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Identification of LL-37 as a Molecular Target for Boswellic Acids

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Gum resin extracts of *Boswellia serrata* have been traditionally applied in folk medicine for the treatment of various inflammatory diseases. Analyses of these extracts identified a group of pentacyclic triterpenes, the boswellic acids (BAs), as active principles that might be responsible for some of the observed anti-inflammatory effects. The molecular background of the beneficial effects of BAs is still incompletely understood. To identify potential new targets of BAs, a target-fishing strategy was established leading to the identification of the antimicrobial peptide LL-37 as a molecular target of BAs. LL-37, a 4.5 kDa peptide, is released from neutrophils after stimulation and, besides its LPS-neutralizing capabilities, is known to be involved in the mediation of several inflammatory responses. Here we demonstrate that the LPS-neutralizing ability of LL-37 is inhibited by BAs in a cell-free assay with EC₅₀ values of 0.2 µM (ABA) and 1 µM (AKBA). Furthermore, supernatants from degranulated neutrophils as well as blood plasma had LPS-neutralizing effects which could be inhibited by addition of BAs as well (ABA: EC₅₀ = 1 µM, AKBA: EC₅₀ = 5 µM). In conclusion, BAs bind to LL-37 which in turn influences the biological activity of LL-37. This effect could contribute to the observed anti-inflammatory actions of BAs.