Lichen planus is an inflammatory disease of the skin and mucous membranes characterized by vacuolization of basal keratinocytes associated with a prominent junctional lymphocyte infiltrate which comprises T lymphocytes, NK cells, myeloid and plasmacytoid dendritic cells. Basal keratinocyte damage is considered as being a consequence of a lymphocytic cytotoxic attack, mostly mediated by perforin+CD8+ T lymphocytes. NK cells have been described to infiltrate inflamed skin and significantly contribute to the amplification of immune-mediated skin diseases, thanks to their cytotoxic activity and the release of pro-inflammatory cytokines. Here, we investigated the characteristics and functional properties of NK lymphocytes involved in lichen planus. Double staining immunohistochemistry showed a considerable number (6.42 ± 2.2% of the total cellular infiltrate) of CD3-CD56+ cells in early lichen planus lesions, mostly distributed in the papillary dermis and at the epidermal-dermal interface. Skin NK cells isolated from lichen planus lesions belong to the CD56highCD16- subset, are highly positive for perforin and natural cytotoxic receptors NKG2D and NKp44, and, in accordance with their phenotype, are negative for KIRs receptors CD158a and CD158b. Skin CD56highCD16- NK cells display a CCR6+CXCR3+CCR5+ChemR23+ chemokine receptor asset for homing into inflamed skin. In terms of cytokine
release, skin CD56highCD16- NK cells are able to secrete IFN-?, TNF-? and hardly release IL-22, IL-17 and IL-4. Overall, our data propose a pro-inflammatory role of NK lymphocytes in lichen planus.