

Increased Th17 inflammatory response to *Streptococcus* and decreased expression of Filaggrin and Loricrin *in vitro* in HLA-Cw*0602 positive compared to HLA-Cw*0602 negative psoriatic patients

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Introduction

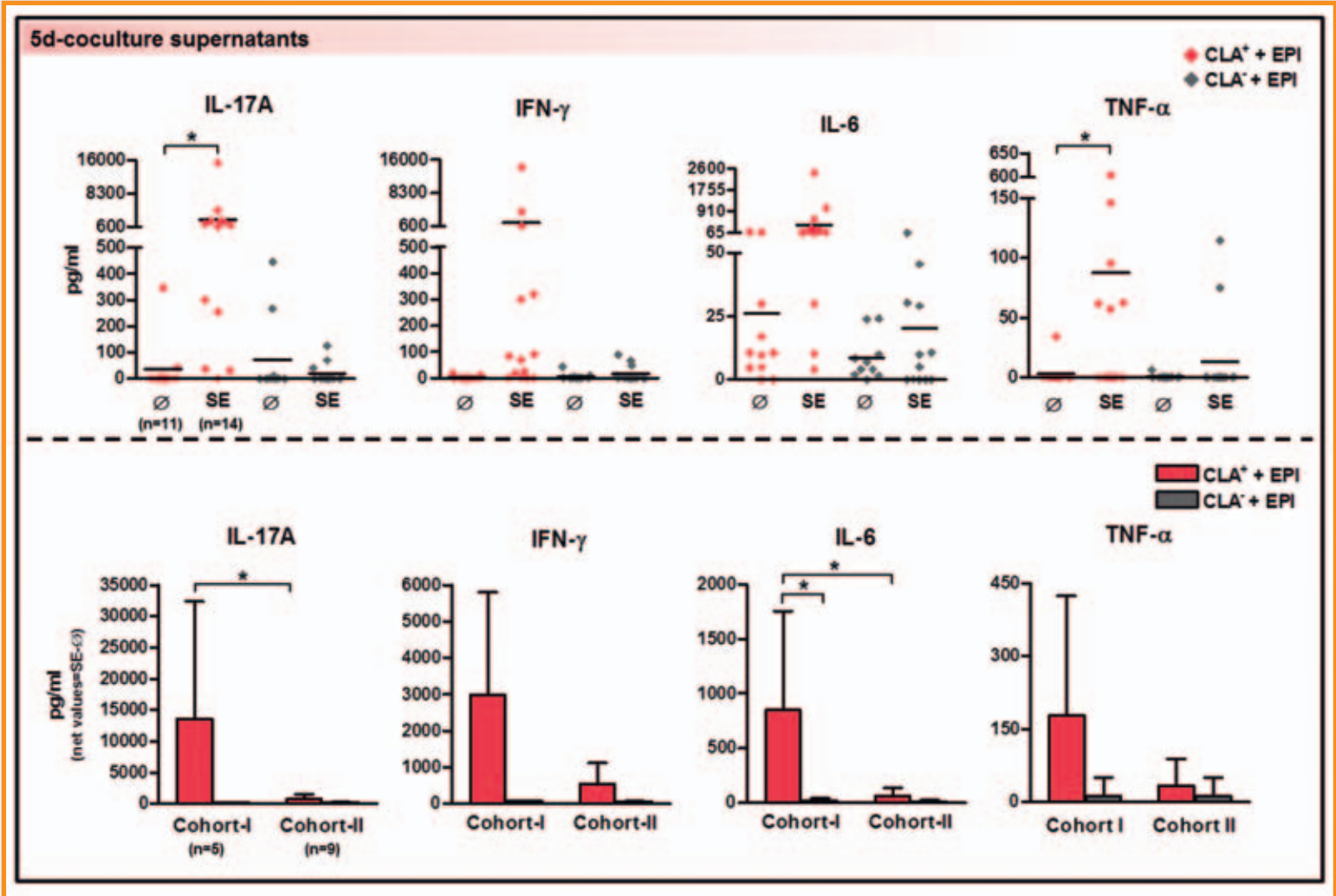
HLA-Cw*0602 positive psoriatic patients present a more severe clinical presentation than HLA-Cw*0602 negative; however the pathological mechanisms behind those differences are not well characterized. We are exploring how a clinically relevant innate stimulus, such as *Streptococcus*, induces psoriatic immune response in *ex vivo* cultures with circulating effector/memory CLA⁺/CLA⁻ T cells and epidermal cells.

Material and methods

These results are part of a study, (M Ferran et al. 2013, *J Invest Dermatol*) with 30 psoriatic patients and 10 controls, from which we have performed additional analysis. Circulating effector/memory-CLA⁺/CLA⁻ T cells from psoriatic patients were cultured together with autologous lesional epidermal cells with or without streptococcal extract (SE), a clinically relevant stimulus in psoriasis. Supernatants were collected at day 5 after the stimuli and were analyzed for relevant cytokines quantification by multiplex immunoassay. Normal keratinocytes were cultured to confluence and then stimulated with 1/10 supernatants from cocultures. mRNA was extracted after 15h of incubation and used for qRT-PCR to evaluate the expression of different genes. Controls did not show cytokine induction.

Results

FIGURE 1.



- A) Streptococcal extract preferentially induces cytokine production in circulating CLA⁺ T cells cultured with lesional autologous epidermal cells.
- B) Cocultures with CLA⁺ T and autologous lesional epidermal cells from psoriatic patients from Cohort-I have a higher cytokine production comparing with patients from Cohort-II.

Patients were grouped in two different cohorts according to three interrelated parameters: **Cohort-I**: presence of the HLA-Cw*0602 allele, guttate type onset and streptococcal throat infection before lesion origin; and **Cohort-II**: patients that lack at least one of them. Net values were calculated subtracting cytokine production of unstimulated conditions (Ø) from those that were stimulated with streptococcal extract (SE). Cohort-I presents a stronger response to SE, being significant for IL-17A and IL-6, which are crucial cytokines in Th17 response.

FIGURE 2. SE stimulated CLA⁺ T + EPI coculture supernatants induce chemokine mRNA upregulation in normal keratinocytes.

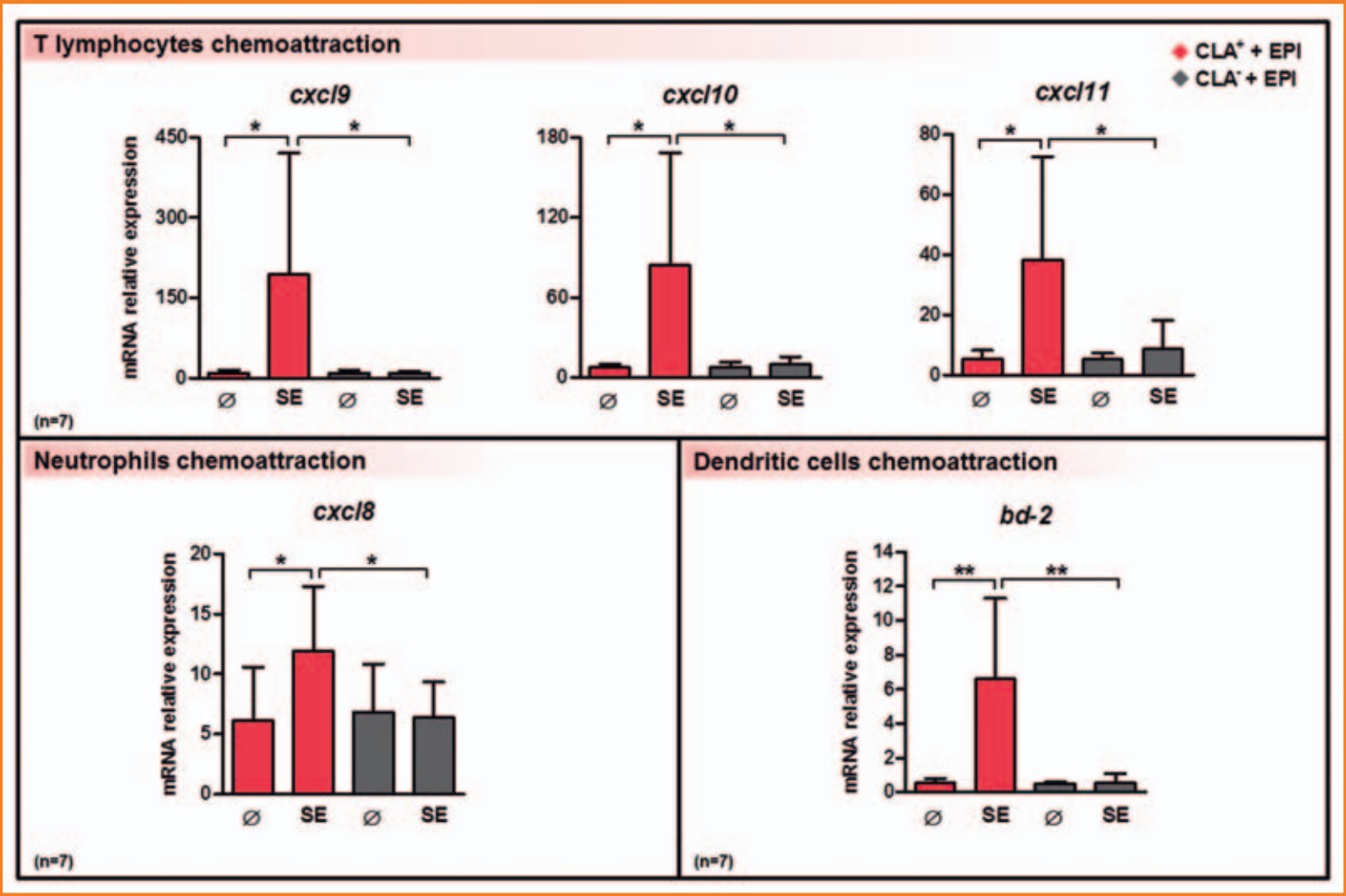


FIGURE 3. Cohort-I coculture supernatants induce downregulation of filaggrin and loricrin mRNA comparing with cohort-II.

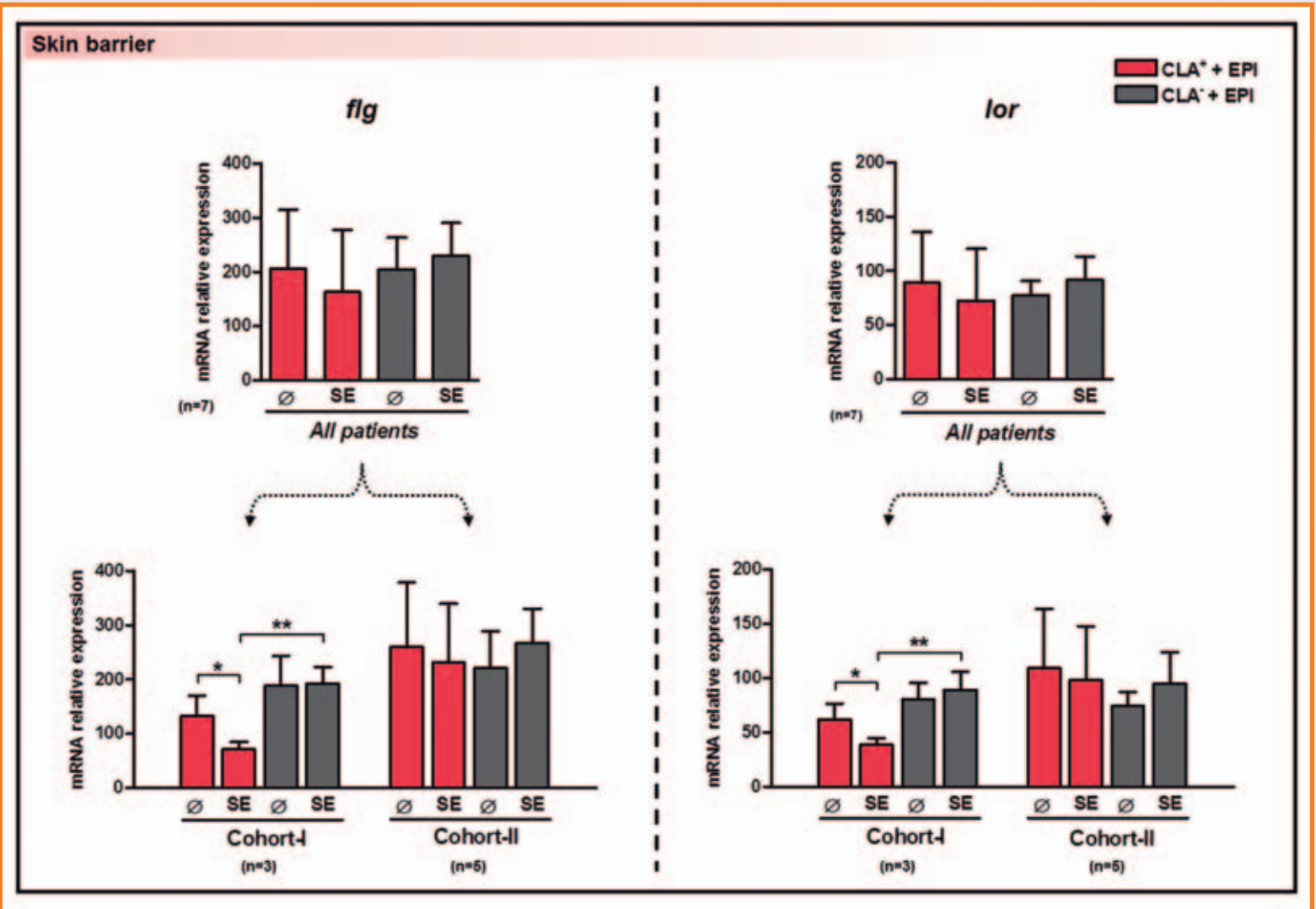
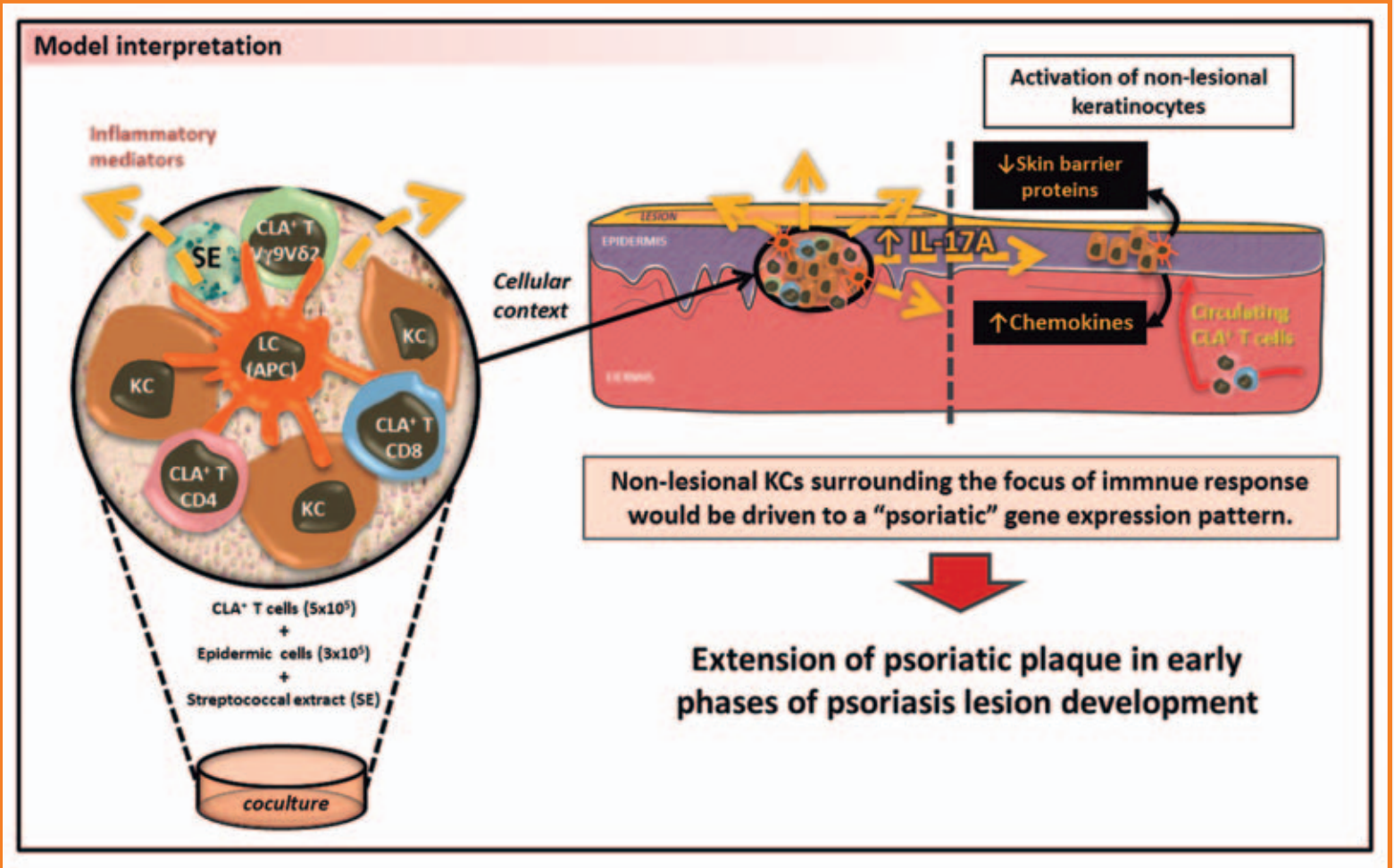


FIGURE 4. Interpretation model.



Conclusions

Cohort-I patients present a more severe spectrum of the disease that would be partly due to the induction of a stronger innate-induced inflammatory Th17 response associated with decreased skin barrier function and subsequent inflammatory amplification by different chemokines and the chemoattractant properties of β -defensin-2.

FUNDING
The study was funded by FIS/ISCIII (Fondo de Investigación Sanitaria ISCIII) 2009.