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P10-13. Increased production of alpha-defensins 1–3 by dendritic cells in HIV-infected individuals is associated with a slower disease progression rate

M Rodriguez-Garcia*, N Climent, H Oliva, C Rovira, L Miralles, A Leon, J Gatell, F Garcia and T Gallart

Address: Immunology, Hospital Clinic, Barcelona, Spain
* Corresponding author

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Background

Defensins are natural peptides with potent anti-HIV activity. In humans two subfamilies exist, α- and β-defensins. α-Defensins 1–3 are mainly secreted by neutrophils, although other leukocytes also produce them. Besides their direct antimicrobial effect, α-defensins 1–3 also exert immunomodulory activities, chemoattracting leukocytes and inducing cytokines and chemokines production. We previously demonstrated that immature monocyte-derived dendritic cells (MDDC produce and secrete α-defensins 1–3 and that these defensins are able to modulate de maturation and differentiation of dendritic cells.

Methods

MDDC were generated *in vitro* from peripheral blood from volunteer healthy controls (HC) and HIV-infected patients, including elite controllers, viremic controllers, untreated viremic noncontrollers and treated patients. To determine α-defensins 1–3 production, culture supernatants were analyzed by ELISA and cells by real time RT-PCR for mRNA expression.

Results

Immature MDDC from HIV-infected patients secreted significantly higher levels of α-defensins 1–3 than HC ($p < 0.0001$). Within the HIV-infected group, this production was statistically increased in untrated HIV-infected controllers ($p < 0.0001$ vs HC) while in untreated viremic and treated HIV-infected patients the production was not significantly increased. The levels of α-defensins 1–3 secreted by immature MDDC positively correlated with CD4 T cell counts in the controllers group ($r = 0.59$; $p < 0.009$), but not in viremic noncontrollers and treated patients. No differences were observed in plasmatic α-defensins 1–3 levels. HIV-infected patients with higher α-defensins 1–3 secretion by immature MDDC showed a slower disease progression, measured as no decrease in the number of CD4+ T-cells below 350 cell/mm3 [HR = 8.9 (CI 1.2–65); $p < 0.035$], fewer increase in plasmatic viral load [HR = 2.67 (CI 1.05–6.74; $p < 0.04$] and no initiation of treatment [HR = 10 (CI 1.02–98.2); $p < 0.05$] along time.

Conclusion

Immature MDDC from HIV-infected patients who spontaneously control the infection produced higher levels of α-defensins 1–3. This increased production of alpha-defensins 1–3 was associated with a slower disease progression.