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SCI
SOCIETAT CATALANA D'IMMUNOLOGIA

XIVth CONGRÉS

Societat Catalana d'Immunologia (SCI)

joint meeting with European Federation of Immunological Societies on Tour (EFIS on TOUR)

Programa Final

Barcelona, 19 i 20 de Novembre de 2020
Acadèmia de Ciències Mèdiques i de la Salut de Catalunya i de Balears

AGAINST THE DOGMA

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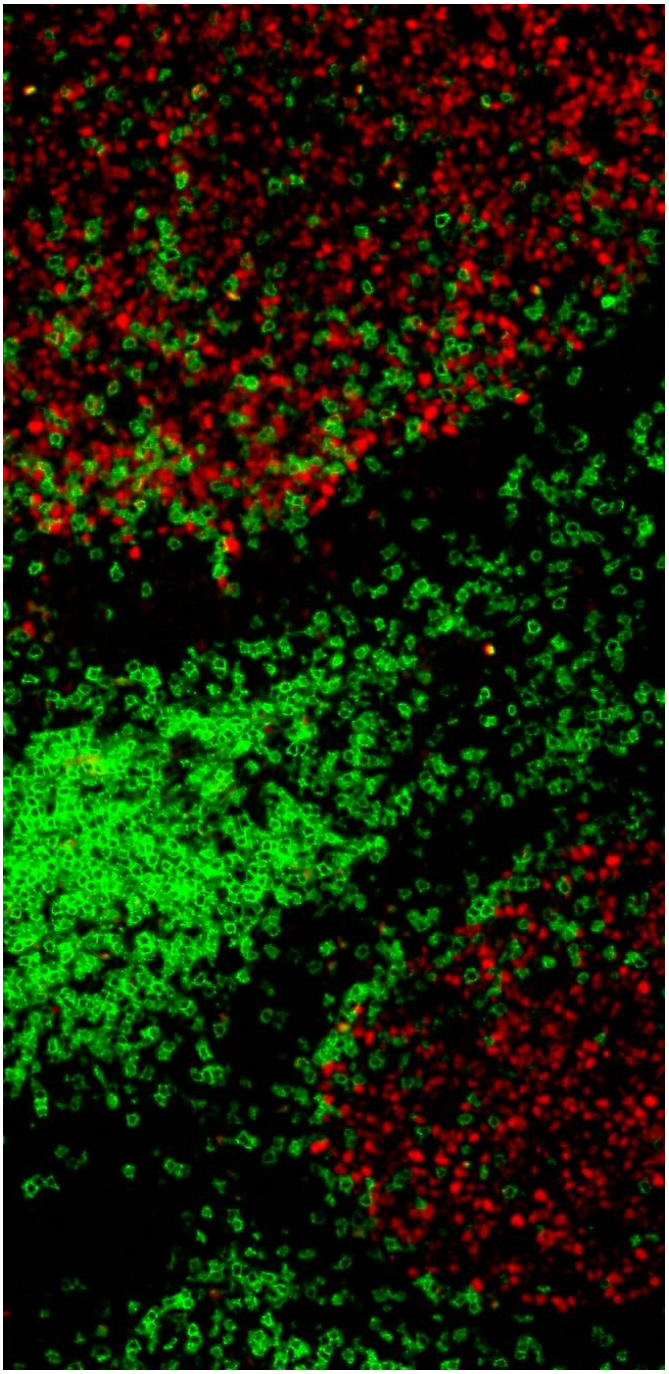

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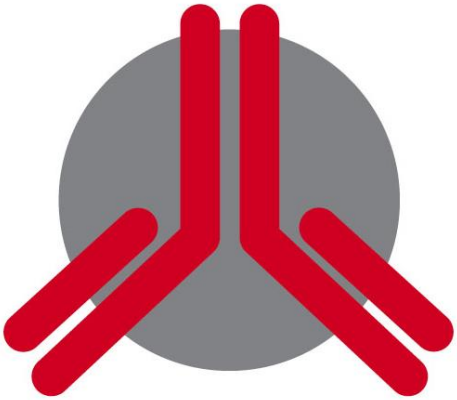

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Welcome to the congress,

On behalf of the organising committee, we would like to warmly welcome you to the XIVth Societat Catalana d'Immunologia Congress (SCI Congress). We believe that our joint meeting with the European Federation of Immunological Societies (EFIS) will present high level scientific knowledge with the contribution of immunologists and specialist who are experts in this field.

Dr. Ricardo Pujol-Borrell
SCI President

XIVth Congress of the Catalan Society of Immunology: Against the Dogma has been accredited by the Catalan Lifelong Learning Board of the Healthcare Professions with 0,4 credits (Record: **09/028725-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. The results will be announced at the end of the congress.

Scheme first day

Thursday, November 19th	
16:00 16:15	**Welcome to the XIIIth CONGRESS of the SCI** **Ricardo Pujol-Borrel** (President of SCI) **Marcos López-Hoyos** (President of SEI)
16:15 17:00	**Opening Lecture –** Speaker: **Andreas Radbruch** (German Rheumatism Research Center Berlin (DRFZ), a Leibniz Institute) (President of EFIS) **Introduction to EFIS on Tour** Title: ***Immunological memory against the dogma.*** Chair: **Pablo Engel** (University of Barcelona)
17:00 17:30	Poster viewing
17:30 18:00	**Plenary Session** Speaker: **Balbino Alarcon** (Centro Biología Molecular Severo Ochoa, Madrid) Title: ***Inter-TCR crosstalk during antigen recognition.*** Chair: **Annabel Valledor**, (University of Barcelona).
18:00 19:45	**Oral Communications, Session-1** – ***Basic and Experimental Immunology*** Chair: **Aura Muntasell** (Autonomous University of Barcelona). - Experimental and genetic evidence for the involvement of *CD6* in inflammatory bowel diseases. **Sergi Casadó-Llombar** et al. - Macrophage mitochondrial MFN2 (mitofusin 2) links immune stress and immune response through reactive oxygen species (ROS) production. **Antonio Celada** et al. - Immunomodulation of type 1 diabetes by 116C-NOD intestinal microbiota. **Estela Rosell-Mases** et al. - siRNA-containing transfection of vitamin D3-induced tolerogenic dendriticcells for the silencing of potential tolerogenic genes. **Íñigo González Larreategui** et al. - Immunomodulatory properties of a soluble cytomegalovirus-encoded CD48 Homolog. **Francesc Poblador** et al. - MRL mice infected with cytomegalovirus (CMV) as an animal model of Sjögren's Syndrome. **Joan Puñet-Ortiz** et al. - HIV-1 enveloped Virus-Like Particles (VLP) displaying high density of HIV-1 Env-derived antigens on their surface induce a functional immune response beyond neutralizing activity. **Ferran Tarrés-Freixas** et al. 19:25–19:45 **Discussion**
19:45 20:15	**Plenary Session** Speaker: **Winfried Pickl** (Medical University of Vienna) Title: ***The role of a new T helper cell type, Th-IL-2 cells, in allergic immune reactions.*** Chair: **Eva Martinez-Carceres** (Autonomus University of Barcelona).

Scheme second day

Friday, November 20th	
09:00 09:30	**Plenary Session** Speaker**:** **René van Lier** (Sanquin Blood Supply. University of Amsterdam) Title**:** ***Tissue memory cells at the center of the immune system*** Chair: **Dolores Jaraquemada** (Autonomous University of Barcelona)
09:30 10:00	**Plenary Session** Speaker**:** **Miguel López-Botet** (University Pompeu Fabra, Barcelona) Title**:** ***Development of human "adaptive" NK cell populations: open issues.*** Chair: **Pablo Engel** (University of Barcelona)
10:00 11:30	**Oral Communications, Session 2:** ***Clinical Immunology*** **I** Chairs: **Cristina Costa** (IDIBELL, Barcelona).; **Rosa Faner** (Hospital Clinic, Barcelona). - Changes induced in lymphocyte subpopulations by dimethyl-fumarate treatment in multiple sclerosis could identify "NEDA" patients. **Aina Teniente Serra** et al. - Lymphocyte subpopulations analysis in psoriatic patients treated with biological drugs. **Marc Boigues-Pons** et al. - Myeloid-Derived Suppressor Cells in Kidney Transplant Recipients and the effect of Maintenance Immunotherapy. **María Iglesias Escudero** et al. - Pretransplant adaptive NKG2C+ NK cells protect against cytomegalovirus infection in kidney transplant recipients. **Michelle Ataya** et al. - Impaired lung NK activity in the lung of Idiopathic Pulmonary Fibrosis patients. **Tamara Cruz** et al. - Immunophenotype in CU patients under omalizumab treatment. **Cristina Alejandra López Rodríguez** et al. 11:15–11:30 **Discussion**
11:30 12:00	**Plenary Session** Speaker**:** **Federica Sallusto** (Institute for Research in Biomedicine Bellinzona) Title**:** ***Conventional and unconventional T cell response to microbial antigens.*** Chair: **Ricardo Pujol** (Autonomous University of Barcelona).
12:00 13:00	**Ordinary General Meeting- Societat Catalana d'Immunologia**
13:00 13:30	Poster viewing

13:30 14:00	**Lunch session sponsored by Becton Dickinson** Speaker: **Werner Rodriguez** (*BD Biosciences | Single Cell Multiomics)* Tilte: ***Resolving immune cell identity one cell at time. The multiomic approach.***
14:30 16:15	**Oral Communications, Session 3:** ***Tumor Immunology and Immunotherapy*** Chair: **Manel Juan** (Hospital Clinic. Barcelona) - Phase I multicenter clinical trial with chimeric antigen receptor with humanized anti-BCMA specific (ARI0002h) in patients with relapsed or refractory multiple myeloma. **Mariona Pascal** et al. - CART19-BE-01: un ensayo académico Europeo sobre la administración de células CAR-T denominadas ARI-0001 en pacientes con trastornos linfoproliferativos CD19**+. Valentín Ortiz-Maldonado** et al. - Humoral immune response in patients with CD19 positive relapsed/refractory B-cell malignances recruited into the CART19-BE-01 clinical trial. **Ariadna Bartoló-Ibars** et al. - Comparative analysis and characterization of TCR repertoires in breast cancer TILs. **Andrea Aran** et al. - HAVCR2 mutations altering TIM-3 underlying hemophagocytic syndrome and subcutaneous panniculitis-like T-cell lymphoma. **Roger Colobran** et al. - Dynamics of T-cell subsets in non-small cell lung cancer patients treated with PD-1/PD-L1 axis blocking mAbs. **Coral Zurera Egea** et al. - NK cell receptors and ligand variants modulate response to tyrosine kinaseinhibitors in patients with chronic myeloid leukemia. **Laia Closa** et al. *15:55–16:15* ***Discussion***
16:15 16:45	**Plenary Session** Speaker**: Antonio Lanzavecchia** (National Institute of Molecular Genetics, Milan) Title**:** ***Unconventional receptor-based antibodies.*** Chair: **Miguel López Botet** (University Pompeu Fabra , Barcelona)
16:45 18:00	**Oral Communications, Session 4:** ***COVID-19*** Chair: **Silvia Vidal** (Santa Creu i Sant Pau Hospital, Barcelona). - Early S2-targeting and rapid development of neutralizing antibodies after SARS-CoV-2 infection. **Carlos Ávila-Nieto** et al. - Antigen-specific lymphocyte proliferation against SARS-CoV-2 in COVID patients with negative antibodies against the virus in serum. **Marc Boigues-Pons** et al. - Immunological Risk Profile in COVID-19, the Experience of a Single Academic Hospital in Catalonia. **Manuel Hernández-González** et al. - Immunopathogenesis of COVID-19-related pediatric inflammatory multisystem syndrome: overlap with Kawasaki disease and identification of a distinct severe group. **Ana Esteve-Solé et al.**

	- Revealing protective T cell immune responses against SARS-CoV-2. **Judith Grau-Expósito** et al. - Inborn errors and autoantibodies against type-I inteferons in patients with life-threatening COVID-19. **Roger Colobran** et al 17:45–18:00 **Discussion**.
18:00 **18:30**	**Prize to the best communication and poster.** **Closing of the Congress** **Ricardo Pujol Borrell (**President of SCI**).**

Abstracts
Oral Communications — Session I
Basic and Experimental Immunology

1 Experimental and genetic evidence for the involvement of *CD6* in inflammatory bowel diseases

Sergi Casadó-Llombart[1]; María Velasco-de Andrés[1]; Cristina Català[1]; Alejandra Leyton-Pereira[1]; Belén Suarez[2]; Noelia Armiger[1]; Esther Carreras[1]; Miriam Esteller[3,4,5]; Javier P Gisbert[6]; Lucía Márquez[7]; Maria Esteve[5,8]; Julián Panés[3,4,5]; Ingrid Ordàs[3,4,5]; Elena Ricart[3,4,5]; Azucena Salas[3,4,5]; Eugeni Domènech[9,10]; Francisco Lozano[1,2,11]

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CD6 is a signal-transducing lymphocyte co-receptor mainly expressed on T cells and a subset of B cells, which has still ill-defined roles in regulation of lymphocyte development, activation and differentiation. The CD6 ligands reported to date cover not only widely expressed endogenous counter-receptors (CD166/ALCAM, CD318/CDCP-1 and Galectin 1 and 3) found in both immune cells and a broad range of other normal and neoplastic cell types (e.g., epithelial, mesenchymal) but also microbial-associated molecular pattern of bacterial, viral and parasitic origin. Multiple lines of evidence are now emerging to implicate CD6 and its ligands in the pathogenesis and potential treatment of human autoimmune diseases. The present work aimed at exploring a putative pathophysiological role of CD6 in inflammatory bowel diseases (IBD) including Crohn's disease (CD) and ulcerative colitis (UC). To this end, we first subjected wild-type (WT) and CD6-deficient (*cd6*$^{-/-}$) mice to dextran sodium sulfate (DSS)-induced colitis, a standard experimental model of IBD. The results showed a more severe form of DSS-induced colitis in *cd6*$^{-/-}$ (including increased weight loss and disease score, as well as altered hematological parameters) compared with WT controls. Since no CD6 deficiencies have been reported in humans, we next studied a putative association of single nucleotide polymorphisms (SNPs) of the CD6 gene (rs17824933, rs11230563, and rs12360861) with clinically relevant parameters from CD (n=1352) and UC (n=1013) patients included in the ENEIDA project of the Spanish GETECCU group. The analysis showed that none of the SNPs included in the study were

associated to susceptibility to CD or UC. Nevertheless, significant associations were found associated to location, extent, presence of extra-intestinal manifestations and prognosis of CD and/or UC patients. Taken together, the results support a role of CD6 in IBD, thus further extending the relevance of its immunomodulatory role in autoimmune disorders.

2 Macrophage mitochondrial MFN2 (mitofusin 2) links immune stress and immune response through reactive oxygen species (ROS) production

Antonio Celada[1]; Juan P. Muñoz,[2,3,4]; María Isabel Hernández-Álvarez,[2,3,4]; Pere-Joan Cardona,[5,6]; Antonio Zorzano,[2,3,4]; Jorge Lloberas[1]

[1]Macrophage Biology Group, Department of Cell Biology, Physiology and Immunology, Facultat de Biolog;
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[4]Departament de Bioquímica i Biomedicina Molecular, Facultat de Biologia, Universitat de Barcelona,;
[5]Unitat de tuberculosi experimental, Institut Germans Trias i Pujol, Badalona, Spain.;
[6]Centro de Investigación Biomédica en Red de Epidemiologia y Salud Pública (CIBERESP), Madrid, Spain

MFN2 (mitofusin 2) is required for mitochondrial fusion and for mitochondria-endoplasmic reticulum interaction. Using myeloid-conditional KO mice models, we found that MFN2 but not MFN1 is a prerequisite for the adaptation of mitochondrial respiration to stress conditions as well as for the production of reactive oxygen species (ROS). The deficient ROS production in the absence of MFN2 impairs the induction of cytokines and nitric oxide, and is associated with dysfunctional autophagy, apoptosis, phagocytosis, and antigen processing. The lack of MFN2 in macrophages causes an impaired response in a model of non-septic inflammation in mice, as well as a failure in protection from Listeria, Mycobacterium tuberculosis or LPS endotoxemia. These results reveal an unexpected role of MFN2 to ROS production in macrophages affecting natural and acquired immunity and the immune response.

3 Immunomodulation of type 1 diabetes by 116C-NOD intestinal microbiota

Estela Rosell-Mases[1]; Alba Santiago[2]; Marta Pozuelo[2]; Marta Corral-Pujol[1]; Catalina Cosovanu[1]; Marina Lleal[2]; Joseane Willamil[2]; Francisca Yáñez[2]; Leire Egia-Mendikute[1]; Enric Cosp[2]; Celeste Santos[1]; Celia Vived[1]; Julia Luna[1]; Conchi Mora[1]; Chaysavanh Manichanh[2]; Joan Verdaguer[1,3]

1Immunology Unit, Faculty of Medicine, University of Lleida and IRBLleida, Lleida, Spain.; 2Department of Gastroenterology, Vall d'Hebron Research Institute, Barcelona, Spain.; 3CIBERDEM, Instituto de Salud Carlos III, Madrid, Spain.

Over the last decades, animal model research and clinical studies have shown the connection between gut microbiota alterations and the autoimmune response in the context of type 1 diabetes (T1D). Nevertheless, the microbiota-driven modulation of the adaptive immune system, the main responsible of the diabetic autoimmune process, remains poorly understood.

To clarify this issue, the islet beta cell-autoreactive B lymphocyte transgenic 116C-NOD mouse model was used. Interestingly, 116C-NOD mice present a decreased T1D incidence compared with NOD mice. Taking advantage of this feature, our objective focused on analysing the impact of the 116C-NOD fecal microbiota natural transfer on the T1D progression and the immune phenotype of recipient NOD mice.

Non-transgenic NOD mice cohoused with their 116C-NOD transgenic littermates for forty weeks displayed a significantly diminished disease incidence compared to that of NOD housed separately from their B-cell transgenic siblings. Furthermore, lymphocytes from cohoused NOD mice developed a Th1/Th17 response, at the halfway point between the Th1 predominant pattern of NOD mice and the prevailing Th17 profile of 116C-NOD.

Taken together, these results suggest that gut microbiota, modulated by the own 116C-NOD lymphocyte repertoire, may modify the diabetic autoimmune process of recipient NOD littermates by means of a Th response change.

4 siRNA-containing transfection of vitamin D3-induced tolerogenic dendritic cells for the silencing of potential tolerogenic genes

Íñigo González Larreategui[1]; Ares Sellés[1,2]; Aina Teniente[1,2]; Bibiana Quirant[1,2]; Silvia Presas[3]; Cristina Ramo-Tello[3]; Eva María Martínez Cáceres[1,2]; María José Mansilla[1,2]

1Germans Trias i Pujol University Hospital and Research Institute; 2Department of Cellular Biology, Physiology and Immunology, Universitat Autònoma de Barcelona; 3Multiple Sclerosis Unit, Department of Neurosciences, Hospital Universitari Germans Trias i Pujol

Background: Reestablishment of the immune tolerance is one of the most promising strategies for autoimmune diseases, which can be achieved by tolerogenic dendritic cells (tolDC). These cells display a semimature state of DC, generating a hyporesponsiveness to allogeneic cells. Moreover, as tolDC can be differentiated in vitro from peripheral blood monocytes by the induction of vitamin D3 (VitD3-tolDC), study of CSF1R and CD209 as potential tolerogenic genes could serve as a control of the proper generation of the cells.

Objective: To set up an easy and fast transfection methodology of monocytes for the study of CSF1R and CD209 genes during VitD3-tolDC generation by siRNA silencing.

Methodology: mDC and VitD3-tolDC were differentiated from monocytes and cultured for 6 days in presence of IL-4, GM-CSF (and vitamin D3 for the VitD3-tolDC). At day 1 (and day 4 for doubled transfection), Viromer blue reagent combined with specific or control siRNA were added to VitD3-tolDC. Maturation was inducted on day 4 and, on day 6, global characterization of gene and protein expression, phenotype markers and functionality were performed by qPCR and flow cytometry.

Results: Optimization of transfection using Viromer blue+siRNA per million of cells resulted in a >80% of transfected cells without affecting phenotypical or functional characteristics of VitD3-tolDC. The introduction of specific siRNA for CSF1R and CD209 genes allowed an 8-fold change down-modulation of both genes compared to non-transfected VitD3-tolDC, although only CD209 protein reduced significantly its expression. A partial reduction in the hyporesponsiveness to allogeneic cells was observed in siCD115-containing tolDC, although no statistical significance was reached (n=3). Besides, neither the combined silencing of CSF1R and CD209 nor a doubled transfection affect this hyporesponsiveness.

Conclusion: Viromer blue is an adequate transfection technology for VitD3-tolDC. CSF1R gene is related (but not essential) with the tolerogenicity of VitD3-tolDC.

Oral Communications
Basic and Experimental Immunology

Session I

5 Immunomodulatory properties of a soluble cytomegalovirus-encoded CD48 homolog

Francesc Poblador[1]; Pablo Martínez-Vicente[1]; Pablo Engel[1]; Ana Angulo[1]

1*Immunology Unit, Department of Biomedical Sciences, Medical School, University of Barcelona, Spain.*

Cytomegaloviruses (CMVs) have evolved a remarkable variety of strategies to evade host immunity and stablish persistence. Some of these strategies are based on genes originally stolen from their host, molded and functionally optimized through evolution in order to interfere with specific immune processes. CD48 is a cell surface protein of the immunoglobulin (Ig) superfamily. Via its N-terminal Ig domain, CD48 interacts with the cell surface receptor 2B4, triggering signal transduction events that regulate T lymphocyte and NK- cell cytotoxicity. Our group recently identified A43, a CMV-encoded CD48 homolog, which is capable to bind human 2B4 with exceptional higher affinity and slower dissociation kinetics than human CD48. A43 masks the 2B4 receptor, impairing NK-cell cytotoxicity and IFN-g production through interfering with the immune synapse. Thus, we proposed that A43 may serve as a functional decoy receptor. Here, we present that this viral protein also interacts, via its N-terminal Ig domain, with human CD2, a T and NK-cell co- stimulatory molecule whose primary ligand is CD58. We have performed a series of structural-functional analysis of these molecular interactions using site-directed mutagenesis and modeling of the N-terminal Ig domain of A43 to understand the basis for this receptor unique binding. The nature of A43, being a soluble molecule with the potential to inhibit both 2B4- and CD2-mediated NK- and T cell-mediated responses, provides an excellent basis to develop new immunosuppressive biotherapeutics for pathologies such as autoimmune diseases.

Oral Communications — Session I
Basic and Experimental Immunology

6 MRL mice infected with cytomegalovirus (CMV) as an animal model of Sjögren's Syndrome

Joan Puñet-Ortiz[1]; Manuel Saez Moya[1]; Rebeca Gutiérrez-Cozar[1]; Ana Angulo[1]; Pablo Engel[1]

[1]*Immunology Unit, Department of Biomedical Sciences, Medical School University of Barcelona. Barcelona.*

Sjögren's Syndrome (SjS) is one of the most common chronic systemic autoimmune diseases. It is characterized by abnormal B-cell hyperproliferation as well as cell infiltration and epithelial damage of exocrine glands. Moreover, it can also present life-threatening extraglandular manifestations, such as pulmonary and renal inflammation. Some authors have postulated that viral infections may act as a trigger of autoimmune diseases in susceptible individuals. Here, we explored if MLR (B6.MRL-Fas_{lpr}/J) mice, which present a mutation in the Fas gene, infected with mouse CMV (MCMV) could serve as a new model for SjS. To this end, 4-week-old female MRL mice were infected with a sublethal dose of MCMV. Thirty days after infection we could observe that infected mice produced antinuclear autoantibodies. These mice presented increased levels of anti-dsDNA antibodies as compared with uninfected mice (0.58 ug/mL vs 0.11 ug/mL). Moreover, antibodies against RO52 were only detected in MCMV infected mice (0.58 O.D. vs 0.05 O.D. vs). MCMV did not significantly altered splenic T or B cell subsets. Notably, infected mice showed the presence of lymphocytic foci within the salivary glands, whereas the non-infected mice did not (6/6 vs 0/4). Immunofluorescence analysis of salivary glands revealed that lymphocyte infiltrates were predominantly comprised of T cells instead of B cells, resembling those found in advanced stages of human SjS. Taken together, these data uncover MCMV as an active promoter of SjS in susceptible animals by redirecting autoimmunity towards the salivary gland. This experimental mouse model may be also useful to test new therapeutic strategies.

7 HIV-1 enveloped Virus-Like Particles (VLP) displaying high density of HIV-1 Env-derived antigens on their surface induce a functional immune response beyond neutralizing activity

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-Nieta[1]; Laura Cervera[2]; Sónia Gutiérrez-Granados[2]; María Mercedes Segura[2]; Francesc Gòdia[2]; Bonaventura Clotet[1,3]; Jorge Carrillo[1]; Julià Blanco[1,3]

[1]Institut de Recerca de la Sida (IrsiCaixa); [2]Grup d'Enginyeria Cel·lular i Bioprocessos, UAB; [3]Universitat de Vic-UCC

HIV-1 Gag-based enveloped Virus-Like Particles (VLPs) stand as a safe and promising vaccine platform to induce potent immune responses against HIV-1. However, low incorporation of immunogens at the VLP surface is a major drawback. The aim of this work is to demonstrate in vivo the efficacy of a VLP-based vaccine strategy that presents a dense array of Env-derived immunogens. These VLPs were generated by fusing HIV-1 p55Gag with a gp41 derived protein (Min).

HEK293F cells were transfected with plasmids coding for p55Gag (control) or the fusion-protein MinGag. VLP immunogenicity was assessed in C57bl/6 mice following two approaches: a) four doses of purified VLPs (VVVV; 90ng p24/dose) and b) two doses of electroporated DNA (20µg DNA/dose) followed by two doses of purified VLPs (DDVV). An in vivo C57Bl/6 model injected with a poorly immunogenic Min- expressing syngeneic melanoma cell line (B16F10) was employed to assess the functionality of the MinGag-induced humoral response.

As previously reported, MinGag-VLPs induced robust antibody responses against Gag and Min proteins, reaching a 10-fold higher antibody concentration in the DDVV regimen. Immunisation did not induce neutralising antibodies; however, anti-Min response was strongly biased to IgG2c, a Th1-like IgG subclass that mediates effector antibody functions. To proof so, C57Bl/6 mice were vaccinated twice with Gag or MinGag-VLPs and then injected with Min-expressing B16F10 tumour cell line. A statistically significant delay in tumour growth and longer survival was observed in MinGag-VLP immunised mice, compared to control groups ($p<0.05$).

Altogether, these results demonstrate that this HIV-based VLP platform with a high-antigen display induces a strong antigen-specific Th1-like response that delays the growth of a

Min-expressing tumour cell-line in vivo. Further studies will unveil the platform's versatility to present other immunogens, even trimeric Env, and its potential to induce broadly protective responses, contributing to the development of a vaccine against HIV-1.

8 CHANGES INDUCED IN LYMPHOCYTE SUBPOPULATIONS BY DIMETHYL FUMARATE TREATMENT IN MULTIPLE SCLEROSIS COULD IDENTIFY "NEDA" PATIENTS

Aina Teniente Serra[1]; Silvia Presas Rodriguez[2]; Ares Selles Rius[1]; M José Mansilla[1]; Bibiana Quirant Sánchez[1]; Cristina Ramo Tello[2]; Eva M Martínez Cáceres[1]

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Background

The optimal response to dimethyl fumarate (DMF) in multiple sclerosis (MS) is mediated by a shift to an antiinflammatory and immunoregulatory profile. In a preliminary study of 22 patients with MS followed for 12 months, we observed that, at 3 months of treatment, patients with "No evidence of disease activity (NEDA)" had a decrease in the Th1-like Th17 effector memory (EM) subpopulation.

Objective

To analyze the long-term effect of DMF on the lymphocyte subpopulations of MS patients and its relationship with the activity of the disease.

Methods

Ongoing longitudinal prospective study in MS patients undergoing DMF treatment. A panel of T and B lymphocyte subpopulations in peripheral blood was analyzed by flow cytometry. Patients with a complete follow-up of more than 1 year are classified as: NEDA, MEDA (minimal clinical or radiological activity) or EDA.

Results

To date, 48 patients have been analyzed. After a 2.66 (1-5) years of follow-up, we found 39.6% in NEDA, 25% in MEDA, and 16.7% in EDA.

The changes induced on the subpopulations (increase of naïve subsets in T [CD4 and CD8] and B-cells, and decrease of central memory (CM) and EM T-cells, and memory B-cells susbsets) remained stable in the long term (> 2 years), being more prominent in

NEDA patients. In these, we found lower percentages of Th1 CM and EM pre-treatment ($p=0.009$, $p=0.002$), as well as of Th1, Th17 and Th1-like Th17 CM ($p<0.001$, $p=0.002$, $p=0.012$) and Th1 and Th17 EM ($p<0.001$, $p=0.034$) during the first 12 months of treatment. MEDA patients appear to behave like EDA patients in changes in Th1/Th17/Th1-like Th17 subsets.

Conclusions

Changes induced by DMF on the lymphocyte subpopulations remain stable over time. NEDA patients have an immunophenotype that seems to identify them. Immunomonitoring detects the true biological effect of the treatments.

9 Lymphocyte subpopulations analysis in psoriatic patients treated with biological drugs

Marc Boigues-Pons[1]; José Manuel Carrascosa[2]; Eva Martínez Cáceres[1]; Joan Climent Martí[1]

[1] *Immunology Department, LCMN. Hospital Germans Trias i Pujol and Research Institute, Badalona (Spain);*
[2] *Dermatology Department. Hospital Germans Trias i Pujol, Badalona (Spain)*

Background

Psoriasis is an autoimmune disease characterized by scaly and itchy skin lesions. It is associated with numerous comorbidities and decreased quality of life of patients suffering from it. In recent years the emergence of new biological drugs has revolutionized its treatment especially in the most severe cases of psoriasis. These new drugs work by blocking the major cytokines involved in the inflammatory response of psoriasis, thereby achieving a drastic reduction in lesions and improving patients' quality of life.

Aim

To analyze changes induced in T-cell subsets in peripheral blood of patients with psoriasis treated with biological drugs.

Methods

Using flow cytometry, we evaluated effector and regulatory T cells subpopulations in fresh peripheral blood. We analyzed patients with psoriasis treated with Adalimumab (anti-TNFα, N=20), Ustekinumab (anti-IL23, N=26) Secukinumab (anti-IL17, N=9), patients with active psoriasis without biological treatment (N=14)

and controls without psoriasis (N=21).

Results

Patients with active psoriasis presented a lymphocyte profile characterized by decreased levels of Th1 central memory (CM), Th2 CM, and regulatory T cells with respect to treated patients and controls without psoriasis. Whereas patients treated with Adalimumab and Ustekinumab showed T-cell profiles similar to controls without psoriasis.

Moreover, patients receiving Secukinumab had a lymphocyte profile similar to controls but with a significant decrease of the number of Th17 effector memory (EM) and Th1 / Th17EM subpopulations.

Conclusion

These findings provide an overview of the effects of the biological treatments over the lymphocyte subsets and can serve as a starting point for the selection of the most appropriate drug and for the evaluation of the risk of opportunistic infectious diseases in psoriatic patients.

10 Myeloid-Derived Suppressor Cells in Kidney Transplant Recipients and the Effect of Maintenance Immunotherapy

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Myeloid-derived suppressor cells (MDSC) represent a heterogeneous group of myeloid regulatory cells that were originally described in cancer. Several studies in animal models point to MDSC as important players in the induction of allograft tolerance due to their immune modulatory function. Most of the published studies have been performed in animal models, and the data addressing MDSCs in human organ transplantation are scarce. We evaluated the phenotype and function of different MDSCs subsets in 38 kidney transplant recipients (KTRs) at different time points. Our data indicate that monocytic MDSCs (Mo-MDSC) increase in KTR at 6 and 12 months posttransplantation. On the contrary, the percentages of polymorphonuclear MDSC (PMN-MDSC) and early-stage MDSC (e-MDSC) are not significantly increased. We evaluated the immunosuppressive activity of Mo-MDSC in KTR and confirmed their ability to increase regulatory T cells (Treg) in vitro. Interestingly, when we compared the ability of Mo-MDSC to suppress T cell proliferation, we observed that tacrolimus, but not rapamycin-treated KTR, was able to inhibit CD4+ T cell proliferation in vitro. This indicates that, although mTOR inhibitors are widely regarded as supportive of regulatory responses, rapamycin may impair Mo-MDSC function, and suggests that the choice of immunosuppressive therapy may determine the tolerogenic pathway and participating immune cells that promote organ transplant acceptance in KTR.This work was supported by grants from the FIS-ISCII (PI16/01585) to ML-H and R01 AI139623-01 to JO. This project also received funding from the European Union's Horizon 2020 Research and Innovation Program under the Marie SkłodowskaCurie grant agreement number 860003 (www.instruct-h2020.eu).

Oral Communications
Clinical Immunology I

Session II

11 Pretransplant adaptive NKG2C+ NK cells protect against cytomegalovirus infection in kidney transplant recipients

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Cytomegalovirus (CMV) infection constitutes a complication for kidney transplant recipients (KTR) and CMV-specific T cells reduce the risk of viral replication in seropositive patients. CMV promotes the adaptive differentiation and expansion of an NK cell subset, hallmarked by expression of the CD94/NKG2C receptor with additional characteristic features. We previously reported an association of pretransplant NKG2C+ NK cells with a reduced incidence of CMV infection. We have strengthened the analysis in cryopreserved peripheral blood mononuclear cells from an enlarged KTR cohort (n = 145) with homogeneous immunosuppression, excluding cases at low risk of infection (ie, CMV D-R-) or receiving antiviral prophylaxis. Moreover, adaptive NKG2C+ NK cell-associated markers (ie, NKG2A, CD57, Immunoglobulin-like transcript 2 [LIR1 or LILRB1], FcεRI γ chain, and Prolymphocytic Leukemia Zinc Finger transcription factor) as well as T lymphocyte subsets were assessed by multicolor flow cytometry. The relation of NKG2C+ NK cells with T cells specific for CMV antigens was analyzed in pretransplant patients (n = 29) and healthy controls (n = 28). Multivariate Cox regression and Kaplan-Meier analyses supported that NKG2C+ NK cells bearing adaptive markers were specifically associated with a reduced incidence of posttransplant symptomatic CMV infection; no correlation between NKG2C+ NK cells and CMV-specific T cells was observed. These results support that adaptive NKG2C+ NK cells contribute to control CMV infection in KTR.

12 Impaired lung NK activity in the lung of Idiopathic Pulmonary Fibrosis patients

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Rationale: Idiopathic Pulmonary Fibrosis (IPF) is an age-related lung disease in which there is an accumulation of senescent cells. Senescent cells are eliminated during tissue repair, whereas with aging, the mechanisms of clearance are impaired, resulting in the accumulation of senescent cells.

Objectives: To determine the proportion and activity of NK cells in the lung of IPF patients as one of the main agents involved in the accumulation of senescent cells.

Methods: NK cell populations were determined in lung tissue and peripheral blood of IPF and controls. Cytotoxic and transwell assays were performed using NK cells and lung fibroblast conditioned media

Results: We observed a decrease in the population of NK cells principally in the IPF lower lobes. Of the remaining lung NK cells, we demonstrated an increase in the percentage of senescent NK-producing IL-6 cells which also have a decrease in the expression of the lung chemoattractant CCR2. Single-cell RNAseq of the IPF lung revealed differences between controls and IPF in the NK cluster, with an increased expression of activation genes in areas of low fibrosis (upper lobes) and a pro-senescent gene pattern in more fibrotic areas (lower lobes). Plasma cytokines showed a decrease in NK lung recruitment and circulating NKs were increased in IPF. In-vitro experiments confirmed the impaired NK recruitment and cytotoxic activity from IPF patients.

Conclusions: We propose that defects in NK activity could be one of the mechanisms responsible for the perpetration of the accumulation of senescent cells in IPF lungs.

13 Immunophenotype in CU patients under omalizumab treatment

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Introduction

Chronic urticaria (CU) is a complex skin disease involving diverse factors and mechanisms. Some patients develop concomitantly autoimmune IgG mediated diseases, such as autoimmune thyroiditis. Omalizumab treatment is useful in CU patients but its effect on the immune profile in these patients is still unknown.

Objective

To characterize the immune profile of CU patients treated with omalizumab

Materials and Methods

Observational study of 38 patients diagnosed of CU under omalizumab treatment (baseline (n=21), post- treatment (n=17)); Patients under non-immunomodulatory drugs (NID; n=27) and 50 healthy donors (HD) were used as controls.

Flow cytometry immunophenotyping of T-cell subpopulations, indirect Basophil Activation Test (BAT; to detect anti-IgE antibodies) and anti-thyroid antibodies were performed.

Results

Only 21 patients (34%)gave a positive result in indirect BAT test,10 of them under omalizumab treatment. None of the healthy donors tested gave a positive result. Regarding the effect of omalizumab in T-cell subsets,CU patients treated with NID showed lower percentages of $CD4^+$central memory ($p<0.001$),and activated subpopulations as $CD4^+DR^+CD38^+$ ($p<0.001$) and $CD4^+DR^+CD38^-$ ($p=<0.001$) compared to HD.Percentages of $CD4^+$ naïve ($p=0.0001$) and $CD8^+DR^-CD38^+$ ($p<0.0001$)subpopulations were increased.On the other hand, omalizumab patients showed higher percentages of Th2 effector memory ($p=0.0061$) and CD8 effector T-cells($p=0.027$) than HD.Lower percentages of $CD8^+$naïve ($p=0.034$) and $CD3^+CD8^+$ ($p=0.025$)total lymphocytes were found during omalizumab treatment when compared with baseline.Whereas an increasing trend on Th17,Th1 and some activated populations such as $CD4^+DR^+CD38^+$was observed.Patients with positive BAT and no antithyroid antibodies had lower levels of $CD8^+$effector memory than negative BAT patients ($p<0.04$).

Conclusions

Omalizumab induces changes in some Tcell subpopulations, notably in T helper subsets. There is not a correlation between BAT results, presence of antithyroid antibodies and the effect of omalizumab. Further functional studies are needed to clarify its effects.

14 PHASE I MULTICENTER CLINICAL TRIAL WITH A CHIMERIC ANTIGEN RECEPTOR WITH HUMANIZED ANTI-BCMA SPECIFICITY (ARI0002h) IN PATIENTS WITH RELAPSED OR REFRACTORY MULTIPLE MYELOMA

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Multiple myeloma (MM) is a disease of the bone marrow responsible for 1% of all cancers and 15-20% of hematologic malignancies and remains incurable. It is characterized by a clonal expansion of plasma cells in the bone marrow, the presence of monoclonal immunoglobulin in the blood or urine, renal dysfunction, osteolytic lesions, hypercalcemia, and associated organ dysfunction. In recent years, immunotherapy based on the infusion of modified T lymphocytes with a chimeric antigen receptor (CART cells) to treat hematologic malignancies has markedly improved the prognosis of some patients with hematologic malignancies. Regarding CART immunotherapy in MM, different clinical trials were started by choosing different targets in MM cells (NKG2D ligands, CD138, CD19, kappa light chain and BCMA). Of all of them, the most promising target is BCMA, and there are currently multiple clinical trials with CART cells against it.

A phase I multicenter clinical trial based on the infusion of expanded autologous peripheral blood T lymphocytes transduced with a lentivirus to express a chimeric antigen receptor with humanized anti-BCMA specificity (TNFRSF17) has recently been initiated and conjugated to the costimulatory region 4-1BB and signal transmission CD3z (ARI0002h) in patients aged 18 to 75 years with measurable multiple myeloma relapsed or refractory at least to previous treatment with proteasome inhibitor, immunomodulator and anti- CD38 antibody and with a life expectancy greater than 3 months (EudraCT: 2019-001472-11).

Four other recruitment centers participate in the study (Clínica Universitaria de Navarra (CUN), Pamplona; Hospital Virgen de Rocío, Sevilla; Biomedical Research Institute of Salamanca and Hospital U. Virgen de la Arrixaca, Murcia). The production of cellular products is carried out in two centers, Hospital Clínic de Barcelona and CUN.

The aim of this study is to assess the safety and efficacy of CARTBCMA ARI0002h in the patients recruited.

Oral Communications — Session III
Tumor Immunology and Immunotherapy

15 CART19-BE-01: un ensayo académico Europeo sobre la administración de células CAR-T denominadas ARI-0001 en pacientes con trastornos linfoproliferativos CD19+.

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Introducción: El pronóstico de la leucemia aguda linfoblástica (LAL) y otras hemopatías CD19+ recaída/refractaria (R/R) es muy pobre. Recientemente, numerosas terapias CAR-T anti-CD19 han sido desarrolladas para pacientes R/R, dos de ellas (tisagenlecleucel y axicabtagene-ciloleucel) aprobados por la EMA en LAL y LDCGB R/R. Sin embargo, numerosos pacientes continúan sin CAR-T disponible.

Métodos: Desarrollamos un CAR-T incorporando el 4-1BB y la secuencia scFv anti-CD19-A3B1. CMN autólogas fueron transducidas (células ARI-0001) usando el sistema CliniMACS Prodigy. Se incluyeron pacientes con LAL, linfoma no Hodgkin (LNH) y leucemia linfocítica crónica (LLC) sin alternativas terapéuticas. Se realizó linfodepleción con fludarabina y ciclofosfamida seguida de 0.4-5x10^6 células ARI-0001/kg administradas de forma única (DU) o fraccionada (DF) en 3 alícuotas (10%, 30% y 60%).

Resultados: 47 pacientes recibieron células ARI-0001 (tabla 1), incluyendo LAL (38), LNH (8) y LLC (1). Luego de 3 casos de toxicidad grado 5 observados en pacientes tratados con DU, se introdujo la enmienda que permitió tratar 28 pacientes con DF (tabla 2). En pacientes con LAL, se observó SLC grado ≥3 en 13.2% (26.7% DU vs 4.3% DF) y neurotoxicidad (ICANS) grado ≥3 en 2.6% (6.7% DU vs 0% DF), y la mortalidad relacionada al procedimiento al día +100 fue de 7.9% (15.8% DU vs 0% DF). Todos los pacientes evaluables desarrollaron aplasia de linfocitos B. La tasa de respuesta completas

al día +100 fue del 71.1%, la SLP al 1er año fue del 47% (95% IC 27-67%), la SG al 1er año fue del 68.6% (95% IC 49.2-88%) y la duración de la respuesta fue de 14.8 m (95% IC 6.0-NA) (tabla 3).

Conclusiones: Fue factible preparar células ARI-0001 en un ambiente académico usando el sistema CliniMACS Prodigy. Los datos de seguridad y eficacia obtenidos estan en línea con lo publicado en otros CAR-T comerciales o en desarrollo.

16 Humoral immune response in patients with CD19 positive relapsed/refractory B-cell malignances recruited into the CART19-BE-01 clinical trial

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Background: The Spanish Agency of Medicine approved our first clinical trial with a fully academic CAR19 on May 2017. B-cell malignances treated in the clinical trial include patients with R/R B-ALL (adult and pediatric), non-Hodgkin's lymphoma (NHL) and chronic lymphocytic leukemia (CLL) who failed the standard therapy. This fully academic CAR19 combines the single-chain variable fragment (scFv) with anti- CD19 specificity, originated from a mouse monoclonal antibody A3B1, conjugated with the co-stimulatory regions 4-1BB and CD3z. Despite deep remissions, there are still major challenges and disparate data are reported about the humoral immunogenicity induced by CART19-cell therapies approved by FDA and EMA.

Methods: The humoral anti-CART response was assessed by a cell-based fluorescence assay to detect human anti-murine antibodies (HAMA) in patients´ sera. Assessment was conducted at different time points: 1) at baseline (pre-dose), 2) on day 14 after the administration of ARI-0001 cells, 3) on day 28, 4) on day 100, and 5) every 3 months thereafter. Subsequently, cytotoxicity assay for positive patients' sera were done so as to appraise the effect of HAMA. Assessment was conducted at different ratios of target/ effector cells previously pre-incubated with patients' sera.

Results: Forty-seven patients (37 adults/10 pediatrics) received ARI-0001 cells. Approximately thirty per cent of the patients tested positive for the presence of anti- CAR antibodies. Of these patients, 3 of them presented pre-dose anti-murine antibodies, 6

patients presented with a weak and 6 patients presented with a strong post-dose presence of HAMA. Despite the fact that some patients tested positive for the HAMA assay, some of them were diminishing the effectiveness of CART-19.

Conclusions: These data suggest the importance of the immunogenicity induced by CART-cell therapies. Immune monitoring should include the assessment of humoral response, especially before considering a second dose after relapse.

Oral Communications — Session III
Tumor Immunology and Immunotherapy

17 Comparative analysis and characterization of TCR repertoires in breast cancer TILs

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Breast cancer (BC) is the most common malignant disease and the leading cause of cancer death in women. The presence of Tumor Infiltrating Lymphocytes (TILs) has shown to be directly correlated with a good prognosis in several cancer types, including BC. A high CD8+/CD4+ TILs ratio has also been described as another determining factor. The characterization of the T Cell Receptors (TCR) expressed by TILs has been gaining interest, since their ability to recognize specifically tumor-antigen expressing cells can be used as a tool of immunotherapy.

In this study, different features of TCR of CD4+ and CD8+ T cells expanded from TILs from BC biopsies have been evaluated. NGS of the TCR has been performed in the initial biopsy-derived T cell cultures, as well as in the sorted CD4+ or CD8+ expanded T cells from TILs. Different properties of the TRAV and TRBV CDR3 regions were evaluated to study whether there were differences among the CD4+ and CD8+ TILs, i.e. length, charge, polarity and hydropathy. Moreover, the analysis of the TCR allows to study the clonality of TILs in the initial cultures and to monitor the in vitro expansions.

Although there is not a significant difference in the diversity of the TCR between the CD8+ and CD4+ samples, there is in some of the CDR3 properties analyzed; (i) the TRBV CDR3 was negatively charged in the CD8+ compared to the $CD4^+$ TILs and (ii) the TRBV CDR3 length of $CD8^+$ TILs was shorter than that of $CD4^+$ TILs and this difference is also significant in the central 5 amino acids of the CDR3, suggesting a shorter N-D-N.

In summary, preliminary data indicate that there are differential attributes in the TCR TILs subpopulations. This suggests that the TCR features of TILs should be further studied and considered for designing better immunotherapies.

Oral Communications — Session III
Tumor Immunology and Immunotherapy

18 HAVCR2 mutations altering TIM-3 underlying hemophagocytic syndrome and subcutaneous panniculitis-like T-cell lymphoma

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Subcutaneous panniculitis-like T-cell lymphoma (SPTCL) is a rare cutaneous T-cell lymphoma characterized by a hypodermal infiltration of CD8 T cells expressing an ab T-cell receptor. SPTCL can be associated with hemophagocytic lymphohistiocytosis (HLH), a life-threatening condition characterized by a hyperinflammatory state and persistent macrophage activation. The presence of HLH accompanying SPTCL is associated with shorter overall survival.

Here we present a case of an 8-years-old child from non-consanguineous parents who was admitted to our hospital with 15 days fever evolution. The laboratory test revealed progressive pancitopenia, splenomegaly, bone marrow hemophagocytosis, hyperferritinemia, absent NK cytotoxicity and impaired degranulation. Microbiology tests detected positive parvovirus B19 PCR in peripheral blood. A diagnosis of HLH secondary to ParvB19 was made. The patient was treated with hig-dose IVIG and HLH-2004 protocol until complete remission. Three years later the patient presented with intermittent high-grade fever and subcutaneous nodules. The skin biopsy revealed a SPTCL. Laboratory test demonstrated a concomitant HLH reactivation with low cytotoxicity and impaired degranulation. Finally, hematopoietic stem-cell transplantation (HSCT) from a matched unrelated donor was performed.

After several targeted sequencing approaches, whole exome sequencing was performed revealing a compound heterozygous mutation in HAVCR2 gene (c.291A>G / p.I97M and c.331C>T / p.R111W). HAVCR2 encodes the T cell immunoglobulin mucin 3 (TIM-3)

molecule, a cell surface receptor acting as a negative immune checkpoint regulating peripheral tolerance, antitumoral immunity, and innate immune responses. Recently, HAVCR2 mutations have been identified as causing SPTCL with HLH. The p.I97M mutation has been reported as a recurrent mutation in patients with European ancestry. It has been demonstrated that this mutation abrogates TIM-3's plasma membrane expression. The p.R111W mutation is novel and we are studying its functional effect.

In summary this case confirm that HLH-SPTCL is a new autosomal recessive genetic entity resulting from TIM-3 deficiency and leading to uncontrolled immune activation.

Oral Communications — Session III
Tumor Immunology and Immunotherapy

19 Dynamics of T-cell subsets in non-small cell lung cancer patients treated with PD-1/PD-L1 axis blocking mAbs

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Immune checkpoint inhibitors are one of the main immunotherapies that are recently used to treat non-small cell lung cancer (NSCLC), by blocking inhibitory pathways of the immune response, such as the PD-1/PD- L1 axis, to reinvigorate the ongoing immune-directed attack of the tumour. These immunotherapies have proven to be effective and safer than chemotherapy and have shown to both increase the survival rate of many cancer types, and expand the median survival of responsive patients. However, there is a need of biomarkers to determine which patients might benefit the most to these therapies, as current biomarkers, such as PD-L1 tumour expression, are not as accurate as desired.

We hypothesize that peripheral blood lymphocytes are directly affected by the treatment and can be used as biomarkers of treatment response. Hence, we evaluated the effects that PD-1/PD-L1 axis blocking immunotherapies induce in peripheral blood T-cell subsets of NSCLC patients, by flow cytometry, during a 12-month follow-up.

RESULTS: Among the main findings we encountered a significant decrease during progression of the Treg and the CD4+ EM Th1/Th17 subsets in periphery, as well as in CD4+ T-cell subsets at different activation stages. We also found a significant decrease throughout time of peripheral activated CD8+ T-cells. And most strikingly, within the worst prognosis group based on PD-L1 tumour expression, we obtained preliminary data on significantly different values of peripheral CD4+ T-cell subsets depending on the outcome.

Based on these results the study of peripheral blood lymphocyte subsets might entail a potential source of biomarkers to select those NSCLC patients that might benefit the most to PD-1/PD-L1 axis blocking immunotherapies.

20 NK cell receptors and ligand variants modulate response to tyrosine kinase inhibitors in patients with chronic myeloid leukemia

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Chronic myeloid leukemia (CML) is a myeloproliferative neoplasm treated with tyrosine kinase inhibitors (TKIs). Although survival rates have improved, response to these treatments is highly heterogeneous. Variations in response rates may be due to different causes such as treatment adherence, mutations in BCR- ABL1 , clonal evolution, amplification of BCR-ABL1, etc. Nevertheless, innate immune response is also considered to play a very important role and, specifically, NK cell activity through their receptors and ligands could be determinant.

The aim of this retrospective study was to explore the role of different KIR genes as well as the activating NKG2D receptor variants, present in NK cells, and also their respective ligands, HLA-A, -B, -C, -G, -F, MICA and MICB, in the evolution of 190 patients with CML and treated at two hospitals from Barcelona. Early molecular response (EMR), major molecular response (MMR) and deep molecular response (DMR) were correlated. Samples from Barcelona Blood Bank healthy donors were analyzed as controls.

The presence of KIR2DL2/KIR2DS2 was associated with the achievement of EMR, MMR and DMR. Carriers of the activating NKG2D variant, and MICA*009:01 were also likely to achieve MMR. The most remarkable difference between CML patients and controls was a higher frequency of the inhibitory NKG2D variant in CML patients.

In summary, our results showed that activating NK receptor phenotypes might help to achieve MMR and DMR in CML patients treated with TKIs.

21 Early S2-targeting and rapid development of neutralizing antibodies after SARS-CoV-2 infection

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The identification of SARS-CoV-2 infected individuals is critical in order to reduce new infections and stablish strategies to control the ongoing COVID-19 pandemic. Currently, diagnosis is mainly based on viral detection by RT-PCR methods using nasopharyngeal swab samples. However, the high cost, the difficulties associated with sample collection and the short timeframe in which viral replication can be accurately detected requires the implementation of alternative diagnostic methods. Among them, the quantification of the humoral response elicited in SARS-CoV-2 infected individuals is very promising since it might also inform about the immune response triggered. However, our knowledge about the features of the anti-SARS- CoV-2 humoral response is limited, hampering the development of instructive serological assays for COVID19 diagnosis and monitoring. Thus, we aimed to analyze the dynamics of humoral responses elicited against several SARS-CoV-2 antigens by ELISA (spike; S1, S2 and receptor binding domain (RBD) subunits and nucleocapsid protein) and their association with the neutralizing activity of plasma samples and the severity of the disease.
We found that anti-SARS-CoV-2 humoral response is characterized by an early elicitation of anti-S2 antibodies and the coexistence of IgM, IgG and IgA isotypes. Anti-S2 antibodies are consistently detected and their testing might improve the sensitivity of the antibody-based assays, especially during the first days after infection. Moreover, SARS-CoV-2

infected individuals develop an early neutralizing humoral response that mostly correlates with anti-S1 and anti-RBD antibodies. Finally, we did not observe any association between anti-SARS-CoV-2 antibody levels and disease severe.

22 Antigen-specific lymphocyte proliferation against SARS-CoV-2 in COVID patients with negative antibodies against the virus in serum

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Background

As the SARS-CoV-2 pandemic spreads out, it becomes more important to evaluate the immune status of the population against the virus. Serological tests that measure specific antibodies against the virus are the most common way to evaluate the immune response. However, as some patients do not develop these antibodies, or they are no detectable, it is necessary to use other approaches to test the cellular immune response.

Aim

To evaluate the antigen-specific lymphocyte proliferation against SARS-CoV-2 in COVID patients with a positive PCR for SARS-CoV-2 but negative antibodies against the virus in serum.

Methods

We performed a dye-based proliferation assay to evaluate the Ag-specific T-cell response against SARS- CoV-2. Fresh PBMCs were incubated for 6 days with peptides from the S (spike), M (membrane) and N (nucleocapsid) proteins of the virus and analysed using flow cytometry. A group of 8 patients with positive PCR for SARS-CoV-2 and negative serology (with a negative result with 3 or more different methods) were analysed and a group with positive PCR and positive serology was used as a control group (n=9).

Results

In the control group, 8 out of 9 patients (89%) showed specific T lymphocyte proliferation. Whereas in the group of patients with positive PCR and negative serology, only 5 out of 8 (63%) showed specific T lymphocyte proliferation against SARS-CoV-2 peptides in the dye-based proliferation assay.

Conclusions

The evaluation of the cellular immune response is crucial to obtain a complete view of the immune response against the SARS-CoV-2 and it is of special relevance in those patients with negative serology. This kind of analysis will be also useful to test the cellular immune response to coming vaccines.

23 Immunological Risk Profile in COVID-19, the Experience of a Single Academic Hospital in Catalonia

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One of the main difficulties in the management of patients with COVID-19 is the shortage of tools to anticipate hyperinflammation or to prioritize ICU beds. Acute phase reactants (APR), hematological parameters and IL-6 have been considered the most suitable. Prognostic power of demographic data and 32 laboratory parameters in relation to the final outcome (discharge home vs exitus) have been analyzed in 1758 consecutive patients >18 years (790F/968M, mean age 62.5 ± 16.9) admitted to the emergency dept of a single hospital during the first wave of pandemic. Patients with major concomitant diseases -but no comorbidities- were excluded. Age was the main demographic determinant of prognosis (mean age discharged 60.86 versus exitus 74.5). IL-6, CRP, Ferritin, D-dimer, Lymphopenia and Neutrophil/Lymphocyte Ratio were associated to outcome in univariate and multivariate analysis. In principal component analysis, the Dm1 and Dm2 explained the 20.8% the 10.8% of the prognosis. Neutrophil and lymphocyte parameters followed by APR were the main determinants. In the random forest model of classification, the parameters with higher coefficients were log IL-6, age, urea, LDH, neutrophils, Hb, monocytes, lymphocytes and CRP. Some parameters typically associated to hemophagocytic lymphohistiocytosis i.e. liver tests, triglycerides and low platelets were less strongly associated. These results indicate that laboratory parameters and age can be used to generate a predictive algorithm but more parameters, e.g. additional inflammatory cytokines, ideally closer to the pathophysiological determinants of severity, may be required to improve prediction power. Obviously, image technique and clinical monitoring remain the cornerstones for prognosis.

24 Immunopathogenesis of COVID-19-related pediatric inflammatory multisystem syndrome: overlap with Kawasaki disease and identification of a distinct severe group.

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Multisystem inflammatory syndrome associated with SARS-CoV-2 pandemics has recently been described in children (MIS-C), partially overlapping with Kawasaki disease (KD). We hypothesized that: 1) cytokine profiles of MIS-C and pre-pandemic KD may be unique and justify the clinical differences observed; 2) SARS-CoV-2-specific immune-complexes (IC) may explain the immunopathology of MIS-C.

Fifty-eight pediatric patients were included: 1) 14 MIS-C; 2) 10 patients with positive SARS-CoV-2-PCR without MIS-C (COVID); 3) 14 pre-pandemic KD and 4) 20 healthy controls (HC). Thirty-four circulating cytokines were quantified in pre-treatment samples (54/56) and the presence of circulating SARS-CoV-2 IC was evaluated in MIS-C patients.

Compared to HC, MIS-C and KD groups displayed significant elevation of most cytokines, of which IFN-γ, IL-18, IP-10 (markers of IFN-γ-induced response) and MCP-1, IL-1α, IL-1RA (markers of inflammatory monocyte activation) were the main triggers of inflammation. With linear discriminant analysis, MIS-C and KD profiles overlapped; however, a subgroup of MIS-C patients differentiated from KD, displaying significant increases in IFN-γ, IL-18, IL-8, GM-CSF, RANTES, and incipient signs of macrophagic activation syndrome. There was no detection of circulating SARS-CoV-2-IC in MIS-C patients.

Our findings suggest a major role of IFN-γ in the pathogenesis of MIS-C, which may be relevant for therapeutic management.

Oral Communications COVID-19

25 Revealing protective T cell immune responses against SARS-CoV-2

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T cell responses are key to protecting against viral infections and necessary for antibody development. Here, in order to inform vaccine development on the correlates of protection against SARS-CoV-2, we studied the acute infection functional profile, migration patterns and caspase-3 expression of antigen-specific T cell responses in three different cohorts of patients (n=46). In depth flow cytometry analyses indicated increased apoptosis in antigen-specific and non-specific T cells associated with disease severity. Pattern variations associated with T cell responses against SARS-CoV-2 where based on two factors, the targeted viral protein and the cohort of patients assessed. Overall, cell stimulation with membrane (M) and nucleoprotein (N) viral peptides induced a Th1 profile exemplified by IFNg in CD4+ T cells and degranulation in CD8+ T cells respectively, whereas spike (S) peptides induced a biased Th2 profile exemplified by IL-4. Hospitalization and disease severity were associated with predominant IFNg and IL-4 responses, as well as increased responses against S peptides, while non-hospitalized outpatients had a dominant IL-10 response produced by CCR7 expressing cells. Importantly, antigen-specific resident memory T cells in the lung were weakly detected in an asymptomatic individual and strongly detected in a severe convalescent patient, in which contemporary blood did not reflect resident profiles. In summary, different SARS-CoV-2 viral proteins elicit unlike T cell functional profiles, which have clear implications for vaccine design. A balanced anti- inflammatory and effector antiviral response may be key to favor infection resolution without major complications during acute infection. Further, while immune responses migrate and establish in the lung as resident memory T cells, which could be determinant for future protection against reinfection, the magnitude and profile of the lung SARS-Cov-2 specific T cells strongly differ from the response detected in blood.

Oral Communications COVID-19

26 Inborn errors and autoantibodies against type-I inteferons in patients with life-threatening COVID-19.

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Clinical outcomes of human SARS-CoV-2 infection range from silent infection to lethal COVID-19. Epidemiological studies have identified three risk factors for severe disease: being male elderly, and having other medical conditions. However, interindividual clinical variability remains huge.

We established the COVID Human Genetic Effort (covidhge.com) to test the general hypothesis that life- threatening COVID-19 may be caused, in some patients, by monogenic inborn errors of immunity to SARS- CoV-2.

Here we present two relevant results:

1-Genetic defects in genes involved in type-1 interferon production: We sequenced the exome or genome of 659 patients with life-threatening COVID-19 pneumonia and 534 subjects with asymptomatic or benign infection. At least 3.5% of patients with life-threatening COVID-19 pneumonia have genetic defects at eight (IRF7, IFNAR1,TLR3, TBK1,...) of the 13 candidate loci involved in the induction and amplification of type I IFNs.

2-A phenocopy phenomena consisting in autoantibodies against type I interferons: We analyzed 987 patients hospitalized for life-threatening COVID-19 pneumonia, 663 asymptomatic or mildly affected individuals infected with SARS-CoV-2, and 1,227 healthy controls. At least 101 of 987 patients (10.2%) with life- threatening COVID-19 pneumonia had neutralizing IgG auto-Abs against IFN-ω (13 patients), the 13 types of IFN-alpha (36 patients), or both (52 patients). These auto-Abs were present before infection in the patients tested and were absent from 663 individuals with asymptomatic or mild SARS-

CoV-2 infection. They were present in only four of 1,227 (0.33%) healthy individuals. Strikingly, 95 of the 101 patients with auto-Abs were men (94%).

In conclusion, almost 15% of patients with life-threatening COVID-19 have genetic defects (≈3,5%) or autoantibodies (≈10%) affecting the type-I inteferon immunity. This discovery reveals essential roles for type I inteferon immunity in the control of SARS-CoV-2 infection. For the autoantibodies results, these findings provide a first explanation for the excess of men among patients with life-threatening COVID-19.

Posters

1 INTESTINAL IMPACT OF POSTBIOTICS IN A MODEL OF SUCKLING RAT ROTAVIRUS INFECTION

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Besides prebiotics and probiotics, in the last years a new concept of microbial modulator has appeared in the form of postbiotics. These are defined as bioactive compounds, inactivated fragments or bacteria metabolites, produced by food-grade micro-organisms in a fermentation process that support health and/or well-being. In a previous rat study, we demonstrated the ability of a particular postbiotic mixture, a milk matrix with postbiotics produced during a specific fermentation process (Lactofidus^{TM}) using the strains Bifidobacterium breve C50 and Streptococcus thermophilus 065, to prevent the clinical symptoms associated with rotavirus (RV) infection in early life.

The aim of the present study consists of evaluating the capacity of this postbiotic (POST) mixture to modulate intestinal homeostasis features during rotavirus infection in a rat model.

Lewis rats (3 litters of 8 pups each/group) were supplemented daily either with the fermented milk matrix containing postbiotics or vehicle by oral gavage which were either not infected (REF group) or infected with a simian RV on day 5 of life (RV and RV/POST groups). Faecal samples were collected and samples of the day of maximum diarrhea were used for establishing the microbiota composition (16S DNA bacterial sequencing), short chain fatty acids (SCFA) production (HPLC-MS) and intestinal permeability by means of analysing faecal α1-antitrypsin (ELISA).

Although no clear dysbiosis was induced by the RV infection, the dietary intervention with POST increased the proportion of the Bifidobacteriaceae family proportion, which was not present in the REF or the RV groups ($p<0.05$). However, no statistical changes were found in the fecal SCFA concentration and intestinal permeability due to the RV infection or the supplementation.

In conclusion, the postbiotics showed some prebiotic properties that suggest the interest of adding these types of components to infant formulas.

Posters

2 Dorsal Root Ganglia sensory neurons: A possible link between neuronal degeneration and Autoimmune Diabetes onset

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Type 1 Diabetes (T1D) is an autoimmune disease characterised by the selective destruction of pancreatic β cells. Previous studies demonstrate there is also cell dysfunction of the sensorial neurons innerving the pancreas, which have their cell bodies in Dorsal Root Ganglia (DRG). In this study, we hypothesize that T1D would originate through a neurodegenerative process which would induce an abnormal neuronal autoantigen release. These autoantigens may be the trigger of the autoimmune response against the peripheral nervous system (PNS), but also against the β cells, thus leading to T1D onset.

mRNA expression analysis in DRG cells from NOD, NOD.Rag2$^{-/-}$ and C57B/6 mice were performed to determine the putative cause and/or the molecules involved in this suspected neurodegenerative process. The results suggest that NOD and NOD.Rag2$^{-/-}$ mice have alterations in the expression of around 80 genes which are involved in a wide range of biological processes, such as metabolism, post-translational modifications and ion homeostasis, among others. This suggests that there is a degenerative defect in GDR cells. This dysfunction of the PNS may predispose it to be a target of the immune system, leading to DT1.

A qPCR analysis was performed in a short group of selected genes to confirm microarray results. Some of the candidate genes that, according to our results in NOD mice, show differences in transcription levels are Scg5 and Vcp, which are respectively up and down-expressed in diabetic prone mice compared to non- diabetic prone mice. If our hypothesis is correct, the GDR cells of individuals susceptible to diabetes would also have alterations in the transcription of a wide range of genes. Because it is not possible to access GDRs in

vivo, gene expression analysis of these genes in the blood could be an easy way to detect individuals susceptible to DT1 before the onset of the disease.

Posters

3 Comparative study between two commercial blots for analysis of antibodies associated to idiopathic inflammatory myopathies (IIM)

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Introduction

Currently, there are several commercial assays for the detection of autoantibodies associated to IIM (IIMAA), but there are concerns about their reliability because of their low sensitivity for some antibody specificities and their high percentage of false positives for others. Some of these antibodies are associated with a specific pattern of disease or cancer, which has important implications for the diagnosis and management of patients.

Objectives

To compare the diagnostic concordance of 2 commercial IIMAA immunoblot kits from different manufacturers and identify differences in the results obtained.

Materials & Methods

Serum samples requiring IIMAA studies were analyzed at the Immunology Laboratory of Bellvitge´s Hospital. Eighteen positive and seven negative samples analyzed with kit EI were selected and analyzed subsequently with kit GA. The specificities involved in the study were: Jo-1, PL-7, PL-12, EJ, SRP, Mi-2, MDA-5, TIF1γ, SS-A/Ro52, SAE1, SAE2, NXP-2.

The concordance between the results of 2 kits was analyzed, as well as between the results of each kit and the diagnosis of the patients.

Results

Eighteen samples (72%) had some positive antibody with kit EI, but only 5 (20%) with kit GA.

10 samples (40%) obtained concordant results, 6 of them negative. 15 samples (60%) were discrepant, 14 of them with some positive antibody with kit EI but negative with kit GA.

Regarding the discrepant samples, kit GA showed greater concordance with diagnosis,

especially those positive with kit EI but negative with kit GA, since those patients had not been diagnosed with IIM. Notably, 5 patients with positive anti-TIF1γ antibodies with kit EI but negative with kit GA had not been diagnosed with dermatomyositis or cancer.

Conclusions

The concordance between the kits is low, with a higher percentage of positive results obtained with kit EI. Kit EI appears to have false positive results, especially for anti-TIF1γ antibodies.

Posters

4 HUMAN IMMUNE FACTORS IN THE TRANSITIONAL BREAST MILK STAGE CHANGE DURING 7-DAYS PERIOD

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Breast milk composition changes during lactation according to the neonatal requirements of the neonate. Previous studies have described differences on immune profile between colostrum and the mature milk, however, little is known about the changes on milk immunoglobulin (Ig) and cytokine (CK) levels within the transitional phase, which is considered from 2-5 days until up to 2 weeks after delivery.

For that, we quantified and compared the Igs (IgA, IgM, IgE, IgG, IgG1, IgG2, IgG3 and IgG4) and some CKs (GM-CSF, IFN-γ, IL-1β, IL-2, IL-4, IL-5, IL-6, IL-9, IL-10, IL-12, IL-13, IL-17, IL-18, IL-21, IL-22, IL-23, IL-27, TNF-α) levels between two sampling days within the transitional phase (day 7 and 15 of breastfeeding) in a mother-infant birth cohort (n = 105) in the Spanish-Mediterranean area by ELISA and Multiplex Bead Immunoassays.

The results showed the dynamic changes of these immune factors, mainly Igs, during a short period (from 7 to 15 days, postpartum). For instance, the overall concentration of total Igs in breast milk samples significantly increased from day 7 to day 15 ($p < 0.05$), due mainly to the high concentration of IgA found at d7, but also IgE, IgG2 and IgM. The great inter- and intra-variability among milk cytokine levels between mothers did not allow to observe differences between the two sampling time points.

The differences found here reinforce the idea that breast milk is a highly dynamic source of these immune factors, and particularly in this period. These results highlight the importance of the milk collection timing in interventional and descriptive studies, as just few days lead to dramatic different levels of breast milk immune composition.

Posters

5 Mechanism of action of Thalidomide in CLE revealed using artificial intelligence

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Background: Cutaneous involvement in Lupus Erythematosus (CLE) is common and encompasses a wide range of dermatologic manifestations. Around 70-80% of patients develop skin lesions at some point during the course of their systemic disease. Standard therapy consists of topical steroids and antimalarials; however, up to 40% of the patients are refractory. Thalidomide has been used successfully to treat several dermatological disorders. Its efficacy in CLE is significant with 80-90% of patients achieving clinical remission; however its use is still limited due to serious side effects.

Objective: To identify mechanism of action of Thalidomide in CLE.

Methods: Skin biopsies from CLE patients before and after thalidomide treatment have been analyzed by RNA-seq (n=10). Data from clinical responder patients was evaluated using artificial neuronal networks following Therapeutic Performance Mapping System protocols to obtain a plausible mechanism of action. Expression gene analyses, immunofluorescence in skin biopsies and in vitro experiments have been performed in order to validate the proposed models.

Results: We discover that Thalidomide acts modulating CRBN and therefore, regulating two molecular pathways: IRF4/NFKB1 and AMPK1/mTOR. Immunofluorescence showed a reduction of CRBN, IRF4, MTOR and NFKB1 in post-thalidomide skin. Notably, IRF4 was localized in the dermis (3-fold intensity; $p<0.01$) and MTOR in the epidermis (1.5-fold intensity; $p<0.0001$) in pre-thalidomide skin. In vitro experiments demonstrated that thalidomide modulates IRF4/NFKB1 signaling in lymphocytes and AMPK1/mTOR in keratinocytes. In addition, co-culture experiments showed a cross-linking between identified pathways: Thalidomide addition in PBMCs promoted a significant reduction of MTOR protein ($p<0.001$) and inflammatory effectors (IL10, TGFβ, TNFα, IL-1β) in keratinocytes, showing that IRF4 targeting may mimic thalidomide dual effect.

Conclusion: Within this study, IRF4 has been identified as molecular target of thalidomide treatment in CLE. This may contribute to the development of novel analogues to treat CLE effectively avoiding thalidomide undesired adverse events.

Posters

6 Estudio de fenotipo linfocitario avanzado en pacientes con COVID-19

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En COVID-19 la gravedad y pronóstico vital de la enfermedad viene determinada por el grado hiperinflamación inducido por la infección por SARS-CoV-2. Disponer de buenos marcadores para pronosticar el desarrollo de hiperinflamación cuando el enfermo entra por primera vez al sistema sanitario puede resultar de gran utilidad para el triage inicial y tratamiento con fármacos inmunoduladores.

En este estudio se ha comparado el fenotipo linfocitario avanzado en 80 pacientes con infección por SARS- CoV-2 incluyendo más de 40 poblaciones diferentes estudiadas por citometría de flujo. Se ha analizado la relación de fenotipo linfocitario en la analítica del paciente al diagnóstico de la infección con el resultado final, y con la severidad clínica mediante ANOVA, siguiendo las siguientes jerarquías en cada caso:

a) En relación con la severidad clínica: intensidad de CD14 en monocitos clásicos e intermedios; número de linfocitos Th17 (CXCR3-CCR6+); número de linfocitos CD4 y CD8 con características "central memory" (CD45RA-CCR7+); número absoluto total de linfocitos CD3 y número de linfocitos Treg (CD4+CD25++CD127-).

b) En relación con el resultado final, alta a domicilio vs fallecimiento: el porcentaje de linfocitos CD3+CD8+CD25+ y el número de linfocitos Th17.

No se ha encontrado influencia de las subpoblaciones B estudiadas ni en la severidad de la enfermedad ni en el resultado final.

Este estudio confirma en nuestra serie que los pacientes más graves tienen un bajo

número absoluto de linfocitos T CD3+. Además, los pacientes con enfermedad leve tienen números absolutos significativamente más altos de linfocitos T CD4 Tregs así como números absolutos más altos de linfocitos T CD4+ y CD8+ con fenotipo de memoria central (CCR7+CD45RA-). También hemos evidenciado que el número absoluto de Th17 disminuye con la gravedad y en los pacientes que son dados de alta, el número absoluto de Th17 es significativamente mayor que los pacientes que fallecen.

Posters

7 Influence of premature delivery on the adipokine profile of human milk

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Human milk is the ideal nutrition for the newborn, and in addition to its nutritional contribution, it contains immune bioactive factors. Among these, there are adipokines such as adiponectin, leptin and resistin. Specifically, leptin and resistin are suggested to be pro-inflammatory whereas adiponectin shows both pro- and anti-inflammatory properties. The aim of the present study was to establish the influence of prematurity on the concentration of adiponectin, leptin and resistin in human milk throughout the lactation period. For this purpose, milk samples from mothers delivering at term (T), preterm (PT) and very preterm (VPT), were collected at three different time points of lactation corresponding to colostrum, transitional and mature milk. Concentrations of adiponectin, leptin and resistin were quantified in milk samples by a multiplex bead- immunoassay technique. Overall, prematurity affected the concentration of all three adipokines in the first milk produced by the lactating mother. Specifically, colostrum from PT group had lower concentration of adiponectin than that from T group. Conversely, all three types of milk from VPT group had the highest concentration of this adipokine. Regarding leptin content, at the three time points of lactation, the milk of the PT group contained higher concentration of this adipokine than that in the T group. However, its concentration in the VPT group was similar to that in the T group. Moreover, in the three groups of study, colostrum had the highest concentration of resistin with respect to transitional or mature milk. Moreover, the colostrum from the VPT group had lower resistin concentration than that from the PT group. Globally, in addition tothe changes observed in milk adipokine composition during lactation, these results also demonstrate the effect of gestational age on the adipokine profile of human milk. Future studies should be directed to ascertain their particular pro- and anti-inflammatory role in prematurity.

Posters

8 Composició del peptidoma de cèl·lules beta pancreàtiques presentat per al·lels d'HLA associats a diabetis tipus 1 humana

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La presentació de pèptids derivats d'autoantígens per les molècules d'MHC de les APCs és un pas clau en el desenvolupament de la resposta autoimmunitària a la diabetis tipus 1 (T1D); certament, l'expressió d'alguns al.lels d'HLA és un dels majors factors de risc en aquesta malaltia. S'ha proposat l'estrès cel.lular en les cèl.lules β pancreàtiques com a inductor de la generació de nous autoantígens.

Amb l'objectiu d'identificar pèptids derivats de cèl.lules β presentats per al.lels d'HLA-DR rellevants en el desenvolupament de la T1D humana, es van analitzar els pèptids associat a HLA-DR3 i -DR4 de moDCs polsades amb extractes proteics de dues línies model de cèl.lules β, usant dos tipus d'extractes: lisats cel.lulars totals i fraccions enriquides en grànuls d'insulina i crinosomes de cèl.lules β cultivades en condicions homeostàtiques o d'estrès cel.lular. Els pèptids units a molècules HLA-DR es van obtenir mitjançant elució àcida a partir de complexes pèptid-HLA-DR purificats per cromatografia d'afinitat. L'anàlisi per espectrometria de masses va permetre identificar més de 200 pèptids derivats dels lisats totals i al voltant de 70 pèptids derivats de fraccions de grànuls de cadascuna de les condicions utilitzades, que suggereixen diferències induïdes per l'estrès cel.lular. De les proteïnes parentals dels pèptids identificats, 51 es van considerar potencialment rellevants per la T1D. Per a dues d'aquestes proteïnes, s'ha descrit la presència d'autoanticossos i/o limfòcits T autoreactius específics en pacients amb T1D. És destacable que la proporció de proteïnes parentals rellevants va ser superior en el peptidoma derivat dels grànuls que en el derivat dels lisats totals.

Els resultats mostren canvis en el repertori peptídic presentat per HLA-DR en condicions d'estrès cel.lular i una predominança de proteïnes parentals potencialment rellevants als compartiments cel.lulars rics en insulina. Futurs experiments han d'ajudar a aclarir si aquestes diferencies donen lloc a la generació de nous pèptids antigènics.

Posters

9 A CLUSTER ANALYSIS OF BRONCHIECTASIS PATIENTS BASED ON THE AIRWAY IMMUNE PROFILE

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Background: Clinical heterogeneity in bronchiectasis remains a challenge to improve the appropriate targeting of therapies and patient management. Antimicrobial peptides (AMPs) have been linked to disease severity and phenotype.

Research Question: Can we identify clusters of patients based on the levels of AMPs, airway inflammation, tissue remodeling and damage; and to establish their relationship with disease severity and clinical outcomes?

Study Design and Methods: A prospective cohort of n=128 stable patients with bronchiectasis were recruited across three centers in three different countries (Spain, Scotland and Italy). Two-step cluster strategy was used to stratify patients according to levels of lactoferrin, lysozyme, LL-37 and SLPI in sputum. Measurements of inflammation (IL-8, TGF-β and IL-6), tissue remodeling and damage (GAGs, MMP-9, neutrophil elastase, total and bacterial DNA) and neutrophil chemotaxis were assessed.

Results: Three clusters of patients were defined according to distinct airway profiles of AMPs. They represented groups of patients with gradually distinct airway infection and disease severity. Each cluster was associated with an airway profile of inflammation, tissue remodeling and damage. The relationships between soluble mediators were also distinct between clusters. This analysis allowed the identification of the cluster with the most deregulated local innate immune response. During follow-up, each cluster showed different risk of suffering three or more exacerbations (p=0.03) and different time to first exacerbation (p=0.03).

Interpretation: Bronchiectasis patients can be stratified in different clusters according to profiles of airway AMPs, inflammation, tissue remodeling and damage. The combination of

these immunological variables shows a relationship with disease severity and future risk of exacerbations.

Posters

10 Ibrutinib therapy modulates the T-cell development in Chronic Lymphocytic leukemia

Alba Mora[1,2,3]; Marta Lafuente[1]; Leticia Alserawan[3,4]; Jorge Sierra[1,2,3]; M. Esther Moga[3,4]; Carol Moreno[3,4]

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Chronic Lymphocytic Leukemia (CLL) is a lymphoproliferative disorder of monoclonal $CD5^+$ B-cells. However, the tumour microenvironment seems to have an important role in the leukemic cell survival. Ibrutinib, a drug used in the treatment of CLL, it is an irreversible inhibitor of Bruton's Tyrosine Kinase (BTK) in B-cells but also inhibits the IL2-inducible T-cell kinase (ITK) moleculein T-cells.

The main objective of this work was to analyze the immunophenotype of circulating lymphocytes by flow cytometry from patients with stable and progressive CLL treated or not with Ibrutinib, and to investigate whether this therapy is capable to restore the unbalanced cell populations.

The percentage of T and NK cells in patients with stable and progressive CLL were low compared to healthy donors. Progressive CLL also showed a decrease of NKT cells. We did not observe significant differences in the $CD4^+/CD8^+$ T-cells ratio between CLL groups or healthy donors, but patients with stable and progressive CLL presented a decrease in the percentage of $CD4^+$Treg cells, $CD4^+$naïve and $CD8^+$ naïve T-cells. Moreover, patients with progressive CLL also evidenced an increase of Th1, $PD1^+$ and effector memory $CD4^+$ T-cells and of $CD8^+$T-cells with an effector and replicative senescence immunophenotype ($CD27^-CD28^-$).Patients treated with Ibrutinib did not show changes on

NKT cells, Th1 polarization or naïve $CD4^+$ subpopulation, but this therapy increased the percentage of $CD3^+$ T-cells, NK cells and Treg cells and decreased exhaustive $PD1^+CD4^+$ and $CD27^-CD28^-CD8^+$ T-cells.

In conclusion, the progression of CLL is characterized by an immune dysregulation which mainly affect to $CD4^+$ T-cells, presenting an unbalance Th1and Treg polarization and an increase of exhausted T-cells. Ibrutinib therapy has a positive impact by modulating the development of these T-cell subsets.

Posters

11 Evaluation of IgG, IgM and IgA anti- SARS-CoV2 ELISA assays

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Background

As the COVID-19 pandemic evolves, the development of immunoassays has become a pressing priority. Serological assays allow the study of immune response to SARS-CoV-2, and the identification of seroconversion. In addition, they help to characterize COVID-19 course, and are essential for epidemiological studies and vaccine trials.

Immunoassays are rapidly being developed with limited validation on clinical samples.

Method

We evaluated 12 ELISA CE-IVD market to detect anti-SARS-CoV-2 antibodies. These included six antibodyassays using IgG, 4 for IgM and 2 for IgA isotypes. The SARS-CoV2 antigens evaluated were nucleocapsid, spike or a mix peptides.

The assays were validated using 38 serum samples from 17 symptomatic and confirmed RT-PCR-positive SARSCoV-2 patients, and 31 serum samples pre- COVID-19 (January-February, 2019) as a control group. RT-PCR-positive individual were classified in four subgroups base on the days from onset of symptoms: Group 1 : 7-10 days, Group 2: 10-14 days, Group 3: 14-21 days and Group 4: >21 days.

Results

Our evaluation showed heterogeneous assay performance. The specificity of the tests ranged from 81-100 % in pre-COVID-19 samples. Possible cross-reactivity with the nucleocapsid protein was observed. All the individuals with positive SARS-CoV-2 RT-PCR

showed seroconversion during the follow-up. Among samples from SARS-CoV-2 RT-PCR positive individuals, seropositivity increased over time, being higher in samples taken > 21 days after symptoms onset.

Conclusion

The variability found in our evaluation study of commercial CE-IVD ELISA kits, in terms of sensitivity and specificity, confirms that validation of the tests is required to facilitate their use and an adequate interpretation of the results in the clinical practice.

Posters

12 Seroprevalence of anti-SARS-CoV2 antibodies in blood donors from Balearic Islands

Cristina Alejandra López Rodríguez[1]; Bibiana Quirant Sánchez[1,2]; Javier Calvo[3]; Sara Contreras-Martos[4]; Alfonso Leiva[4]; Oana Bulilete[4]; Enrique Girona[5]; Joan Llobera[4]; Eva Martínez- Cáceres[1,2]; Antoni Gaya[3]

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Background

The fast spread of the COVID-19 forced to prioritize the SARS-CoV2 diagnostic tests only for symptomatic people during the first months of the pandemics in Spain.This study aims at estimating the SARS-CoV2 seroprevalence in asymptomatic blood donors from the island of Majorca(Balearic islands).

Method

A total of 1414 serum samples from anonymized blood donors of the Blood Bank of the Balearic Islands were analyzed.Serum samples were collected between April 1st and April 30th, 2020.One hundred pre- pandemic serum samples from the same blood bank collected between 29th and 30th January 2020 were also analysed.

IgA anti-SARS-CoV-2 antibodies were studied by ELISA (Diapro®, Italy), according to the manufacturer's instructions. All sera that gave either a positive or indeterminate index value for IgA anti SARS-CoV-2 antibodies were further analysed to determine IgG- and IgM- SARS-CoV-2 antibodies. Finally, those sera positive for IgG anti-SARS-CoV-2 antibodies were re-analysed by an independent confirmatory ELISA (Diapro®, Italy).

Results

IgA anti-SARS-CoV-2 antibodies were detected in 88 out of the 1414 serum samples (6.2%). From them, 48 sera resulted IgG positive, and 17 sera, IgM positive. Triple positivity was detected in 17 out of the 88 (19.81%) serum samples. A total of 27 serum

samples were only positive for IgA anti-SARS-CoV-2 antibodies.

The analysis of pre-pandemic samples showed a 98% of specificity for IgA ELISA in our population.

We found that the most prevalent antigen recognized by IgG antibodies was the N antigen:95.1% were positive against N protein, 31.1% were positive against S1 glycoprotein and 19.7% were positive against S2 glycoprotein.

Conclusion

Our study has analysed the IgA anti-SARS-CoV-2 seroprevalence in blood donors from a specific region of Spain.These results show that specific IgA anti-SARS-CoV-2 antibodies is present in asymptomatic patients and highlights the relevance of this immunoglobulin in the context of COVID-19 infection.

Posters
Diagnostic Immunology 8 - 13

13 Different T helper profile in convalescent COVID-19 patients vs other pneumonia

Teresa Franco Leyva[1,5]; M Encarna Saez[2,5]; Gemma Boera Carnicero[1,5]; Sandra Clotet[3]; Manuela Agustí Martí[1,5]; Daniel Albert Jares[1,5]; Laura Feltrer[4,5]; Cándido Juárez[1,5]; Jordi Casademont[4,5]; Olga H Torres[2,5]; Laura Martinez- Martinez[1,5]

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Introduction: The SARS-COV-2 (COVID) pandemic has caused an explosion of viral pneumonia cases affecting mainly elderly people. Other community-acquired pneumonia (CAP) already used to cause great morbi-mortality in patients ≥ 65 years old.

Objective: To study and compare cellular components of the immune response in a cohort of recovered COVID patients vs a cohort of recovered CAP patients.

Material and methods: 44 patients >65years old were included: 20 suffered from COVID and 24 from other CAP. CAP patients had been stratified into Bad (BE) or Good (GE) evolution according to whether they were readmitted to hospital/died within 6 months after the episode or not. Samples were collected 1-2 months after pneumonia hospitalization. Hemogram, lymphocyte subpopulations, T helper immunophenotyping and senescent T lymphocytes were studied.

Results: PostCOVID patients had fewer leukocytes (6755/µL) than those with BE (8498/µL), at the expense of neutrophils(COVID 4116/µL, BE 6239/µL) and monocytes (COVID 497/µL, BE 647/µL). Instead, they had more B lymphocytes(COVID 182/µL, BE 87/µL). Although there weren't significant differences in the total T lymphocytes(COVID 1260/µL, BE 1155/µL, GE 1557/µL), their composition was different. COVID patients had lower Th0 lymphocytes(COVID 169/µL(24.5%), BE 211/µL(33.3%), GE 397/µL(43.2%)) and Th2 lymphocytes(COVID 93/µL (13.7%),BE 129/µL(21.4%), GE 205/µL(22.9%) but higher Th1/2(COVID 102/µL(15.1%), BE 56/µL(8.5%), GE 70/µL(7.1%)), Th1/17(COVID 30/µL (3.5%), BE 7/µL(1.2%), GE 13/µL(1.5%)), Th17(COVID 33/µL(4.7%), BE 15/µL(2.5%), GE 25/µL(2.7%)), Th9(COVID 39/µL(5.5%), BE 12/µL(1.9%), GE 28/µL(3.1%)) and Th22(COVID 7/µL(1.0%), BE 2/µL(0.3%), GE 3/µL(0.4%)) than patients with CAP. No significant differences were observed in the senescence study.

Conclusion: Patients recovered from SARS-COV-2 pneumonia have an expansion of CCR6+ T helper lymphocytes compared to those recovered from CAP due to other etiologies.

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 In vitro evidence for the negative immunomodulatory function of the CD6 lymphocyte co-receptor

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The CD6 glycoprotein is a surface co-receptor reported to be involved in lymphocyte activation, proliferation and survival processes following stimulation with supra-physiological polyclonal T-cell activators. However, its ultimate stimulatory/inhibitory role as well as the molecular signaling mechanisms involved is still controversial. Here, we analyze the modulatory role of CD6 in peripheral T lymphocytes under antigen-specific stimulation conditions. To this end, MHC class II-restricted and ovalbumin (OVA)-specific TCR-transgenic mice expressing normal (OT-II cd6$^{+/+}$) or deficient (OT-II cd6$^{-/-}$) surface expression were analyzed. Splenocytes from both mouse lines were cultured in the presence of $OVA_{323-339}$ peptide (ISQ), soluble anti-CD3ε mAb (positive control) and $OVA_{257-264}$ peptide (SIINFEKL; negative control) at different time-points. The results show that OVA-activated CD4^{+} T-cells from OT-II cd6$^{-/-}$ mice express higher surface levels of T cell activation (CD25 and CD69) and exhaustion (PD-1) markers. Moreover, while cell proliferation was found significantly increased in CD4^{+} T-cells from OT-II cd6$^{-/-}$ mice, no significant differences were observed regarding cell apoptosis compared with OT-II cd6$^{+/+}$ controls. In summary, in vitro evidence supports the negative regulatory role of CD6 on early and late events following antigen-specific lymphocyte activation.

Posters

15 Study of the transplacental immunoglobulin transfer: relationship between plasma concentrations in maternal and umbilical cord blood

Karla Rio[1,2], Ignasi Azagra-Boronat[1,2]*, Malen Massot-Cladera[1,2], Margarida Castell[1,2], Marta Selma-Royo[3], Izaskun Mantrana[3], María J Rodríguez-Lagunas[1,2], M Carmen Collado[3], Francisco J Pérez-Cano[1,2]

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Mothers confer natural passive immunization to their infants by transplacental pathway during the gestation period and through breast milk after birth.

The objective of the present study was to establish the concentration and relationship of immunoglobulins (Igs) at birth in plasma of mothers and in cord blood samples of infants, belonging to the Mediterranean birth-cohort (MAMI cohort).

A total of 27 mothers and 23 infants were recruited into the study. At the day of delivery, plasma from the mothers and cord blood from the infants were obtained. The concentrations of total Igs and Ig classes (IgA, IgE, IgG and IgM) as well as the subclasses of IgG (IgG1, IgG2, IgG3 and IgG4) were assessed by means of a multiplex bead-immunoassay. The Pearson's correlation coefficient between both samples was also calculated.

The concentration of Igs was higher in the maternal plasma than those observed on neonatal cord blood ($p<0.05$). Particularly, we found significant higher maternal values of IgM, IgG2, IgE and IgA ($p<0.05$), although the amount of IgG was similar in both mother and neonatal samples. Moreover, total Igs, all IgG subtypes and IgE positively correlated in the mother-infant pair. Conversely, it was not the case for IgM and IgA. When clustering IgG subtypes into Th1- or Th2-associated Igs it was observed that the %Th1, %Th2 and the Th1/Th2 ratio in the neonatal cord blood displayed a positive correlation with those in the maternal plasma ($p<0.05$).

In conclusion, we established the concentration of Igs in the maternal-neonatal pair at birth. Although their levels were lower in cord blood, we established positive associations between the concentrations in the mother and the infant, suggesting that the immune status during pregnancy, in terms of Ig levels, would influence the immune status of the infant at birth.

Posters

16 Myeloid-Derived Suppressor Cells in Lung Transplant Recipients

María Iglesias Escudero[1]; David San Segundo Arribas[2]; David Merino Fernández[2]; Patricia Lamadrid Perojo[2]; Victor Manuel Mora[2]; David Iturbe Fernández[2]; Sonia Fernández-Rozas[2]; José Manuel Cifrian Martínez[2]; Marcos López Hoyos[2]

[1]Hospital Germans Trias i Pujol; [2]Hospital Universitario Marqués de Valdecilla

Myeloid Derived Suppressor Cells (MDSCs) represent a heterogeneous group of myeloid regulatory cells that were originally described in cancer. Several studies in animal models point to MDSC as important players in the induction of allograft tolerance due to their immune modulatory function; however, studies addressing MDSCs in human organ transplantation are sparse. We evaluated phenotype and function of MDSCs subsets in peripheral blood from 82 lung transplant recipients and its relationship to post transplant clinical events and confirmed the ability of Mo-MDSC subsets from tacrolimus treated LTR to suppress T cell proliferation in vitro. We found that percentages of total MDSC were increased in LTR 3 months after transplantation up to a year. When we studied the effect of transplantation on MDSC subsets in our cohort, Mo-MDSC percentages increased promptly after transplantation and decreased gradually during the timecourse follow up. On the contrary, PMN-MDSC percentages decrease in the short term after trasplantation, and increase during the follow up. Although the effect of immunosuppressive therapy on MDSC remains unknown, we hypothesize that corticosteroids are increasing Mo-MDSC populations in peripheral blood immediately after transplantation. No effect of MDSC subsets on short-term clinical events was observed ir our cohort, but our results determine Mo-MDSC frequencies are increased after acute cellular rejection (ACR), suggesting a possible role for Mo-MDSC in the development of chronic lung allograft dysfunction (CLAD). Therefore, whether MDSC subsets play a role as biomarkers of chronic rejection or not, remains unknown and require further investigations.

2021 Events
Lifelong Learning SCI Program 2021

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

04-02-2021
18:00-20:00
Immunometabolism during inflammation and aging (Taula rodona)
Professor/a: Maria Mittelbrunn

04-03-2021
18:00-20:00
Scavenger receptors as targets for immune-based therapies (Sessió)
Professor/a: Francisco Lozano Soto

29-04-2021
16:00-20:00
Dia de la Immunologia
"Autoimmunity and Autoinflammation"

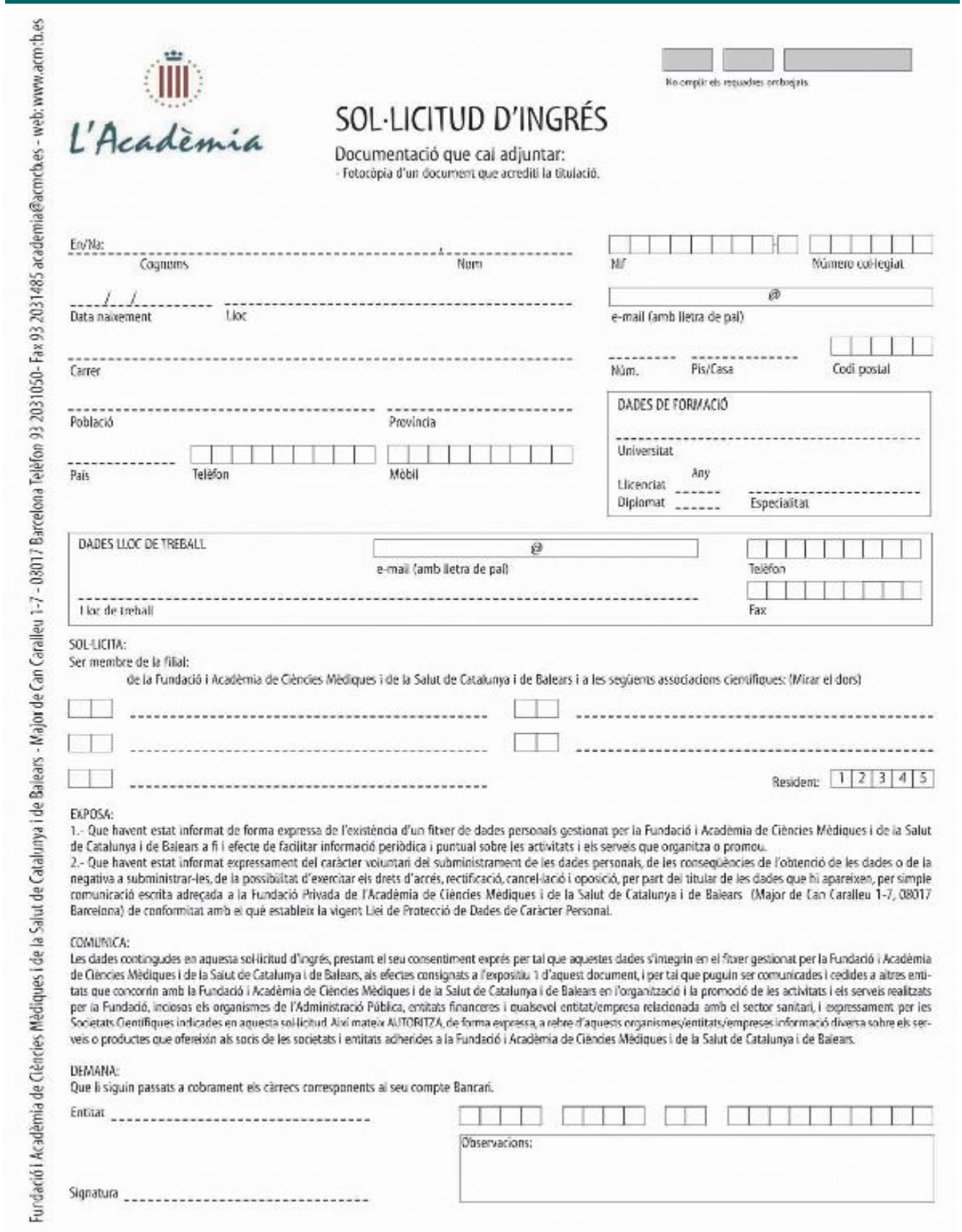
Stratification of systemic autoimmune diseases (Sessió)
Marta Alarcon- Riquelme
The relevance of DNA methylation alterations in immune-mediated disease (Sessió)
Professor/a: Esteban Ballestar
Advances in rheumatoid arthritis (Sessió)
Juan Cañete

06-05-2021
18:30-19:30
New Technologies: Immunoprofiling cyToff mass cytometry: opportunities and challenges (Taula rodona)
Tomas Kalina
Bulk and single cell molecular profiling or normal and neoplàstic B cells (Sessió)
Iñaki Martin-Subero

03-06-2021
18:00-20:00
New roles of the transcription factor NFAT5 (Sessió)
Cristina López Rodríguez

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



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Data naixement _____ Lloc _____

e-mail (amb lletra de pal) @

Carrer _____ Núm. _____ Pis/Casa _____ Codi postal

Població _____ Provincia _____

País _____ Telèfon _____ Mòbil _____

DADES DE FORMACIÓ

Universitat _____

Llicenciat _____ Any _____

Diplomat _____ Especialitat _____

DADES LLOC DE TREBALL

e-mail (amb lletra de pal) @

Telèfon

Lloc de treball _____

Fax

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'expositiu 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 _____

Signatura _____

Observacions:

List of authors and participants

L'Acadèmia
FUNDACIÓ ACADÈMIA DE CIÈNCIES MÈDIQUES
I DE LA SALUT DE CATALUNYA I DE BALEARS

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XIII CONGRÉS

Societat Catalana d'Immunologia (SCI)

Barcelona, 19 i 20 de novembre 2020

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