European Crohn's and Colitis Organisation

Adipose-derived stem cells from Crohn's disease patients show antigen presenting cell-like properties

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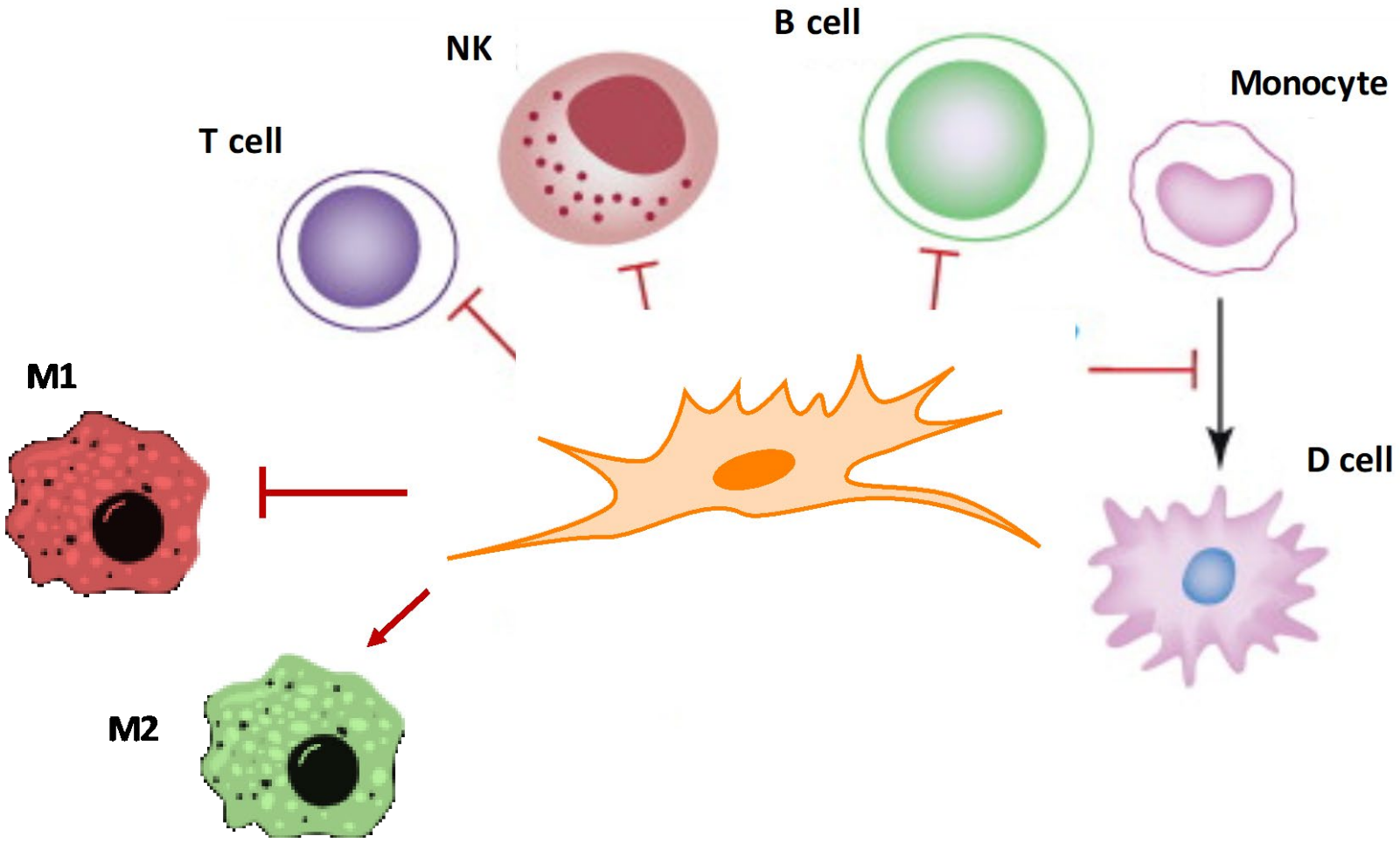
Copenhagen, March 7th 2019

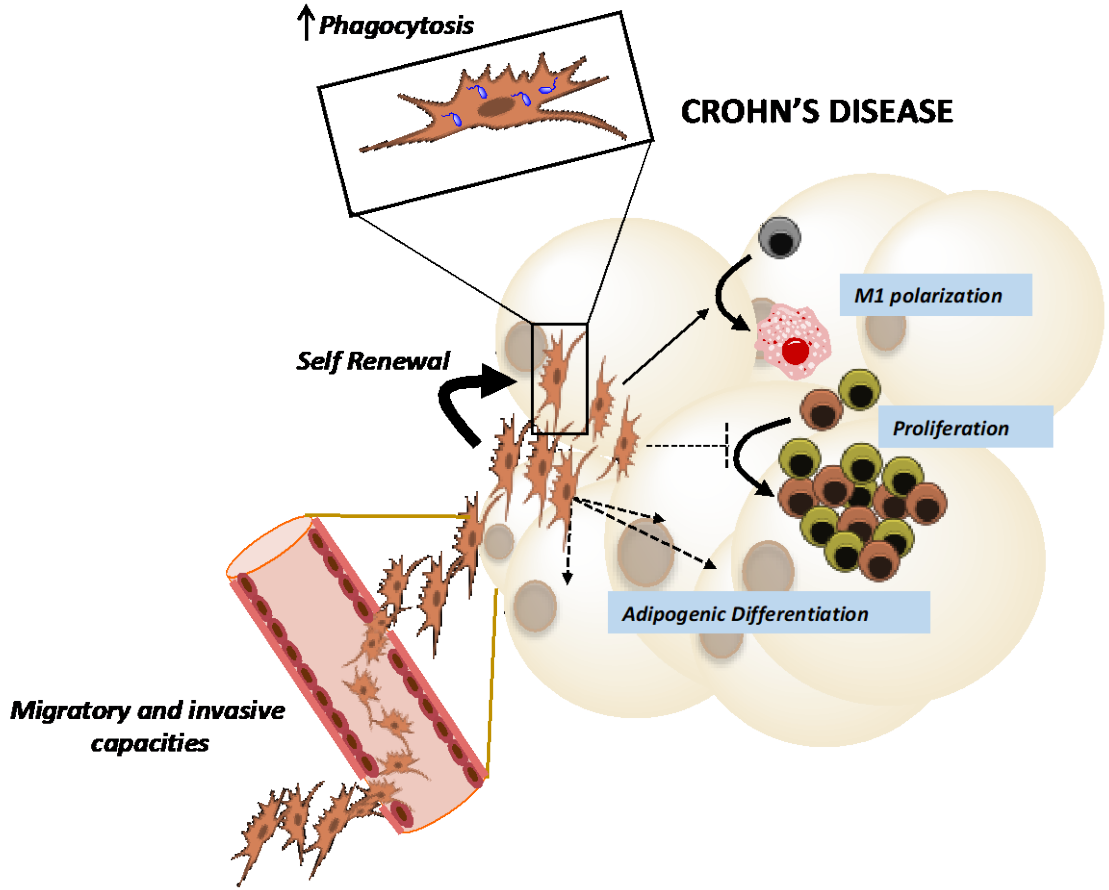
Adipose-stem cells

- **Physiological conditions**



Adipose-stem cells

- **Inflammatory millie: Crohn's Disease**

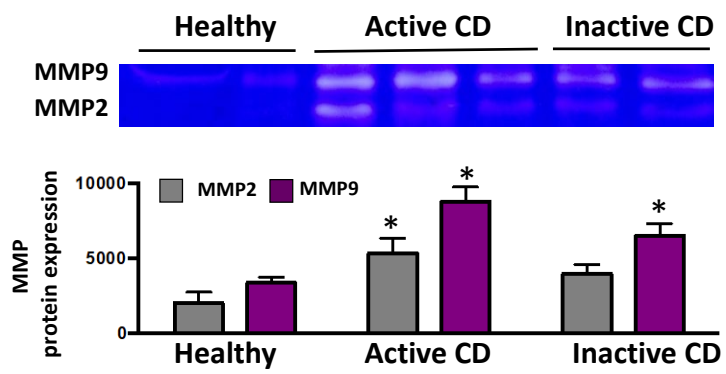


Stem Cell Reports
Article
OPEN ACCESS

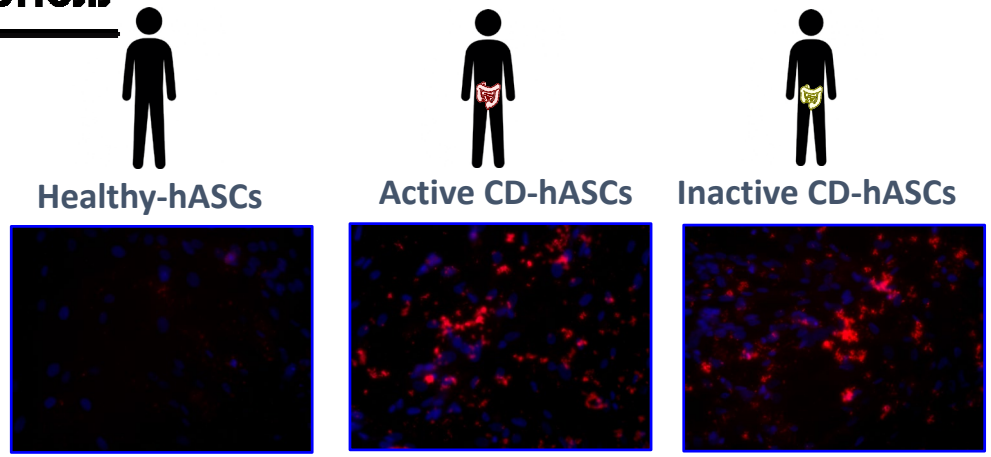
Crohn's Disease Disturbs the Immune Properties of Human Adipose-Derived Stem Cells Related to Inflammasome Activation

Carolina Serena,[1,2,*] Noelia Keiran,[1,2,9] Ana Madeira,[1,2,9] Elsa Maymó-Masip,[1,2] Miriam Ejarque,[1,2] Margarida Terrón-Puig,[1] Eloy Espin,[3] Marc Martí,[3] Natalia Borruel,[4] Francisco Guarner,[4] Margarida Menacho,[5] Antonio Zorzano,[2,6,7] Monica Millan,[8] Sonia Fernández-Veledo,[1,2] and Joan Vendrell[1,2,*]

INVASION

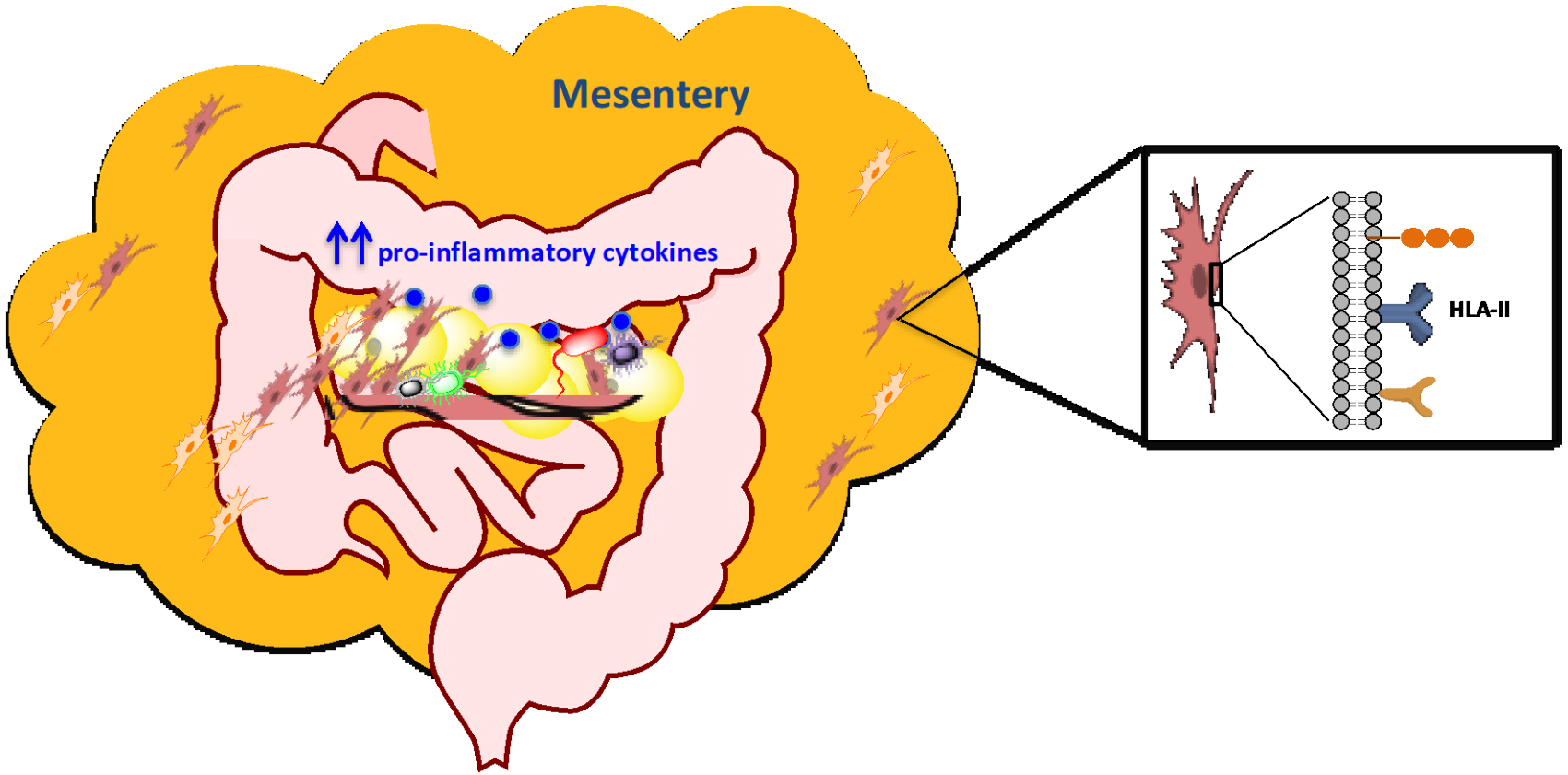


PHAGOCYTOSIS



In red, phagocyted bacteria. In blue, nucleus

HYPOTHESIS



Dysbiotic bacteria

Immune activated adipose-stem cell

Mature adipocytes (*creeping fat*)

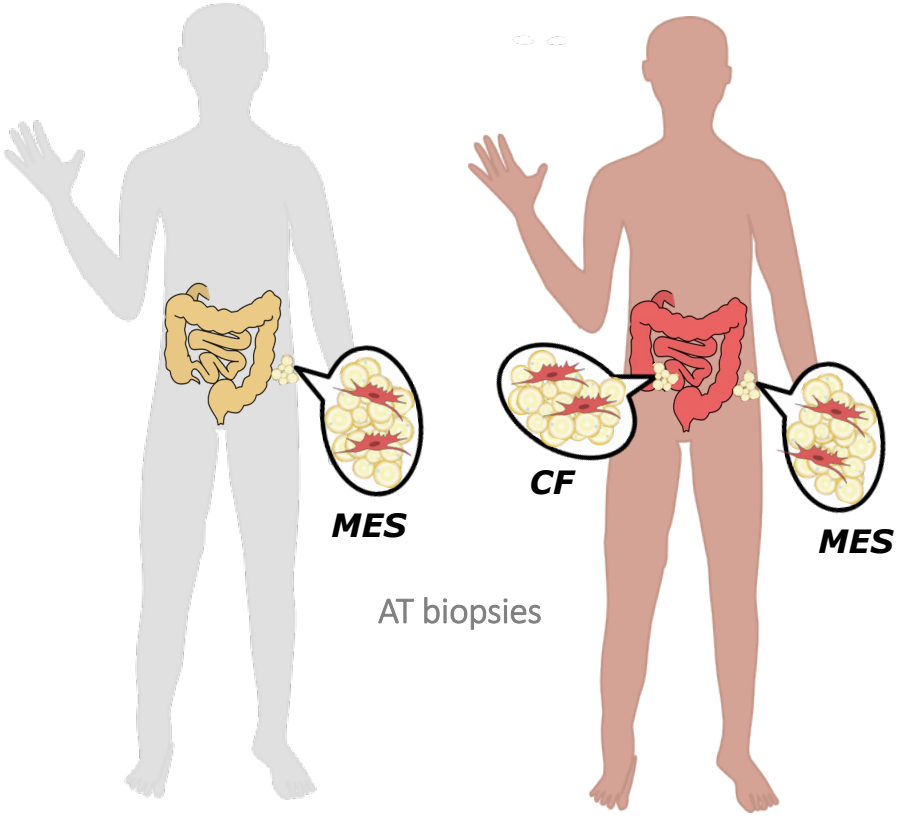
METHODS

HJ23
Hospital Universitari Joan XXIII
ICS Camp de Tarragona

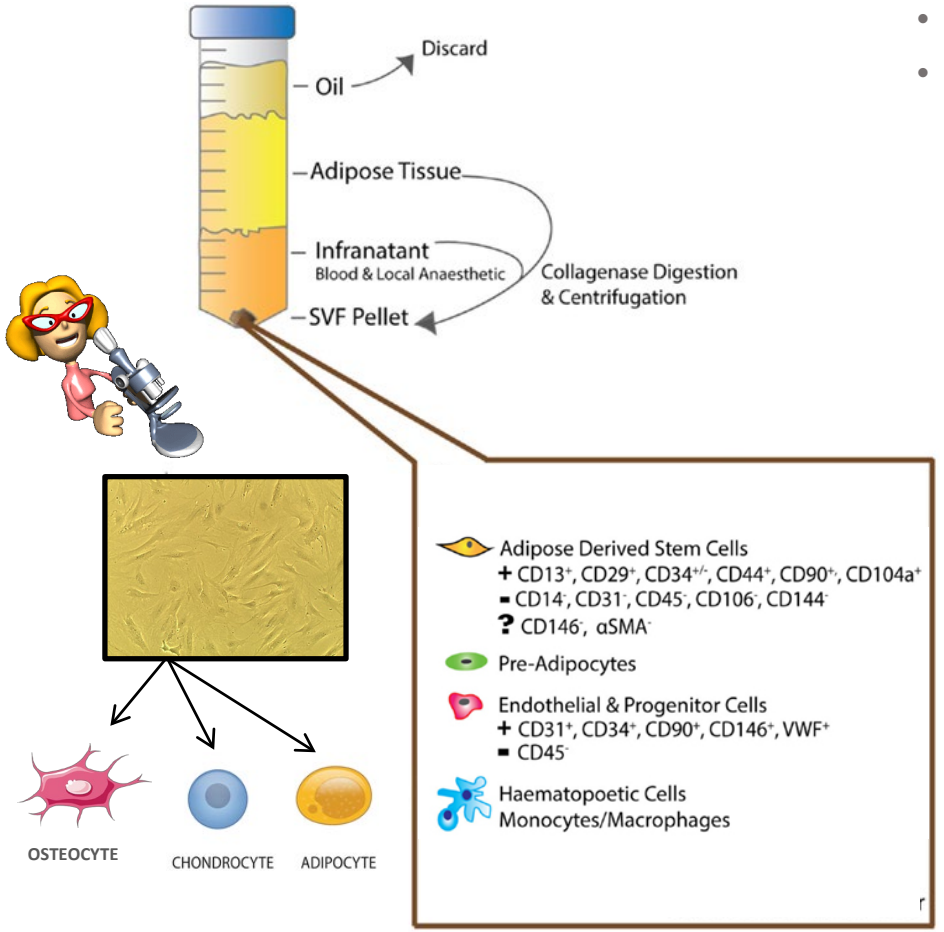
Vall d'Hebron
Hospital

Non-Crohn
(n=10)

Crohn
(n=10)



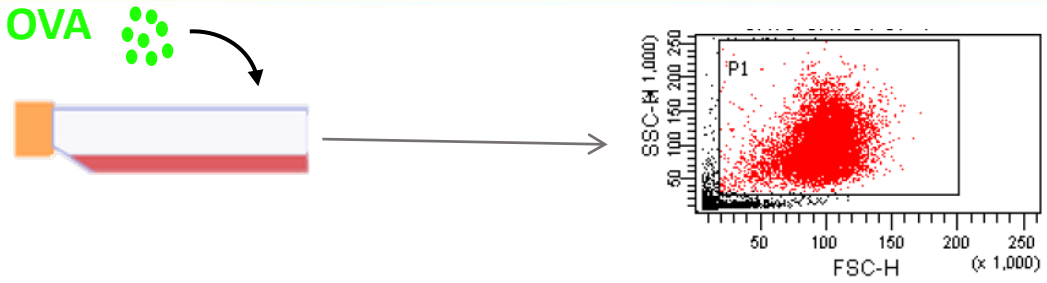
AT biopsies



Antigen-presenting cell properties:

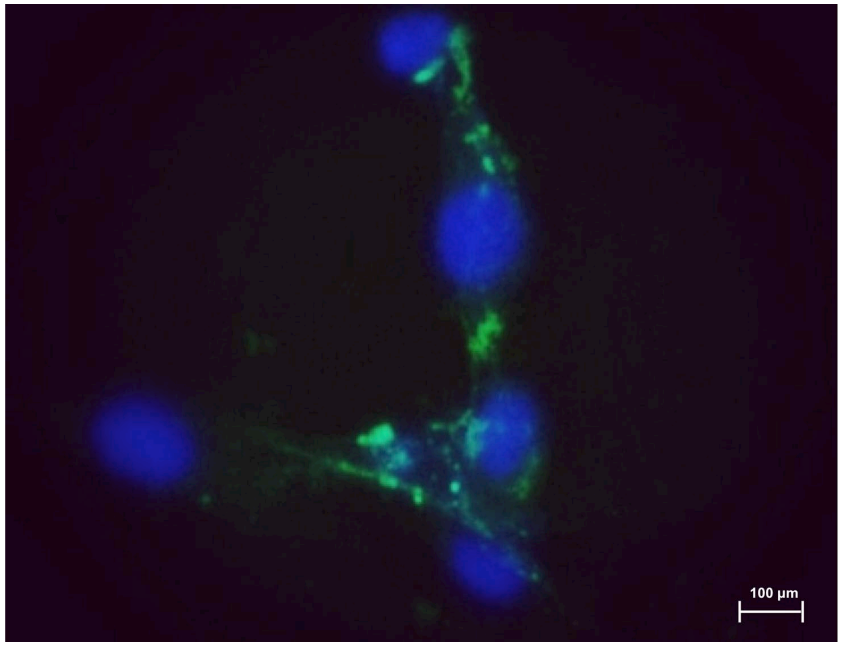
- **Flow citometry**
- **Gene expression**
- **Immunofluorescence**

RESULTS



Surface markers	Non-Crohn		Crohn			
	Mesenteric		Mesenteric		Creeping Fat	
	%	MFI	%	MFI	%	MFI
OVA	86±9.1	7047±316	89.3±15	5296±1720	95±2.2	8318±206
HLA-DR	32,00±5,90	760±50	88,53±3,50*	1988±156*	85,43±5,09*	2087±114*
CD86	1,90±0,29	246±11.7	62,78±7,27*	1267±259*	69,25±4,53*	628±212*
CD34	0,63±0,31	120±19.3	0,91±0,41	260±45	1,15±0,35	224±36
CD45	0,28±0,09	80±15.5	0,52±0,07	1267±259	0,97±0,22	112±17
CD14	0,84±0,23	110±20	3,00±1,41	115±19	2,13±1,37	105±30
CD90	92,60±1,76	25539±1200	97,22±0,95	22939±890	97,70±1,14	26010±1400
CD73	79,90±7,66	5758±298	86,61±4,50	6100±125	85,68±8,00	5900±110
CD36	34,58±7,02	250±25	29,37±6,94	190±30	25,83±9,48	90±45

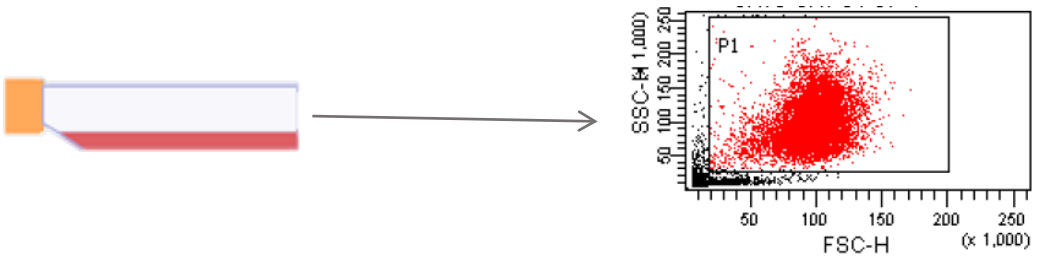
Immunophenotypic profile of human adipose-derived stem cells (ASC). ASC were obtained from ten non-Crohn and Crohn patients and were stained with the panel of antibodies described and analyzed by flow cytometry using the FACS II ARIA cytometer. Values are reported as the mean and SD and were compared with Student's t test.* $p < 0.05$.
MFI: median fluorescence intensity



In blue, nucleus of ASCs. In green, ovalbumin uptake

Representative fluorescent image of OVA uptake by ASCs
OVA:ovalbumin; ASCs:adipose-stem cells

RESULTS



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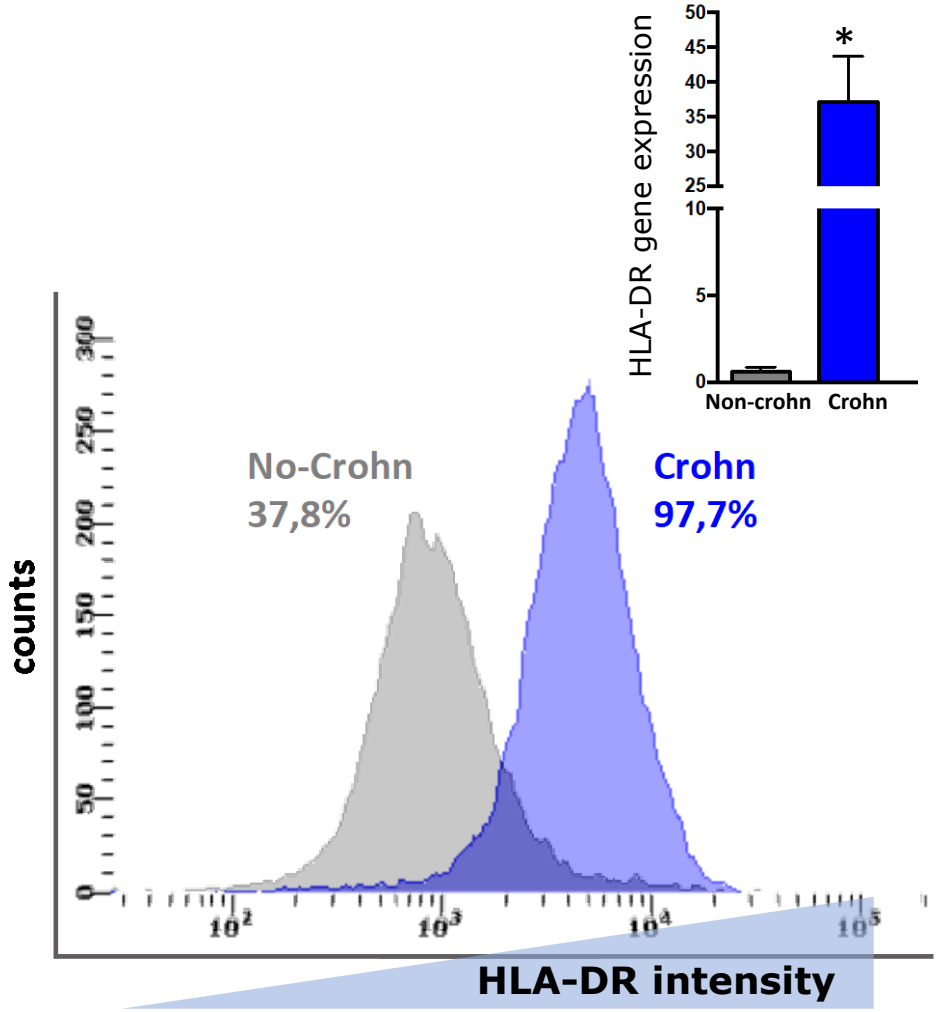
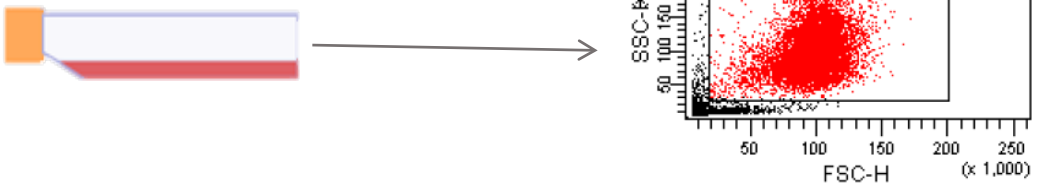


Representative histogram obtained by flow citometry of ASC isolated from non-Crohn and Crohn patients and incubated with HLA-DR.

RESULTS



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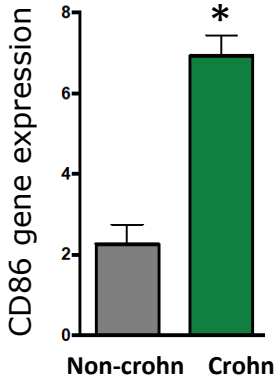
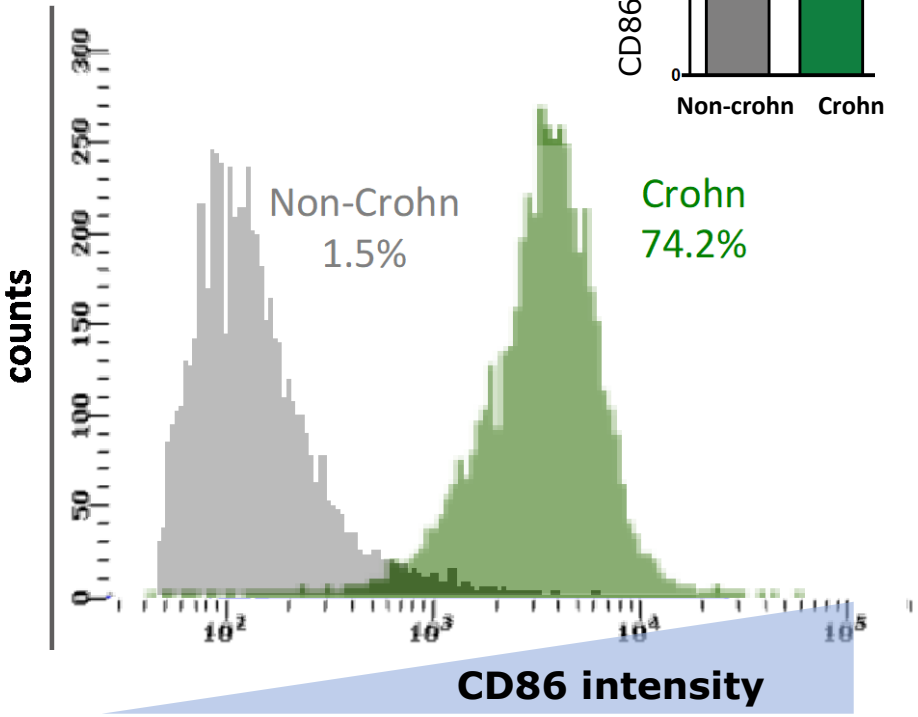
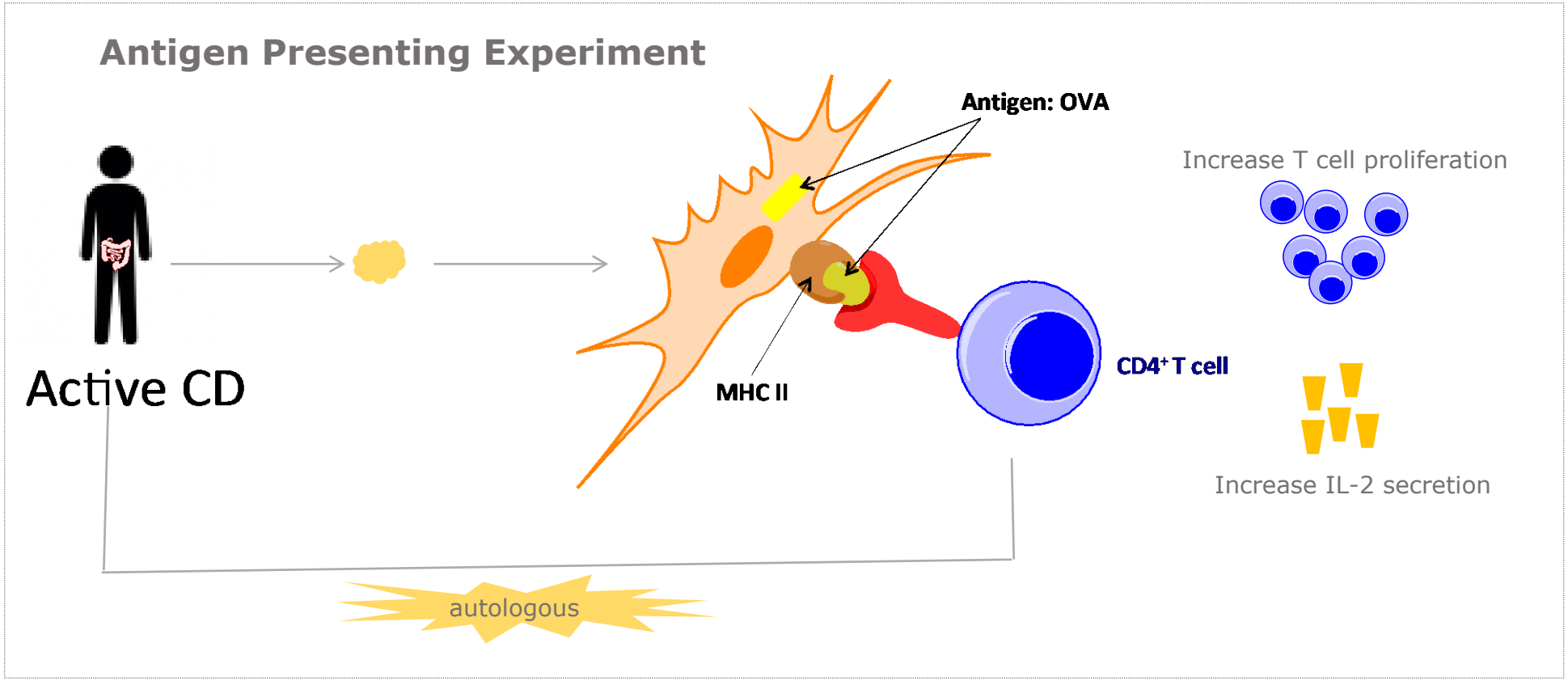


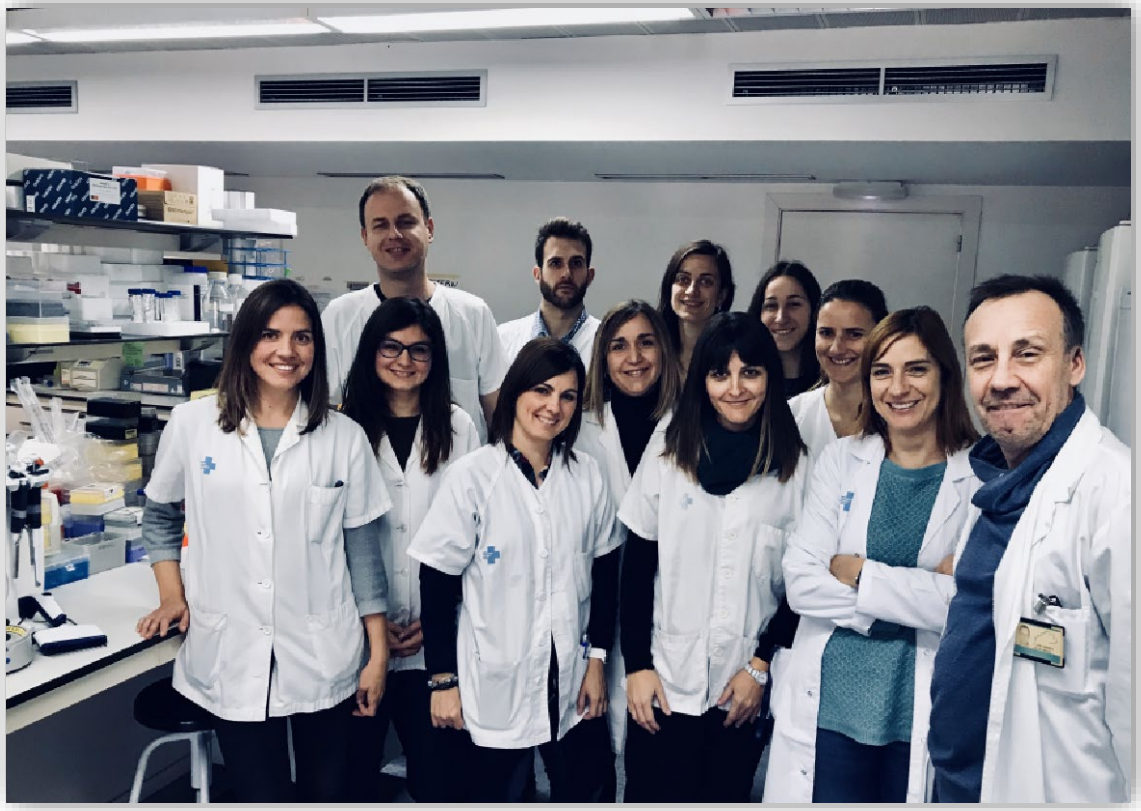


Representative histogram obtained by flow citometry of ASC isolated from non-Crohn and Crohn patients and incubated with CD86.



Adipose stem cells may act as antigen-presenting cell in Crohn's subjects promoting the immune system activation, influencing Crohn's outcome and disease progression.

DIABETES AND METABOLIC ASSOCIATED DISEASES RESEARCH GROUP



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Collaborators:

Vall d'Hebron Hospital

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Universitat de Barcelona

Adipoplast
PLASTICIDAD ADIPOSA Y PATOLOGIAS ASOCIADAS. RED TEMATICA DE EXCELENCIA

Funding:

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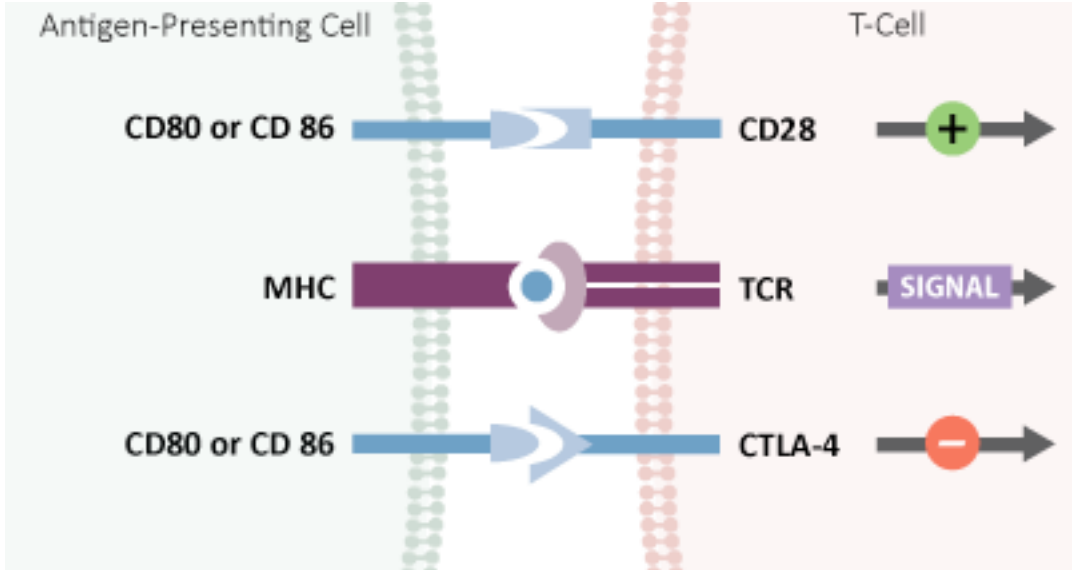
"Una manera de hacer Europa"

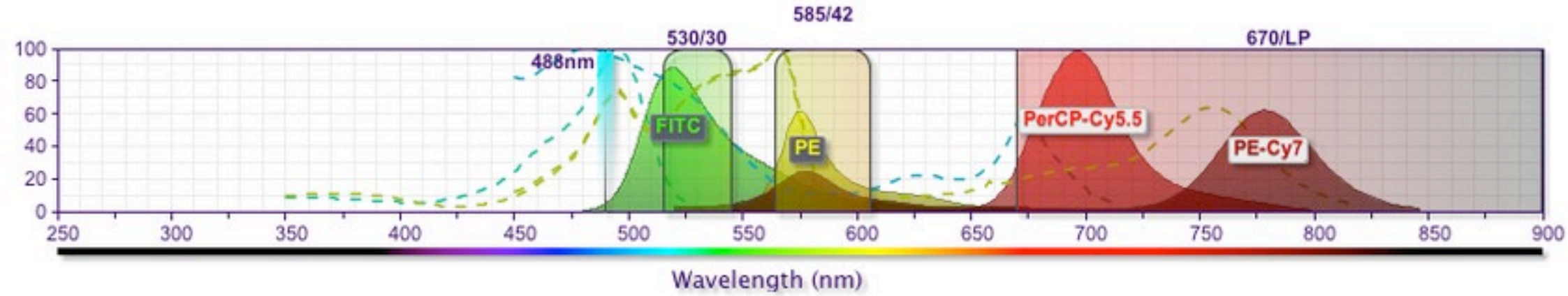
Fondo de Investigación en Salud
Instituto de Salud Carlos III

Fundació La Marató de TV3

European Crohn's and Colitis Organisation

AGAUR
Agència de Gestió d'Ajuts Universitaris i de Recerca


Antigen-Presenting Cell
T-Cell
CD80 or CD 86
CD28
+
MHC
TCR
SIGNAL
CD80 or CD 86
CTLA-4
−



	Fluorochrome	% Max	Ex	Em	Filters	FITC	PE	PerCP-...	PE-Cy7
1	FITC	88.0	☑	☑	530/30	☑	47.0 %	0.6 %	--	--
2	PE	61.6	☑	☑	585/42	☑	26.8 %	70.4 %	--	--
3	PerCP-Cy5.5	98.4	☑	☑	670/LP	☑	--	*3.6 %*	*95.8 %*	--
4	PE-Cy7	61.8	☑	☑	None	☑	--	--	--	--