Induction of Th1 and Th17 cytokines in cultures of circulating CLA+ T cells and epidermal psoriatic cells activated by *Streptococcus* depends on MHC class II and MCHC class I

Marta Ferran[1], Ester R Romeu[2], Marc Sacrista[1], Ana M Giménez-Arnau[1], Antonio Celada[2], Ramon M Pujol[1], Luis F Santamaria-Babi[1,2]

1. Department of Dermatology. Hospital del Mar. Institut Municipal d'Investigació Mèdica (IMIM), Parc de Salut Mar, Barcelona, Spain.
2 Biomedical Research Institute (IRB), Barcelona, Spain, and Department of Fisiologia i Immunologia. Universitat de Barcelona (Spain)

INTRODUCTION

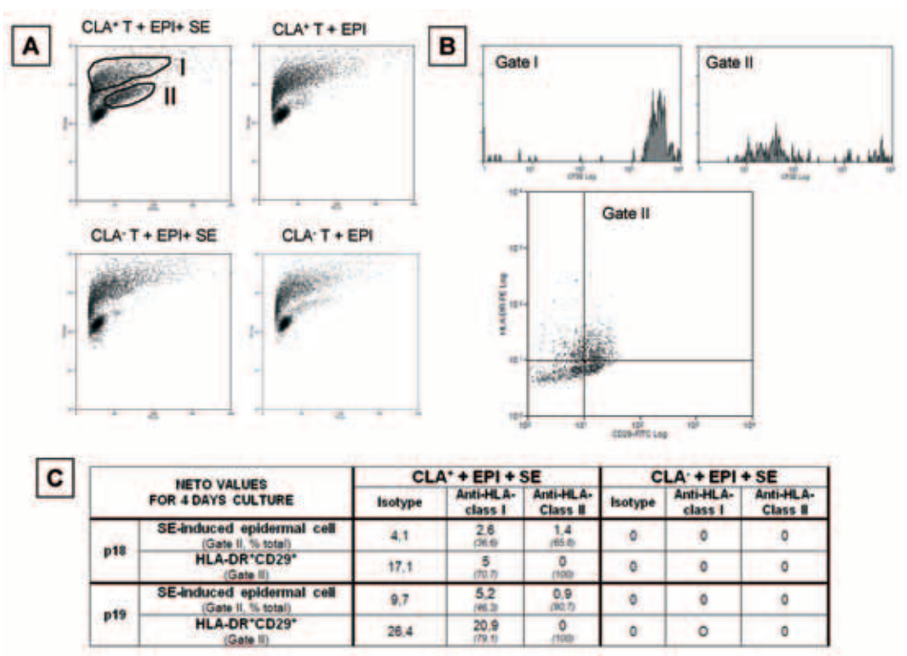
Streptococcus pyogenes infection is associated with the onset of psoriasis; however the mechanisms generating Th17 response and keratinocyte activation/proliferation under such circumstances are poorly characterized due to the lack or relevant models. We have previously shown that *ex vivo* activation of circulating CLA+ T cells and epidermal cells derived from autologous lesional skin with streptococcus extract (SE) induces Th1/Th17 cytokine production together with epidermal cell activation and hyperplasia, in contrast to CLA- from same patients and memory T cells from controls. In this study we have determined the role of MHC class I and MHC class II in our model.

MATERIAL AND METHODS

These results are part of an study (J Invest Dermatology, in press) with 27 non-treated moderate-to-severe psoriasis patients and 6 healthy controls that were enrolled in the study after giving written informed consent. CLA^+/CLA^- $CD45R0^+CD3^+$ were isolated by immunomagnetic separation from peripheral blood and epidermal cell suspensions were obtained from dispase/tryptase treatment of skin punch biopsies. Streptococcal extract was isolated from bacteria from the throat of psoriatic patients.

RESULTS

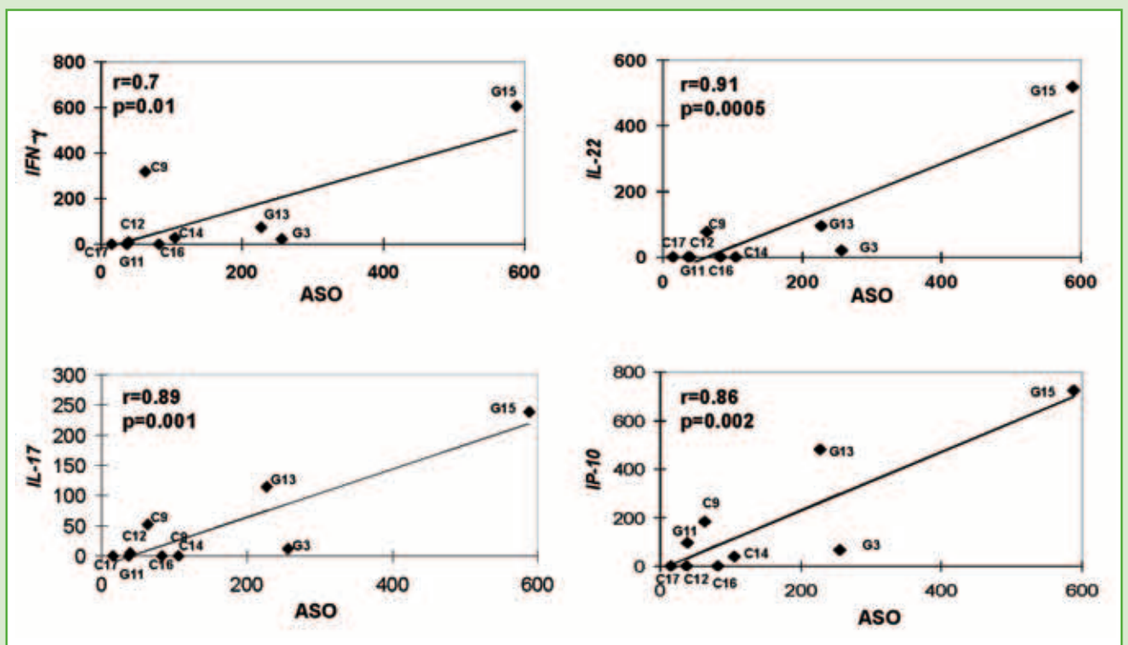
Figure 1. SE together with CLA+ memory T-cells induce proliferation of epidermal cells that express HLA-DR and CD29, and depends on HLA-Class I and Class II interaction



	NETO VALUES FOR 4 DAYS CULTURE	CLA+ + EPI + SE			CLA- + EPI + SE		
		Isotype	Anti-HLA-class I	Anti-HLA-Class II	Isotype	Anti-HLA-class I	Anti-HLA-Class II
p18	SE-induced epidermal cell (Gate II, % total)	4,1	2,6 (36,6)	1,4 (65,6)	0	0	0
	HLA-DR+CD29+ (Gate II)	17,1	5 (70,7)	0 (100)	0	0	0
p19	SE-induced epidermal cell (Gate II, % total)	9,7	5,2 (46,3)	0,9 (90,7)	0	0	0
	HLA-DR+CD29+ (Gate II)	26,4	20,9 (79,1)	0 (100)	0	O	0

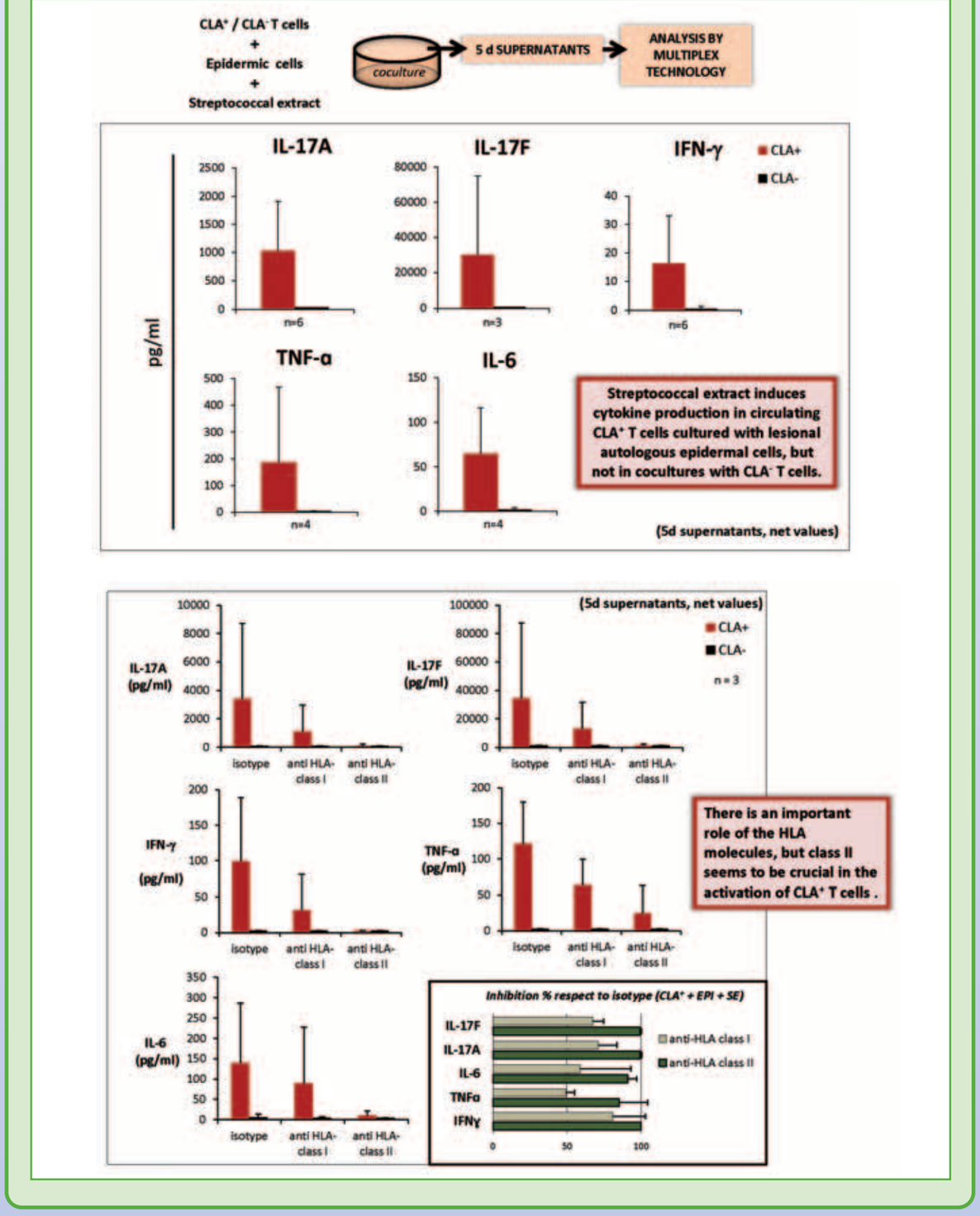
A representative FACS result obtained with a SE-responsive psoriatic patient. In the culture condition with SE together with CLA+ T cell an epidermal cells novel population (II) appears after 4 days of culture (Fig 1A). Such population presents a decrease in CFSE staining c ompared to the main subset of epidermal cells (I) and contains cells expressing CD29 ad HLA-DR (Fig 1B). The induction of population (II) could be inhibited by blocking antibodies against HLA-Class I and Class II (Figa 1C) in two different patients.

Figure 4 SE-induced upregulation in gene transcription for ifn-γ, il-17a, il-22 and ip-10 after 24h of activation of CLA+ memory T cells and epidermal cells correlates with ASO levels in psoriatic patients

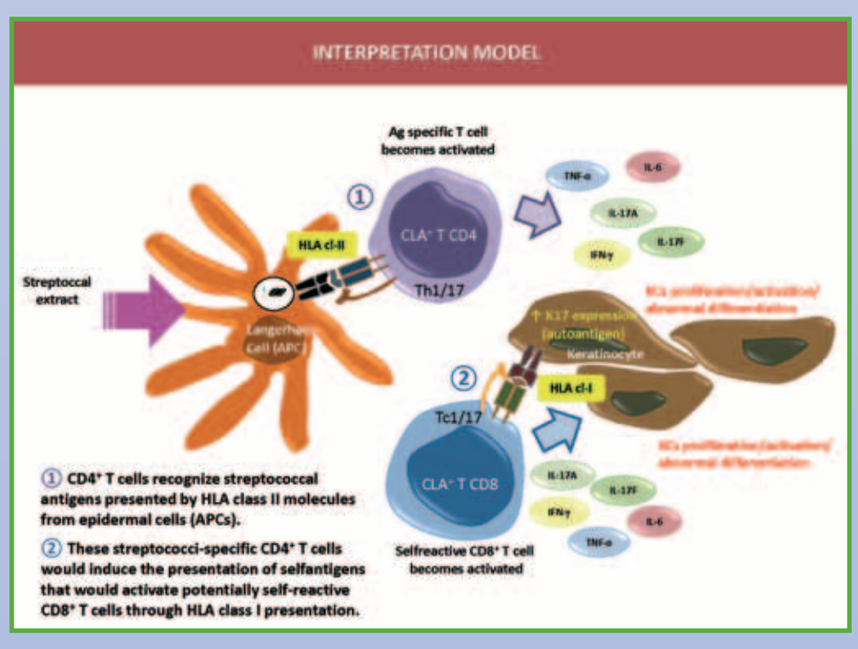


Patients are identified by numbers and psoriasis type (c, chronic; g, guttate).

Figure 2 and Fig. 3. SE induces IL-17A/F, IFN-γ, TNF-α, and IL-6 production that depends on HLA class I and HLA class II in psoriatic CLA+ T cell cultures



Cytokines were measured by multiplex fluorescence bead-based immunoassay in 5 days supernatants. The blockade of MHC class II or class I with specific antibodies reduced the generation of novel basal keratinocytes and cytokine production by 90% and 50%, respectively.



CONCLUSIONS

SE-induced circulating CLA+ effector memory T-cell dependent epidermal cell activation in psoriasis depends on MHC class I and MHC class II.

FUNDING

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Hospital del Mar

Parc de Salut MAR Barcelona