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Human keratinocytes release and respond to danger signals in cutaneous lupus erythematosus.

Lupus erythematosus (LE) is a chronic multisystem disease and cutaneous manifestations belong to the most common clinical features. It was the aim of this study to further decipher the role of keratinocytes in autoinflammation. In immunohistochemistry we found a high expression of inducible HSP70, IL-18R and IL-18 in lesional LE skin. Increased expression of TNFalpha and high mobility group box-1 (HMGB-1) has been described previously. Studies with cultured, patient derived keratinocytes showed that IL-18 stimulation results in significant TNFalpha production in LE derived but not in healthy keratinocytes. Furthermore, we could show that keratinocytes release high levels of HSP70 into the supernatant which was not due to apoptosis. Here we provide evidence, that HSP70-peptide complexes are internalised by keratinocytes and that autoantigenic peptides induce the production of IFNgamma in T cells via this route. Of note, HMGB-1 as well as TNFalpha significantly enhanced the uptake of HSP70 into human primary keratinocytes. In conclusion, we provide evidence that skin resident cells play an active part in maintaining LE inflammation also by means of secretion of molecules which belong to the danger-associated molecular pattern (DAMP) family. This study was supported by DFG grant Wi 1822/5-1.