TNF receptor I on human keratinocytes is a binding partner for staphylococcal protein A resulting in the activation of NF kappa B, AP-1, and downstream gene transcription.

Primary human keratinocytes and immortalized HaCaT cells were analysed for their capacity to bind purified staphylococcal protein A (SpA). Co-incubation with FITC-labelled SpA led to a dose-depending attachment. Pull-down experiments with cellular extracts revealed the TNF? receptor I (TNF RI) as binding partner on keratinocytes. Thus, we next looked for expression of this receptor in human epidermis and cultured keratinocytes. TNF RI is strongly expressed on all keratinocytes analysed, both at the mRNA and protein level and activation by SpA at optimal doses of 50-100 ?g/ml resulted in the phosphorylation of the TNF RI downstream kinases MEK1/2, JNK1/2, and p38 subsequently leading to translocation of the p65 NF kappa B subunit and AP-1 into the nucleus. This translocation was then followed by increased expression of IL-8 and COX-2, two known NF kappa B-induced pro-inflammatory genes. To further test the relevance of our findings, we analysed in vitro production of over 100 strains isolated from atopic eczema showing that more than 85% of the tested strains produced extracellular SpA in substantial amounts. Thus, besides superantigens, haemolysins, and other cell wall components, Staphylococcus aureus exerts pro-inflammatory stimuli on human
keratinocytes through the production of SpA signalling through TNF RI.