Berraondo[3]; Ana Rovira[1,4]; Joan Albanell[1,2,4]; Ignacio Melero3,[5]; Miguel López-Botet[1,2]; Aura Muntasell[1]

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We have shown an association between tumor-infiltrating NK cells and response to anti-HER2 antibodies (i.e. trastuzumab, pertuzumab) in breast cancer patients, supporting their contribution to treatment efficacy. In addition, NK cell dysfunction owing to immunosuppressive factors (i.e. TGF-β1) has been related to disease progression in metastatic patients. Hence, strengthening NK cell function and persistence in the tumor microenvironment is envisaged as a relevant option for enhancing the clinical efficacy of anti-HER2 antibodies.

Microarray analysis of CD16-stimulated human NK cells identified CD137 as the TNFRSF member showing the highest induction upon activation. Coculture with trastuzumab-coated SKBR3 cells triggered NK cell degranulation and CD137 expression, but not PD-1. CD137 expression was sustained by autocrine TNF-α signaling through TNF-RI/TNFR-II, as evidenced by the effect of blocking mAbs. NK cells from individuals harboring adaptive NKG2C+ NK cell expansions displayed greater CD137 upregulation, according to their proficient ADCC and TNF-α secretion. CD137 co-stimulation in CD16-activated NK cells by the agonist mAb urelumab reversed TGF-β1-inhibition of IL2-dependent proliferation, restoring CD25 expression and NK cell numbers. Urelumab-treatment prevented TGF-β1-induced differentiation of CD16-activated NK cells towards an ILC1-like profile, partially preserving their cytotoxic potential (e.g. NKG2D and GzmB) while maintaining the acquisition of tissue-resident features (e.g. CD103, CXCR3) as indicated by GSEA of transcriptomic data and phenotypic analysis. Accordingly, CD137-costimulation in CD16-activated NK cells preserved their subsequent antitumor function by sustaining CCL5 secretion, direct and antibody-dependent tumor cell cytotoxicity and IL-12-dependent IFN-γ production, regardless of TGF-β1. Of note, addition of trastuzumab into multicellular suspensions from treatment-naïve breast human tumors recapitulated the induction of CD137 in the absence of PD-1 in tumor-associated CD16+ NK cells. Overall, our data reveals CD137 as a costimulatory receptor capable of overturning TGF-β1 immunosuppression by promoting NK cell proliferation and sequential tumor cell killing, providing the rationale for combinatorial therapeutic strategies including CD137 agonists.

Posters
Acquired Response 20 - 25

The authors will attend the poster on **14/11/2019**: 17:00-17:30h, 18:30-19:00h Panel 2

21 Protective effect of the flavonoid hesperidin on mesenteric lymph node lymphocyte changes induced by intensive training in rats

Patricia Ruiz-Iglesias[1]; Sheila Estruel-Amades[1]; Malen Massot-Cladera[1]; Mariona Camps-Bossacoma[1]; Margarida Castell[1]; Francisco J. Pérez-Cano[1]

[1]Dept de Bioquímica i Fisiologia, Fac. de Farmàcia i Ciències de l'Alimentació (UB); INSA-UB.

It is known that intense physical activity can induce adverse effects on health. In this sense, high-intensity exercise and exhaustion has shown detrimental effects on immune and gastrointestinal functions (1). Bioactive components of the diet could prevent these effects (2). In this context, hesperidin, the main flavonoid found in citrus fruits, has shown an immunomodulatory role in the gut-associated lymphoid tissue in healthy rats (3). The aim of this study was to establish the effect of hesperidin supplementation on mesenteric lymph node (MLN) lymphocytes in a rat model of high-intensity exercise.

For this purpose, Wistar rats were intensively trained in a treadmill throughout 5 days per week for 5 weeks, including 2 exhausting tests a week. During this period, hesperidin (200 mg/ kg of body weight) was administered by oral gavage three times per week. At the end, samples were obtained after performing a regular training (*trained* group), immediately after carrying out a final exhaustion test (*exhausted* group) and 24 h later (*24 h post-exhaustion* group) to assess the MLN lymphocytes composition and functionality.

The results showed that the high-intensity training decreased MLN T-lymphocytes proliferative capacity. Nevertheless, hesperidin administration attenuated this effect, maintaining similar proliferation rate as that found in sedentary rats. Concerning MLN lymphocytes composition, high-intensity training and exhaustion increased the T/B cell ratio. However, hesperidin supplementation reduced the T/B lymphocyte ratio in the exhausted group, probably due to a T cell mobilization from the MLN to the blood. Moreover, hesperidin increased NK and NKT cell proportions in exhausted animals.

Overall, hesperidin administration contributes to maintaining T lymphocyte function during exhaustion after an intense training period.

1. Walsh NP. Eur J Sport Sci. 2018;(6):820-31.
2. Nieman DC, et al. Nutrients. 2017;(9) :513.
3. Estruel-Amades S, et al. Nutrients. 2019;(11):324

Posters
Acquired Response 20 - 25

The authors will attend the poster on **14/11/2019**: 17:00-17:30h, 18:30-19:00h Panel 2

22 Memory B cells include an IgD class-switched subset that gives rise to IgD-secreting plasma cells possibly involved in mucosal homeostasis

Roser Tachó-Piñot[1]; Giuliana Magri[1]; Daniel Segura-Garzón[1]; Sonia Tejedor[1]; Andrea Cerutti[1,2]

[1]Fundació Institut Hospital del Mar d'Investigacions Mèdiques; [2]Catalan Institute for Research and Advanced Studies (ICREA).

IgD is a signal-transducing receptor co-expressed with IgM on mature naïve B cells via alternative splicing of a long precursor mRNA. However, a fraction of antigen-experienced B cells from the upper-respiratory mucosa selectively expresses IgD after losing IgM through a process now characterized as IgM-to-IgD classswitch recombination. In adults, the resulting IgD class-switched B cells are highly mutated and differentiate into IgD-secreting plasmablasts (PBs) and plasma cells (PCs) through a germinal center reaction that typically occurs in the aerodigestive mucosa, including tonsils. Whether this germinal center pathway also gives rise to IgD class-switched memory (D-ME) B cells remains unknown. Here, we identified unconventional D-ME B cells in human tonsils and peripheral blood. These D-ME B cells showed biased Igλ light chain usage and phenotypic properties that were reminiscent of tissue-based activated memory B cells, including elevated CD11c, CD95, CD69 and CXCR3 expression. When exposed to conventional T celldependent signals, D-ME B cells did not undergo robust proliferation, which likely reflects a functional state of anergy. However, T cell-dependent signals efficiently induced the differentiation of D-ME B cells into IgD-secreting plasmablasts/plasma cells (PB/PCs). Consistent with these *in vitro* findings, additional *ex vivo* data showed that some IgD-secreting PBs/PCs occupied germinal centers, which represent a specialized T cell-dependent follicular microenvironment that also generates memory B cells. IgD-secreting PBs/PCs further inhabited extrafollicular areas such as the crypt epithelium, which is a tonsillar site specialized in antigen entry as well as an effector site for secreted IgD. Accordingly, we found that secreted IgD recognized both microbial and non-microbial aerodigestive antigens, including commensal bacteria and possibly some airborne allergens. Thus, tonsillar IgD responses may be implicated in the homeostasis of the aerodigestive mucosa and could be harnessed to develop new therapeutic strategies against allergic and perhaps infectious disorders.

Posters
Acquired Response 20 - 25

The authors will attend the poster on **14/11/2019**: 17:00-17:30h, 18:30-19:00h Panel 3

23 PF4 levels in malignant pleural effusion as an indicator of poor prognosis in lung cancer patients

Maria Mulet[1]; Carlos Zamora[1]; Juan C. Nieto[1]; José M. Porcel[2]; Elisabet Cantó[1]; M. Angels Ortiz[1]; Lídia Perea[1]; Virginia Pajares[3]; Ana Muñoz[3]; Nuria Calvo[4]; Iñigo Espinosa[5]; Mónica Pascual[5]; Silvia Bielsa[2]; Silvia Vidal[1]

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Background

Malignant pleural effusion (MPE) is defined as the accumulation of tumor cells in the pleural fluid and it is a common complication of advanced lung cancer, especially adenocarcinoma. The MPE represents a singular milieu for direct interactions between tumor cells and host lymphoid cells. Some evidence reveal the presence of immune suppressors that impair the immune system in this metastatic microenvironment. We hypothesise that some of these factors could help to predict the evolution of lung adenocarcinoma (LC) patients.

Aim

Our general aim was to investigate the mechanisms by which MPE from LC modulate T lymphocyte functions, specifically proliferation, cytotoxicity and cytokine production. Among immunomodulatory soluble factors of pleural fluids, we evaluated the potential prognostic roles of those altered in pleural fluids from LC patients compared to heart failure (HF) ones (as a control).

Methods

PBMCs from healthy donors were labeled with CFSE, stimulated and cultured with medium supplemented with HF or LC pleural fluids for 72h. Proliferation and cytotoxic phenotype of T lymphocytes were determined by flow cytometry. Pleural fluids and culture supernatants were analyzed for cytokine content by ELISA.

Results

The presence of MPE inhibited the T lymphocyte proliferation and granzyme B expression. We found that levels of soluble mediators derived mainly by platelets (PF4, P-selectin, VEGF, TGF-β) were increased in pleural fluids from LC patients compared to HF ones. Specifically, PF4 was implicated in the immunosuppression of T lymphocyte functions and was associated with less survival.

Conclusions

The high content of PF4 in the MPE may be responsible for the modulation of the immune response against the tumor and could have clinical relevance as a predictor of poor prognosis in LC patients with MPE. An impaired proliferative and cytotoxic response of T lymphocytes induced by PF4 could provide a significant advantage for the tumor to progress.

Posters
Acquired Response 20 - 25

The authors will attend the poster on **14/11/2019**: 17:00-17:30h, 18:30-19:00h Panel 3

24 Administration of Lactobacillus fermentum CECT5716 in pregnant and lactating rats influences their systemic and intestinal immunoglobulin and cytokine profile and impacts their offspring

Ignasi Azagra-Boronat[1,2]; Malén Massot-Cladera[1,2]; Àngels Franch[1,2]; Margarida Castell[1,2]; Francisco J. Pérez-Cano[1,2]; Maria J. Rodríguez-Lagunas[1,2]

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It is well known that the immune system is influenced by the sensing of intestinal microbiota both in intestinal and systemic levels. Therefore, the administration of probiotics during pregnancy and lactation periods might be a good strategy to improve immunity of the mother.

This study aimed to analyze whether the supplementation of rats during pregnancy and lactation periods with *Lactobacillus fermentum* CECT5716 enhances the immune system of the mother and if these can be transmitted to their offspring.

Animals were monitored and daily p.o. supplemented with the probiotic during the three weeks of gestation and two weeks of lactation. Then, mothers and pups were sacrificed in order to obtain plasma and intestinal samples (gut wash, feces, cecal content and mesenteric lymph nodes). Fecal pH was measured. Moreover, several organs were collected to assess their weight. The quantification of intestinal and systemic immunoglobulins was performed by ELISA and Luminex techniques, respectively. The quantification of cytokines by Luminex technique was performed at systemic (dams and pups) and intestinal (dams) levels.

Probiotic supplementation did not influence organ weight or fecal pH in either dams or pups. However, we observed a tendency to increase IgG2a in dams' plasma, which was also significantly increased in pups. Moreover, significative reduction of systemic IgG2c in the pups was observed, therefore increasing Th2 type Ig and reducing the Th1/Th2 ratio. Although we did not detect changes in systemic cytokines, we observed that the dams displayed less IL-12 in the cecal content and higher IFNγ in the gut wash.

Overall, *Lactobacillus fermentum* CECT5716 supplementation induced changes in the Ig profile of dams that resemble the pattern found in the pup, therefore suggesting an active transmission of the effects. Hence, nutritional interventions aimed at improving the quality of the immune system of the mother might be beneficial for their offspring.

Posters
Acquired Response 20 - 25

The authors will attend the poster on **14/11/2019**: 17:00-17:30h, 18:30-19:00h Panel 3

25 Characterization of AIRE-protein domains in antigenic processing and presentation

Adrián Tirado Herranz[1]; Alba Pastor Moreno[1]; Iñaki Álvarez[1]

[1]Institut de Biotecnologia i Biomedicina, Univesritat Autònoma de Barcelona.

Central tolerance is based on the elimination of autorreactive thymocytes during the thymic selection. To be an efficient process, it is necessary the MHC presentation of ideally all the proteins of the organism by the medullary thymic epithelial cells (mTECs). The Autoimmune Regulator (AIRE) is mainly expressed in mTECs. This protein partially leads the ectopic expression of a wide bunch of tissue restricted antigens (TRAs) to avoid the egress of potentially-autorreactive T cells into the periphery tissues that could cause autoimmune responses.

AIRE is a multi-domain protein involved in different activities that allow the establishment of central tolerance such as regulation of the expression machinery, RNA processing, maturation and differentiation of mTECs, apoptosis or cell cycle regulation. Mutations on *AIRE* gene lead the development of Autoimmune Polyendocrine Syndrome 1 (APS1) causing the detection of autoantibodies and infiltrated-lymphocytes on glandular tissue. Most of the mutations affect the activity of AIRE protein altering the subcellular localization and therefore the thymic selection. AIRE is principally expressed in the nucleus. In addition to the nuclear location, a fibrillary cytoplasmic localization has also been described in transfected cells.

Previous findings of our research group showed differences in the proteome between untransfected cells and cells transfected with AIRE. AIRE transfected cells increased the levels of different pro-apoptotic proteins and chaperones. In addition, cell-death in transfected cells was also increased. One of the proteins with an increased presence in the proteome was SIAH1-interacting protein (SIP), an adaptor protein involved in ubiquitination. The Seven in Absentia Homologue (SIAH) is an E3 ubiquitin family involved in proteasome-mediated degradation of specific proteins. Most of the proteins that interact with SIAHs E3 ubiquitin ligases present a specific union motif to SIAH which is present in SIP and AIRE. All of this strongly indicates a relation between AIRE and SIAHs proteins.

2020 Events
Lifelong Learning SCI Program 2020

Academic activities that are part of the Advanced Immunology Training Course organized by the SCI

Data i hora: 6 de febrer de 2020, a les 18.00h
Frontiers in Malaria Research
Dr. Alfonso Mayor (ISGlobal)
Dr. Xavier Fernández-Busquets (Institut de Bioenginyeria de Catalunya (IBEC))
Lloc: Sala 8, Acadèmia de Ciències Mèdiques (Major de Can Caralleu 1-7, Barcelona).

Data i hora: 5 de març de 2020, a les 18.00h
CD300 receptor family in viral infections
Dr. Francisco Borrego (Hospital Universitario Cruces)
Lloc: Sala 8, Acadèmia de Ciències Mèdiques (Major de Can Caralleu 1-7, Barcelona).

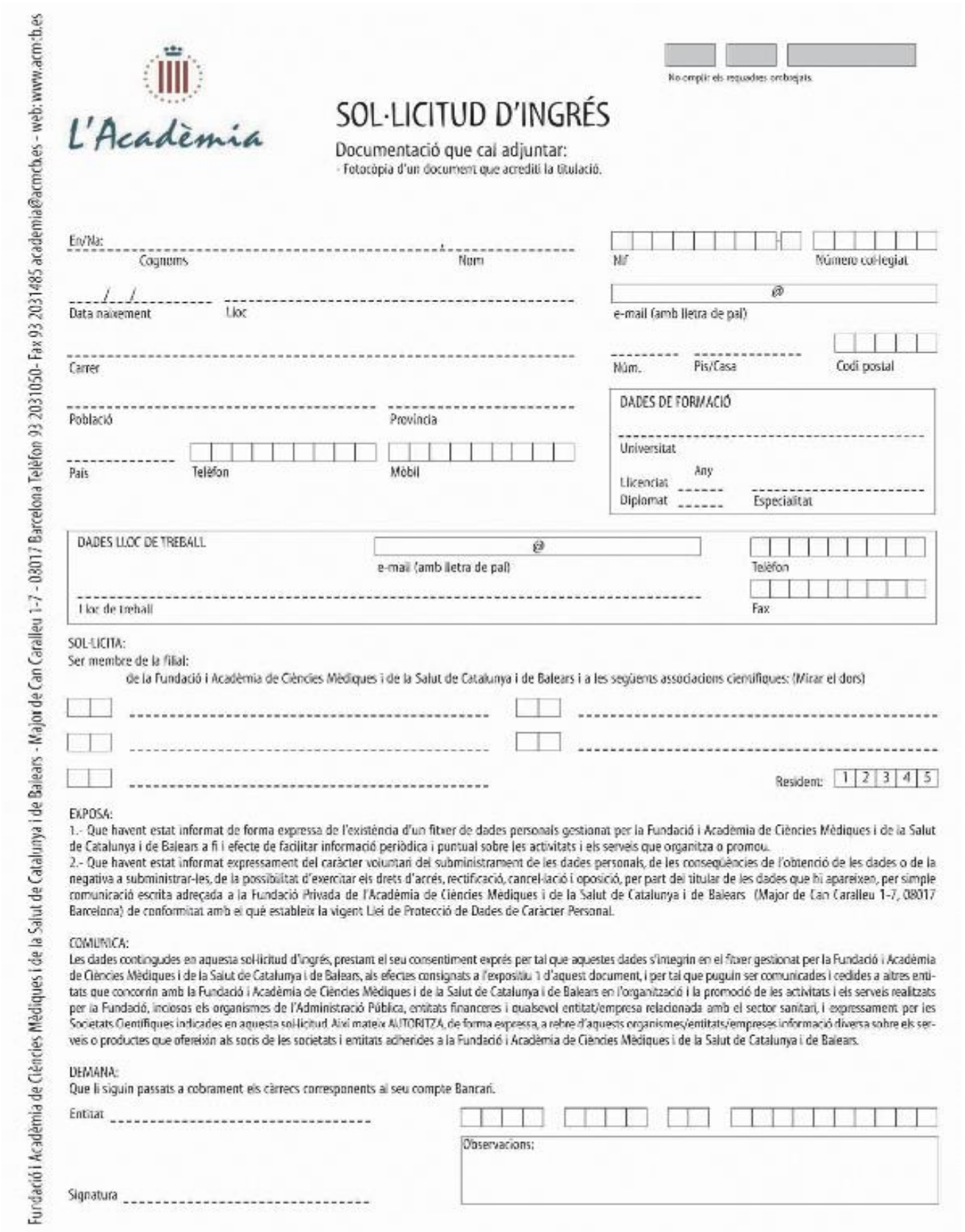
Data i hora: 30 d'abril de 2020, a les 15.00h
Cancer Immunotherapy. DIA DE L'IMMUNOLOGIA.
Dr. Manuel Juan Otero (Hospital Clínic de Barcelona), **Dr. Pablo Menéndez** (Josep Carreras, Leukaemia Research Institute), **Dra. Susana Rives** (Hospital de Sant Joan de Déu, Barcelona).
Lloc: Sala 8, Acadèmia de Ciències Mèdiques (Major de Can Caralleu 1-7, Barcelona).

Data i hora: 7 de maig de 2020, a les 18.00h
The microbiota and the immune system
Dra. Giuliana Magri (Institut Hospital del Mar d'Investigacions Mèdiques (IMIM))
Dr. Joan Verdaguer (Institut de Recrca Biomèdica de Lleida (IRBLleida), UdL)
Lloc: Sala 8, Acadèmia de Ciències Mèdiques (Major de Can Caralleu 1-7, Barcelona).

Data i hora: 4 de juny de 2020, a les 18.00h
Designed antibodies: New Partners in HIV Eradication Strategies
Dr. Jorge Carrillo (Virología e Inmunología Celular, IrsiCaixa)
Lloc: Sala 8, Acadèmia de Ciències Mèdiques (Major de Can Caralleu 1-7, Barcelona).

The Advanced Immunology Training Course has been accredited by the Catalan Lifelong Learning Board of the Healthcare Professions with 1,4 credits (Record: 09/026185-MD).

New members Registration form to SCI



Fundació i Acadèmia de Ciències Mèdiques i de la Salut de Catalunya i de Balears - Major de Can Caralleu 1-7 - 08017 Barcelona Telèfon 93 2031050- Fax 93 2031485 academia@acmcb.es - web: www.acmcb.es

No omplir els requadres ombrejats

L'Acadèmia

SOL·LICITUD D'INGRÉS

Documentació que cal adjuntar:
- Fotocòpia d'un document que acrediti la titulació.

En/Na: _____
Cognoms / Nom

NIF / Número col·legiat

_____ / _____ / _____
Data naixement / Lloc

e-mail (amb lletra de pal)

Carrer

Núm. / Pis/Casa / Codi postal

Població / Provincia

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DADES DE FORMACIÓ
Universitat
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Diplomat / Especialitat

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SOL·LICITA:
Ser membre de la filial:
de la Fundació i Acadèmia de Ciències Mèdiques i de la Salut de Catalunya i de Balears i a les següents associacions científiques: (Mirar el dors)

Resident: 1 2 3 4 5

EXPOSA:
1.- Que havent estat informat de forma expressa de l'existència d'un fitxer de dades personals gestionat per la Fundació i Acadèmia de Ciències Mèdiques i de la Salut de Catalunya i de Balears a fi i efecte de facilitar informació periòdica i puntual sobre les activitats i els serveis que organitza o promou.
2.- Que havent estat informat expressament del caràcter voluntari del subministrament de les dades personals, de les conseqüències de l'obtenció de les dades o de la negativa a subministrar-les, de la possibilitat d'exercitar els drets d'accés, rectificació, cancel·lació i oposició, per part del titular de les dades que hi apareixen, per simple comunicació escrita adreçada a la Fundació Privada de l'Acadèmia de Ciències Mèdiques i de la Salut de Catalunya i de Balears (Major de Can Caralleu 1-7, 08017 Barcelona) de conformitat amb el què estableix la vigent Llei de Protecció de Dades de Caràcter Personal.

COMUNICA:
Les dades contingudes en aquesta sol·licitud d'ingrés, prestant el seu consentiment exprés per tal que aquestes dades s'integrin en el fitxer gestionat per la Fundació i Acadèmia de Ciències Mèdiques i de la Salut de Catalunya i de Balears, als efectes consignats a l'exposítiu 1 d'aquest document, i per tal que puguin ser comunicades i cedides a altres entitats que concorrin amb la Fundació i Acadèmia de Ciències Mèdiques i de la Salut de Catalunya i de Balears en l'organització i la promoció de les activitats i els serveis realitzats per la Fundació, inclosos els organismes de l'Administració Pública, entitats financeres i qualsevol entitat/empresa relacionada amb el sector sanitari, i expressament per les Societats Científiques indicades en aquesta sol·licitud. Així mateix AUTORITZA, de forma expressa, a rebre d'aquests organismes/entitats/empreses informació diversa sobre els serveis o productes que ofereixin als socis de les societats i entitats adherides a la Fundació i Acadèmia de Ciències Mèdiques i de la Salut de Catalunya i de Balears.

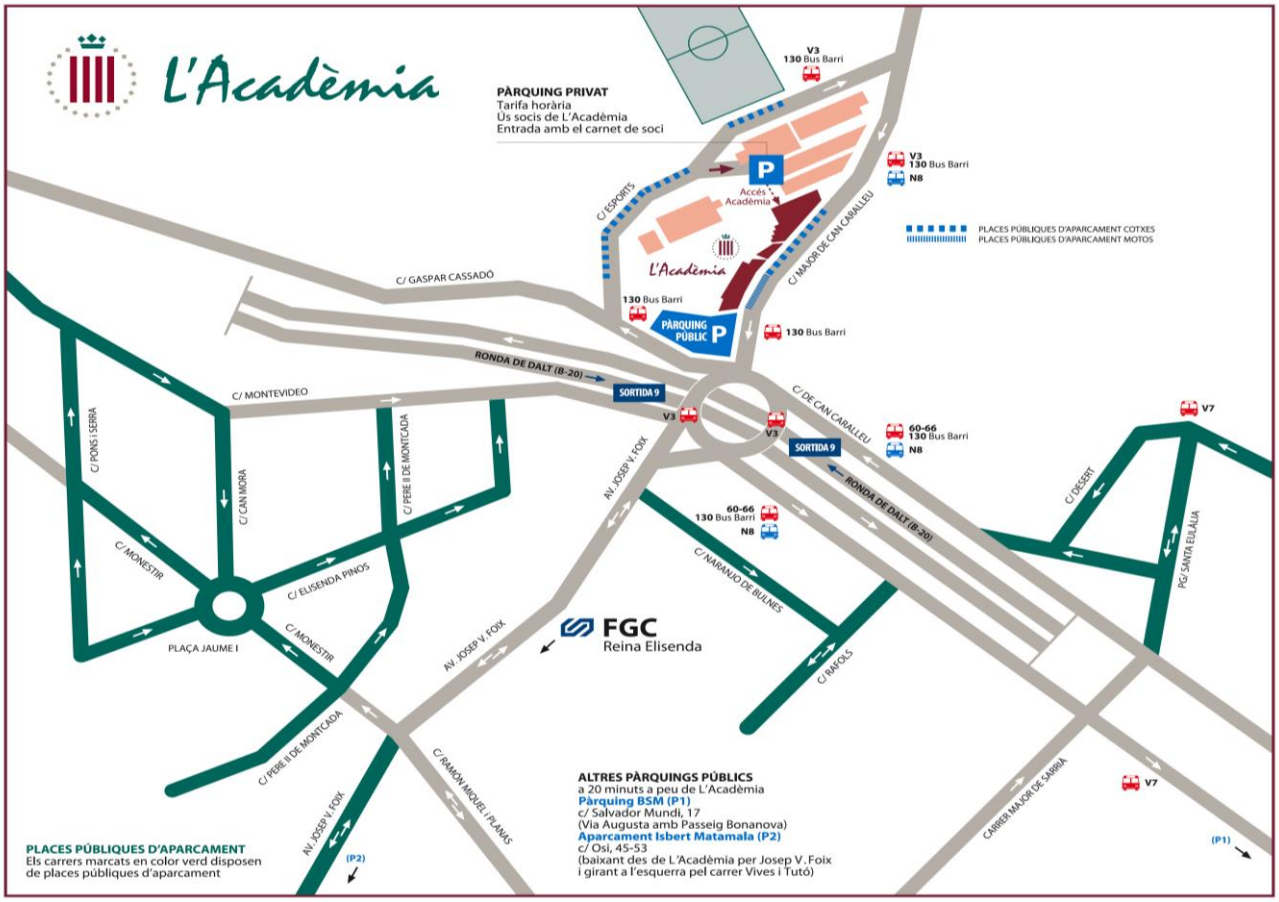
DEMANA:
Que li siguin passats a cobrament els càrrecs corresponents al seu compte Bancari.

Entitat _____

Observacions:

Signatura _____

Participant information: useful information



Congress Venue:
Academia de Ciències Mèdiques, Auditori de l'Acadèmia
c/ Major de Can Caralleu1
08017 Barcelona.

Transportation:

- **By car**: Ronda de Dalt, exit 9
- **By bus**:
  - Line 66 (Pl. Catalunya – Sarrià)
  - Line 60 (Pl. Glòries – Zona Universitaria)
  - Line V3 (Zona Franca –Can Caralleu)
  - Line 130 (Pl. Artós – Can Caralleu))
- **By subway**: Ferrocarrils de la Generalitat de Catalunya (FGC): Line 6: Reina Elisenda station

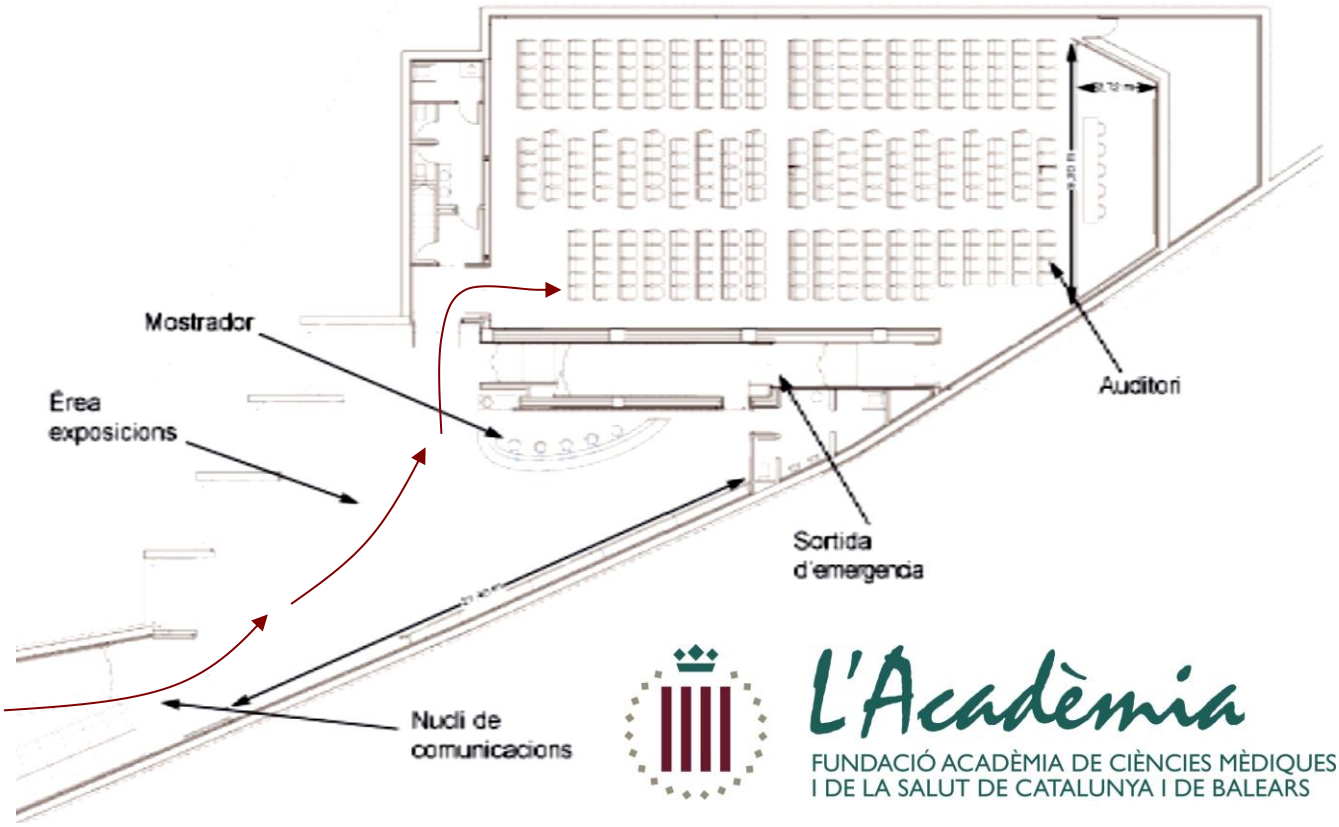
Parking: Small open area between the Academy and the city ring (only for members of the Academy: Parking fees apply).

Congress Office:

Sr. Xavier Nieves
Tel: 00 34 93.203.13.18; FAX: 00 34 93 212 35 69
xnieves@academia.cat

List of authors and participants

Other useful information and notes



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SCI
SOCIETAT CATALANA D'IMMUNOLOGIA
ACM Barcelona

XIII CONGRÉS

Societat Catalana d'Immunologia (SCI)

Barcelona, 14 i 15 de novembre 2019

The contents of this congress will be accessible in https://www.youtube.com/channel/UC95jw_G-ms-okbfMSK1Dtrw/playlists

The new YouTube chanel offered by Societat Catala d'Immunologia

You can follow the activity of the SCI

- **Facebook:** https://www.facebook.com/SCImmunologia
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