

Characterization of regulatory T cells in patients suffering from Chronic Fatigue Syndrome /Myalgic Encephalomyelitis

Dra. Cecilia Cabrera

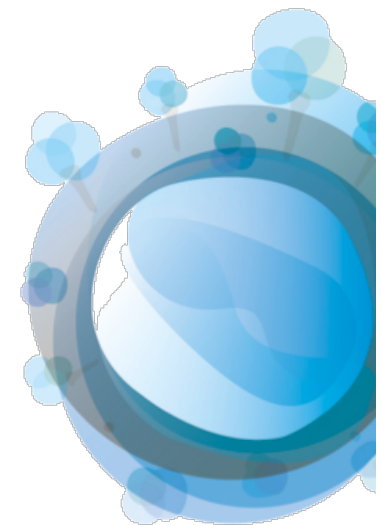
Dr. Julià Blanco

Dr. Bonaventura Clotet

IrsiCaixa

Institut de Recerca de la Sida

 **IGTP**



Who?

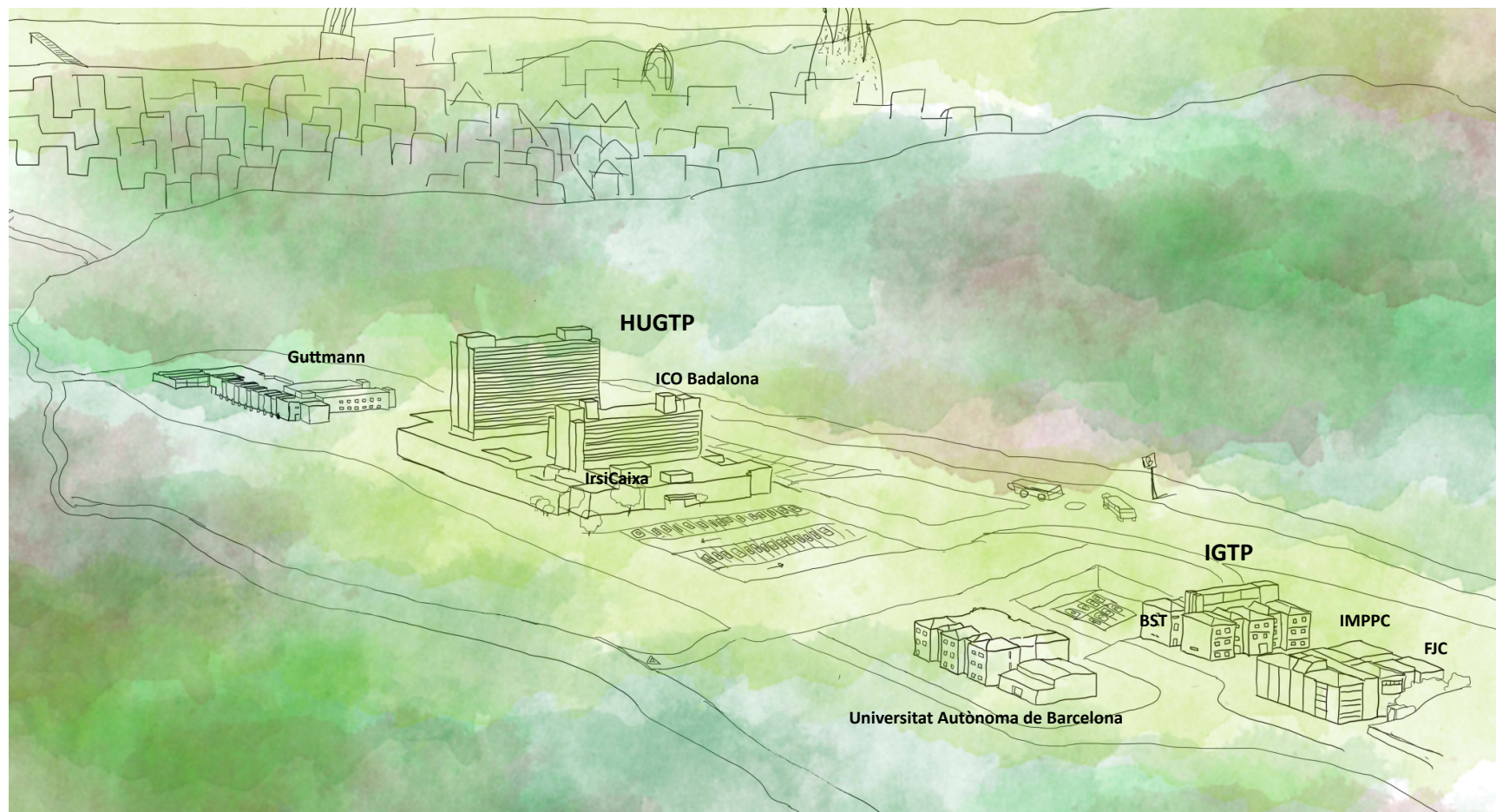
**Virologia i
Immunologia Cel·lular**
Investigador Responsable
Julià Blanco



2010

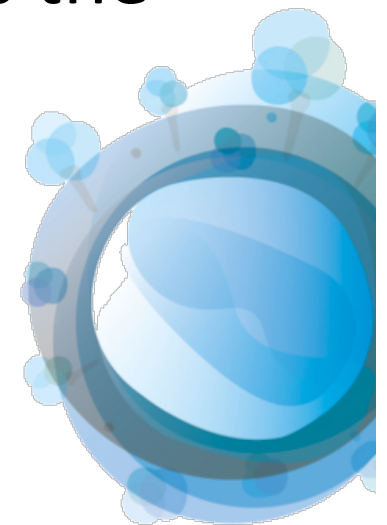
our first contact with CFS reseach

Where?

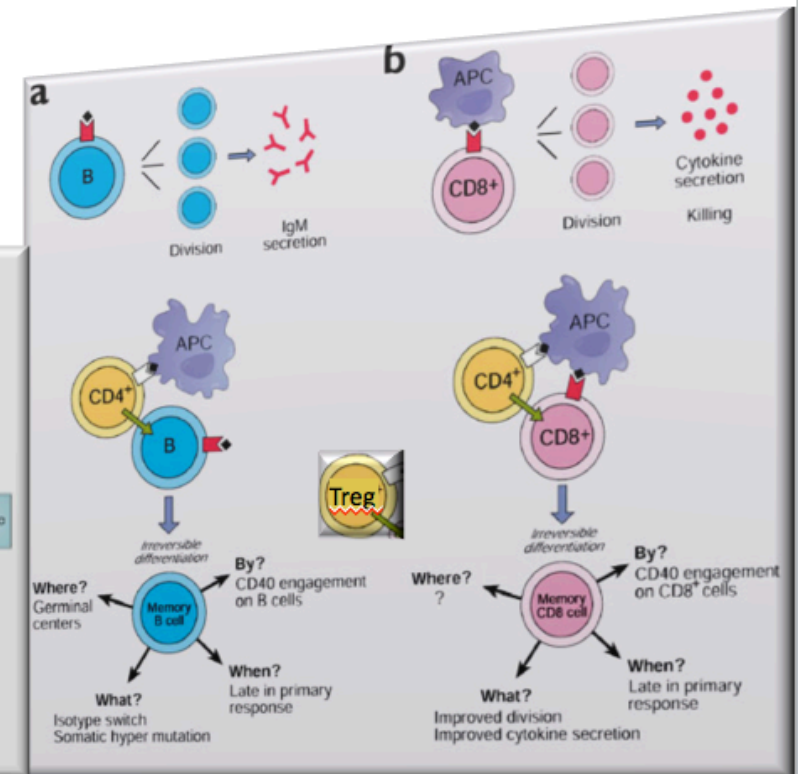
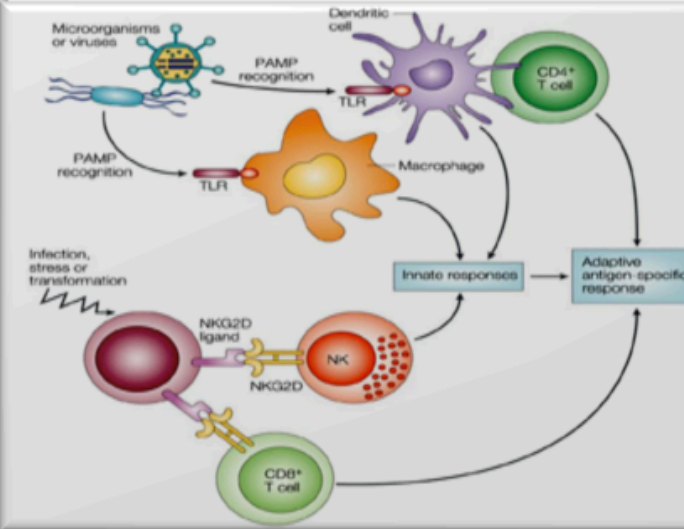
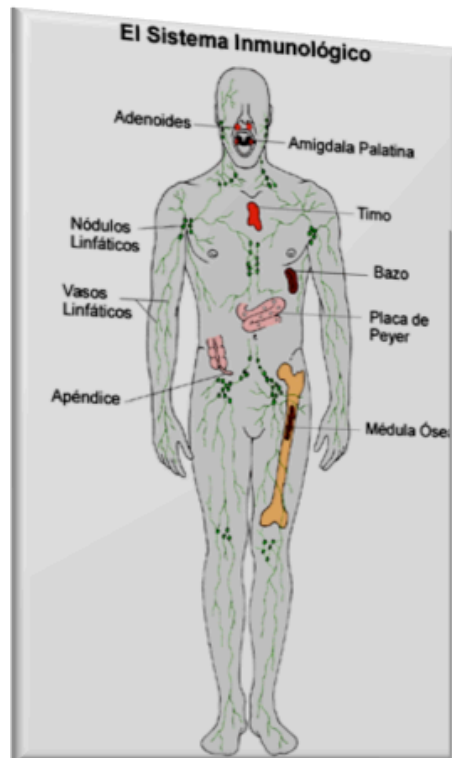


What??

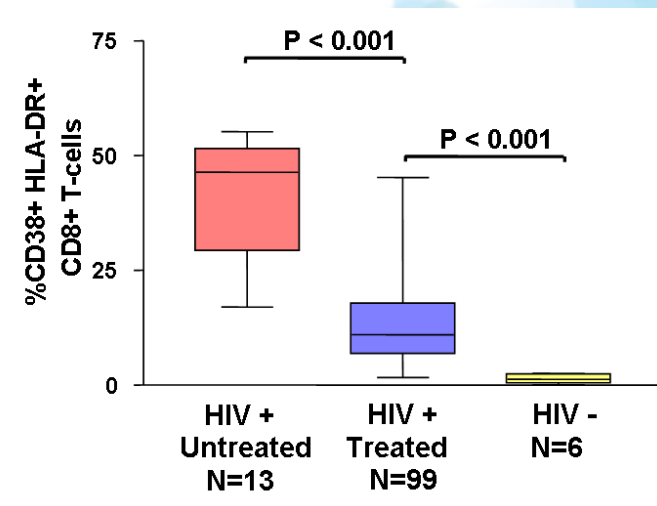
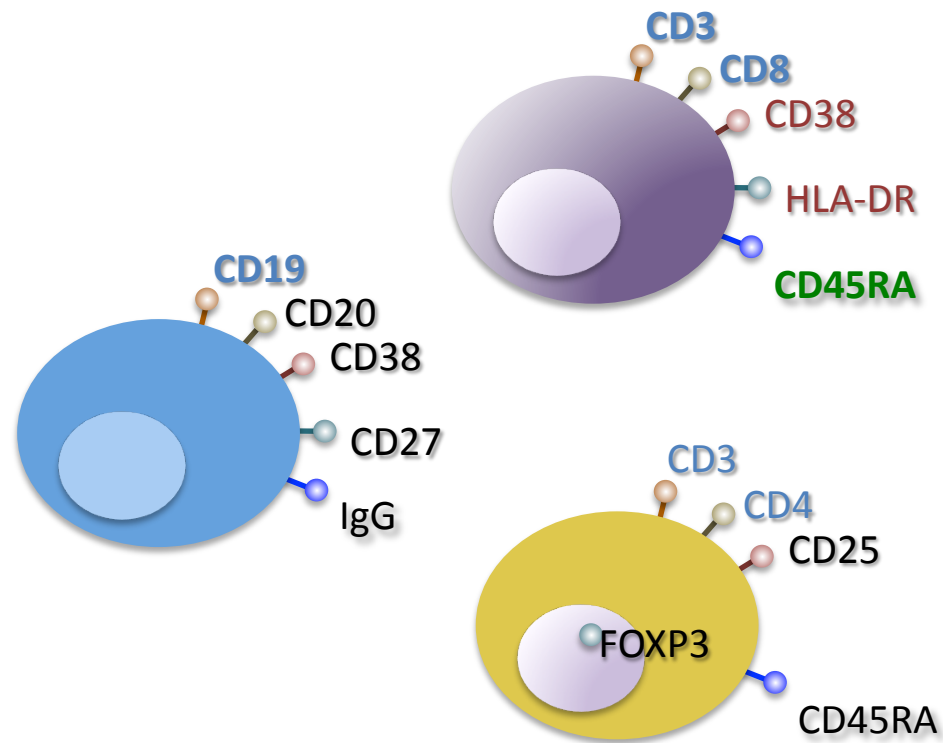
- We study immune alterations occurring after infection by Human Immunodeficiency Virus (HIV).
- HIV destroys lymphocytes and damages the immune system



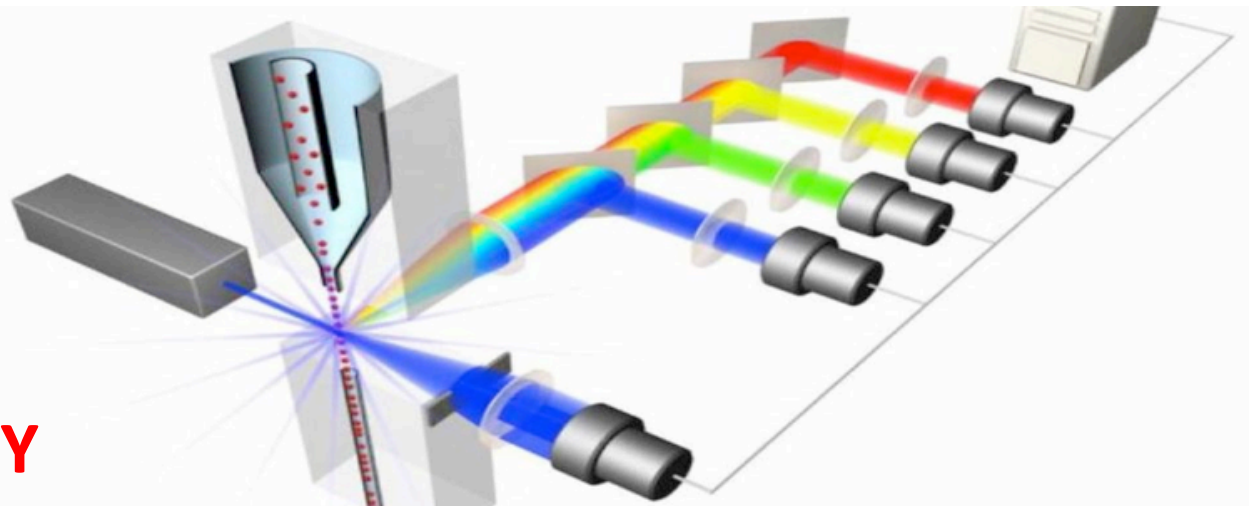
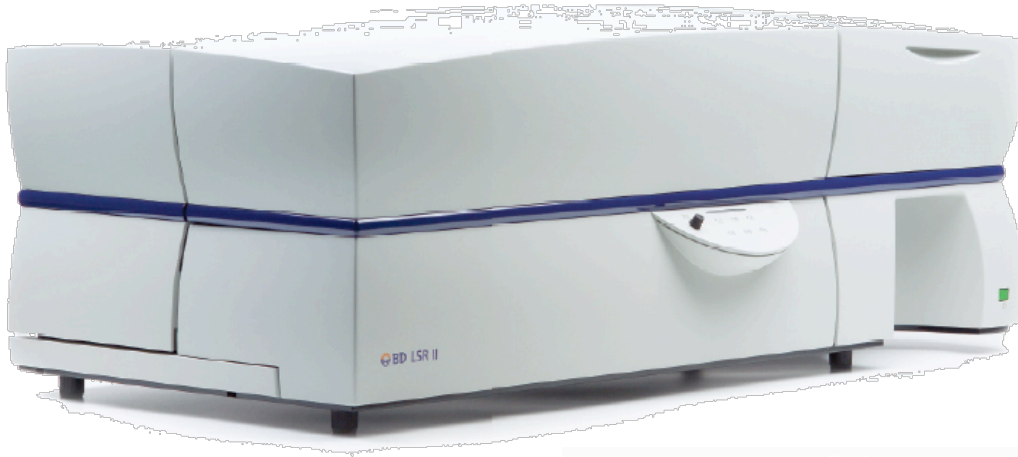
The complexity of the immune system. Many organs and many cell types



Different cells are identified by the presence of specific molecules on their surface



Evaluating changes in Immune cells



FLOW CYTOMETRY

Analysis of millions of individuals cells

Myalgic encephalomyelitis

**FIND THE CURE
FOR CHRONIC
FATIGUE SYNDROME**
Someone I Love Is Waiting....

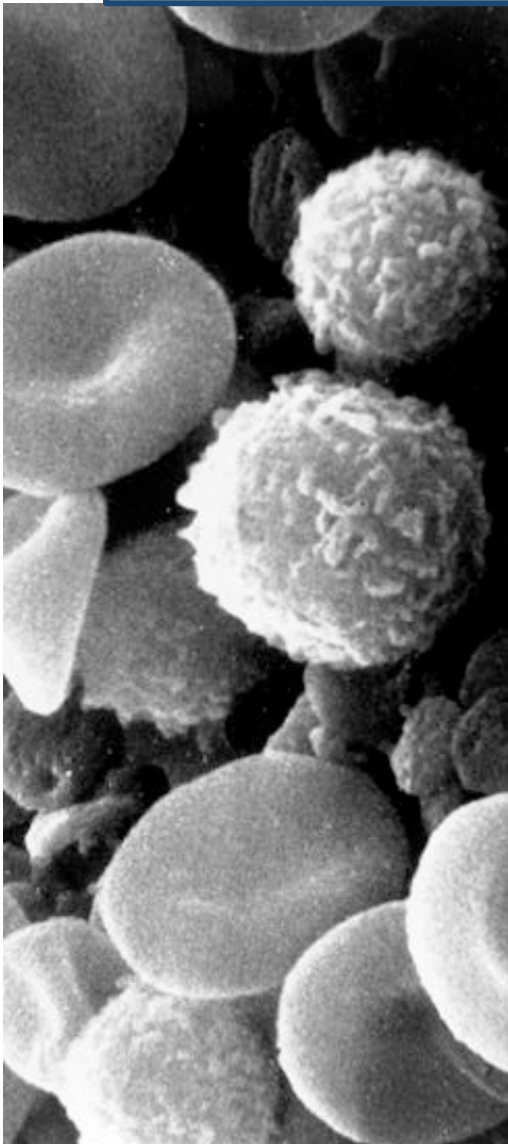


Neuromotor

Immunological

Other

Immunological abnormalities

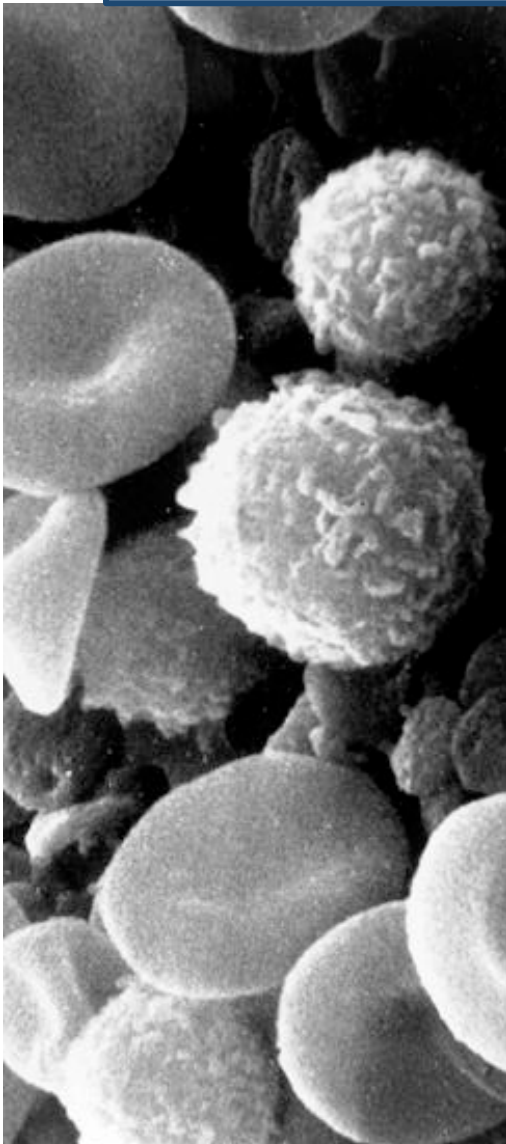


Hipersensitivity

Recurrent infections

Autoimmunity

Immunological abnormalities



NK cells,
antitumoral, defence

T cells, defence
against viruses

B cells, defence,
autoimmunity

Pilot Study to identify immunological abnormalities in patients suffering from CFS

DESIGN:

Cross sectional study, comparative, characterizing immunological status of:

- GROUP A patients suffering from CFS (n=22),
- GROUP B Healthy individuals (n=30)

OBJETIVES:

1. To identify differences in activation and function in B, T, and NK cells among groups.

2010



RESEARCH

Open Access

Screening NK-, B- and T-cell phenotype and function in patients suffering from Chronic Fatigue Syndrome

Marta Curriu^{1†}, Jorge Carrillo^{1†}, Marta Massanella^{1†}, Josepa Rigau², José Alegre³, Jordi Puig⁴, Ana M Garcia-Quintana⁵, Jesus Castro-Marrero³, Eugènia Negredo⁴, Bonaventura Clotet^{1,4}, Cecilia Cabrera¹ and Julià Blanco^{1,6*}

2013

Conclusions

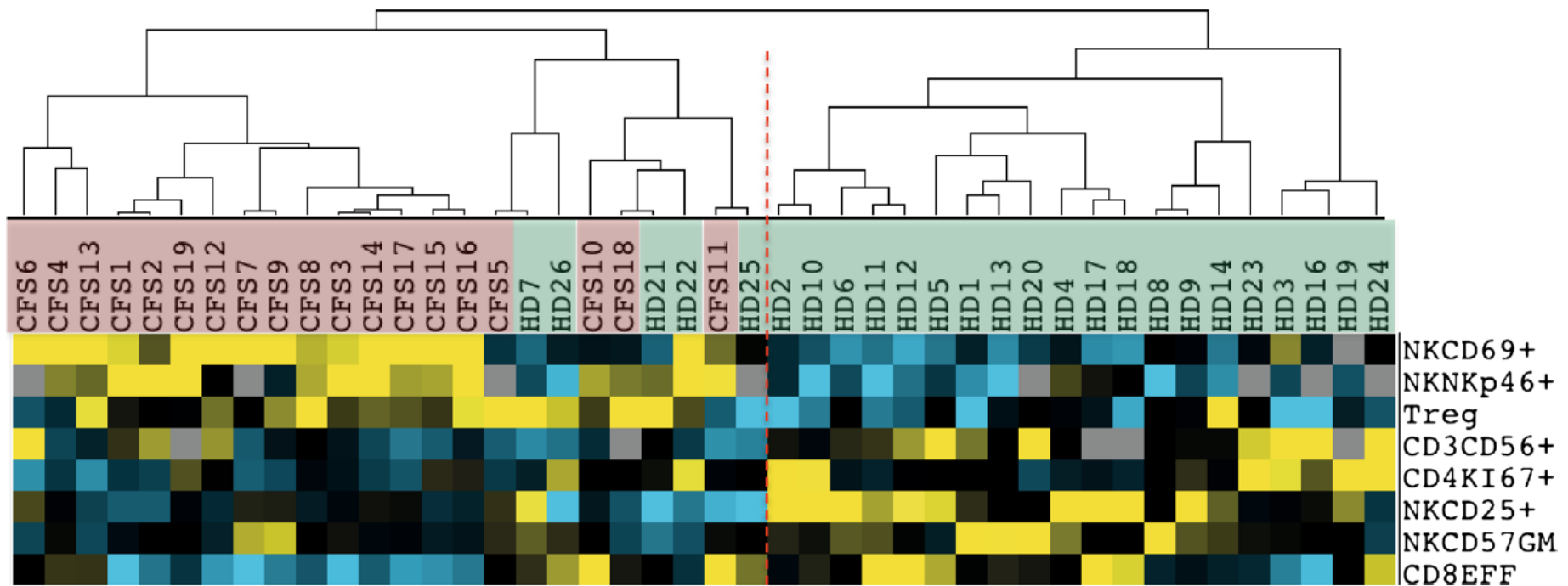


Figure 5 Clustering CFS individuals according to NK and T cell phenotypic markers. A subset of 19 CFS (red labels) and 25 control individuals (green labels) was analyzed. Figure shows normalized centered data in yellow (for positive values, above median) and blue (for negative values, below median). Two groups of CFS and Control individuals were clearly differentiated, while a heterogeneous subgroup was clustered with CFS individuals.

Conclusions

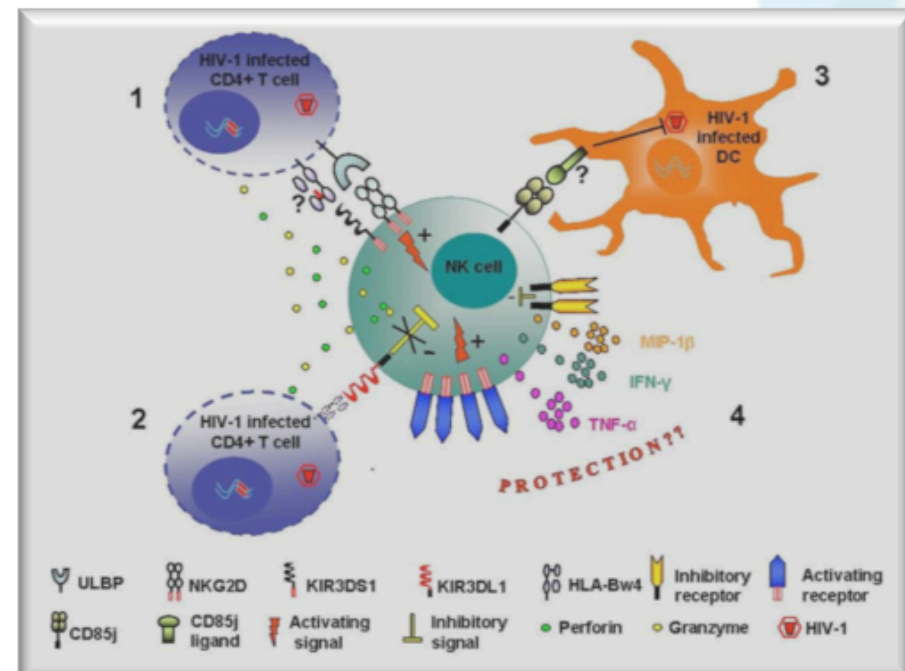
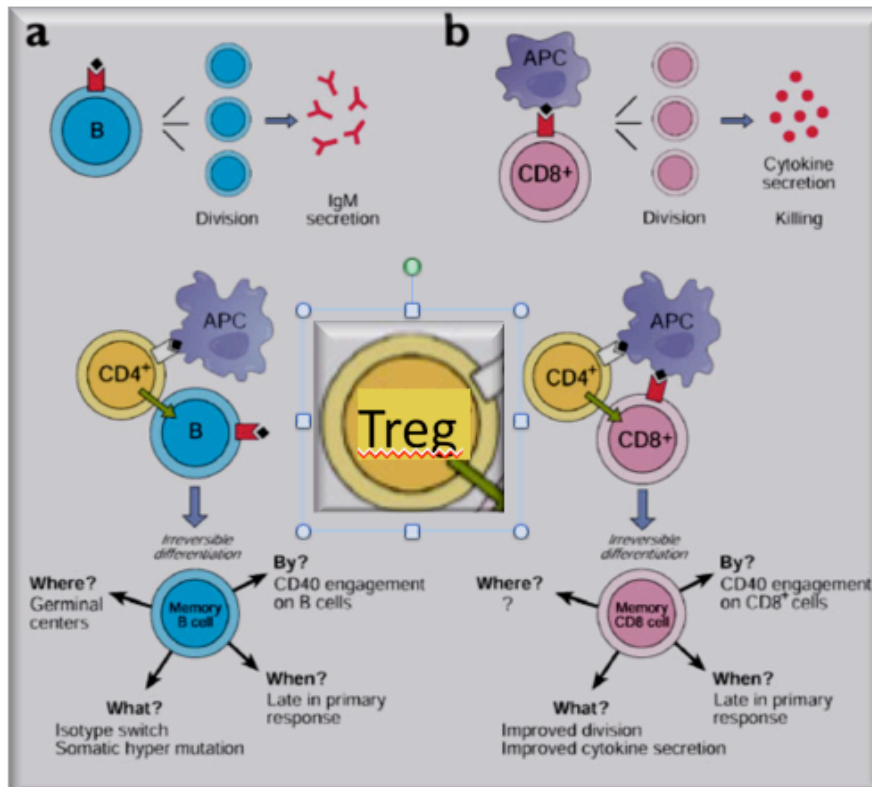
- B cells do not show significant phenotypic or functional alterations
- T cells show a lack of responsiveness in both CD4 and CD8 subsets:
 - In CD4: increased numbers of Treg and lower proliferation in vivo and in vitro
 - In CD8: increased CD5 expression, reduced CD38 expression and numbers of effector cells.
- NK cells show an altered activation pattern.

A reduced T cell response seems to be a major feature of CFS



Our working model

Overexpression of Treg may reduce T cell activity and may impact NK cells



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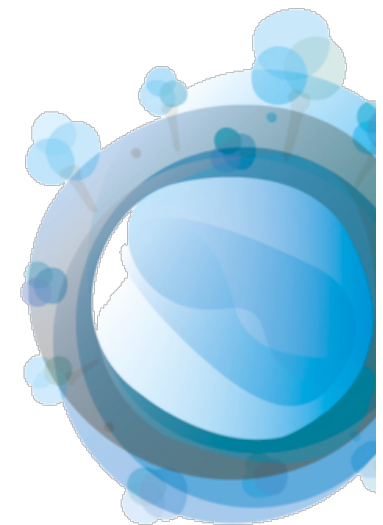
Dr. Bonaventura Clotet

2014

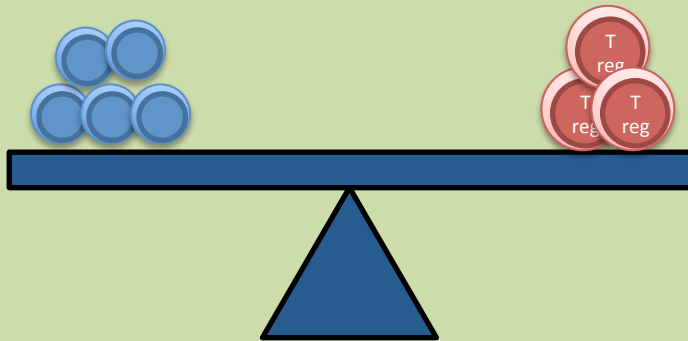
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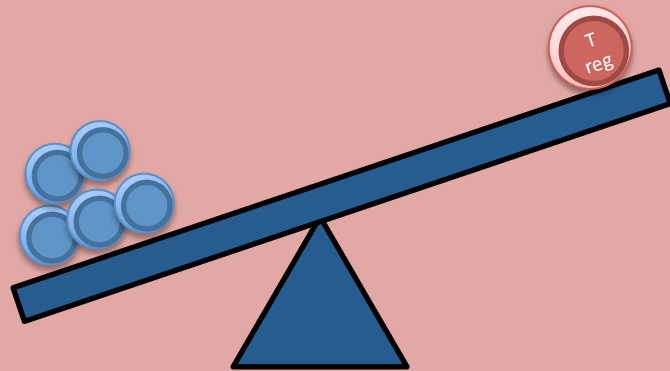
IGTP



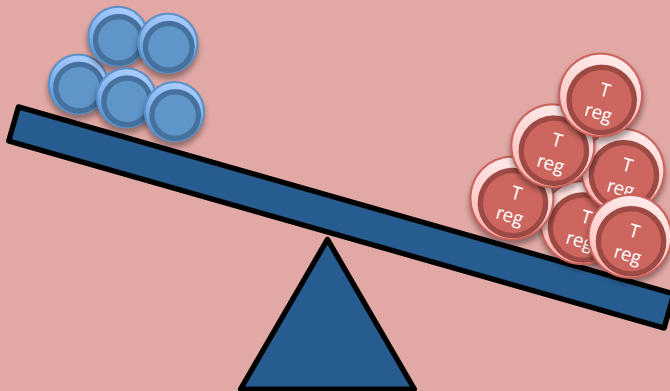
Treg



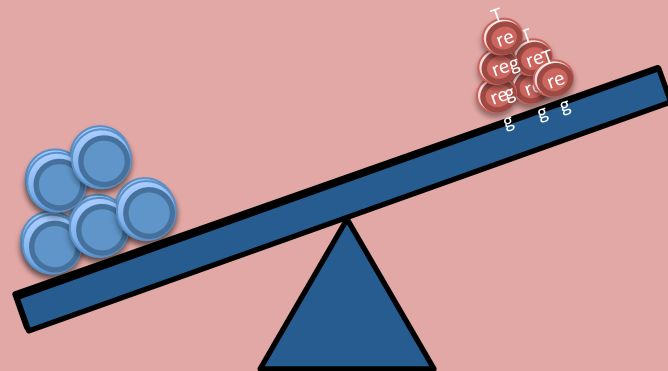
Balanced response



Unbalanced response (autoimmunity)



Unbalanced response (infections)



Unbalanced response (autoimmunity)

Working plan

- Analyze phenotype and function of Treg in patients suffering from CFS (n=22) and controls (n=30).

- ☐ Numbers

- ☐ Ability to control immune responses

- ☐ Mechanisms of control

We will learn on

- ✧ Treg dysfunction in CFS.
- ✧ Association of Treg dysfunction with other immune alterations
- ✧ Our ability to modulate Treg function



Colabora con la investigación biomédica en SFC/EM

We will also increase

✧ Local visibility

✧ International impact

✧ Future perspectives

Positive visibility!

PRESS

- ***El País*** - Edición Nacional – 27/03/2013
- ***El Punt Avui*** – 27/03/2013
- ***Regió 7*** – 27/03/2013
- ***Heraldo de Aragón*** – 27/03/2013
- ***Diario de León*** – 27/03/2013
- ***Diari de Girona (Salut)*** – 28/03/2013
- ***La Vanguardia*** – 28/03/2013
- ***Diario de Cádiz*** – 29/03/2013
- ***Diario de Sevilla*** – 29/03/2013
- ***Canarias 7*** – 31/03/2013
- ***La Gaceta de los Negocios*** – 01/04/2013
- ***Gaceta Médica*** – 01/04/2013
- ***El Semanario de Diario Médico*** – 01/04/2013
- ***Diari de Girona (Suplement especial)*** – 07/04/2013
- ***El País*** - Edición Nacional – 09/04/2013
- ***El País*** - English edition – 15/04/2013

TV

- ***Televisió de Badalona*** – 03/04/2013
- ***Telecinco*** – 09/04/2013

RADIO

- ***Catalunya Ràdio*** – 28/03/2013
- ***Radio Castilla La Mancha*** – 28/03/2013

International impact

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Phoenix Rising

Supporting People with Chronic Fatigue Syndrome (ME/CFS)

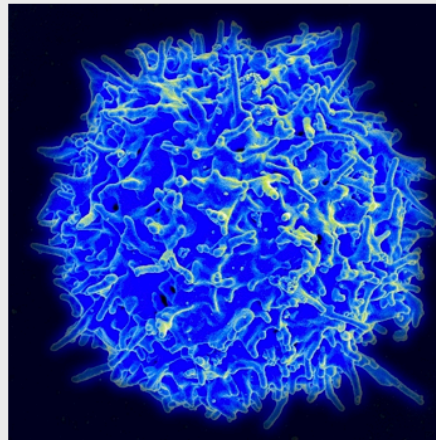
Spanish HIV Experts Give Aid to ME/CFS

APRIL 13, 2013

Joel (Snowathlete) talks with Dr Blanco, from IrsiCaixa, about the Spanish AIDS Research Institute's latest research on ME/CFS

Back in 2009 when XMRV hit the headlines a number of groups around the world took an interest in ME/CFS for the first time. One of these groups was the AIDS Research Institute [IrsiCaixa](#), in Spain. Then XMRV tripped itself up and ME/CFS became invisible again...Except, it didn't...

IrsiCaixa were still interested. Dr Blanco and his colleagues had taken a look at ME/CFS in 2010 and spotted a bunch of problems in the immune system. These guys really know their stuff when it comes to immunology and they knew that they were on to something. Here's what Dr Blanco had to say about it:



T-lymphocyte (T-cell)

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International impact

MEETING PROGRAMME

PRE-MEETING - WEDNESDAY 29 MAY 2013

For those who have arrived by Wednesday evening we will be able to meet up in the hotel bar for an informal get-together on the evening of 29th May.



THURSDAY 30 MAY 2013 – RESEARCH MEETING AGENDA

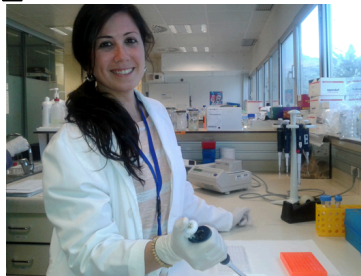
Time	Session	Presenter
0900	Welcome and introductions	(Chairs: Ian Gibson/Hugh Perry)
0915	Pathogen Discovery and Pathogenesis CFI	(Mady Hornig)
0930	Retroviruses and ME	(Greg Towers)
0945	Pathogen Discovery	(Jonas Blomberg)
1000	Gut Microbiota Study UEA	(Simon Carding)
1010	Chaired Discussion	(Ian Gibson/Hugh Perry)
1020	Morning Tea/ Coffee Break	
1040	Review of experience of Rituximab in ME/CFS and present a case for extending clinical trials as per Norwegian protocols or other parallel trials	(Oystein Fluge/ Olav Mella)
1055	Rituximab in autoimmune diseases	(Jo Cambridge)
1115	Update on immunological derangement that may dovetail with the Fluge et al findings.	(Sonya Marshall- Gradisnik)
1130	Screening NK-, B- and T-cell phenotype and function in patients suffering from ME	(Julià Blanco)
1145	Chaired Discussion	(Ian Gibson/Hugh Perry)
1200	Update on ANS studies	(Julia Newton)
1215	FDA Meeting outcome /Treatment with Vistide	(Dan Peterson)
1230	Lunch(hotel restaurant)	

Future

- International collaborations
- European Projects...

Future: 2014-...

- Cecilia Cabrera
- Jorge Carrillo
- Elisabet García
- Silvia Marfil
- Luis M Molinos
- Dan Ouchi
- Marisa Rodriguez
- Lucía Pastor
- **Elisabet Gómez**
- Julià Blanco
- Bonaventura Clotet



- José Alegre
- Jesús Castro
- Josepa Rigau
- ASSEM

OUR YOUNG EXPERT ON FLOW CYTOMETRY

- THANKS TO ALL PATIENTS !!!!



Colabora con la investigación biomédica en SFC/EM