**Nod1, a cytosolic sensor of the innate immunity.**

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The innate immune system in mammals relies on the specific detection of highly conserved molecules from microbes by several classes of host receptors (pattern recognition molecules, PRMs). Among the well described PRMs are the members of the membrane spanning Toll-like receptor (TLR) as well as the cytosolic Nod-like receptor (NLR) families. TLRs have been extensively studied in the past decade, and a clear picture of the function of each member (10 TLRs in humans) in innate immune detection of microbial products is arising. In contrast, the role of NLRs in the innate immunity is only beginning to be investigated. In our studies, we have identified the bacterial molecular motif recognized by Nod1 as the unique muropeptide from Gram-negative bacterial peptidoglycan: GlcNAc-MurNAc-L-Ala-D-Glu-meso-DAP (GM-triDAP). Furthermore, using *in vitro* and *ex vivo* experimental designs we have investigated the role of Nod1 in the innate immune response to several Gram-negative bacteria (*Shigella flexneri*, *Pseudomonas aeruginosa* and *Helicobacter muridarum*). We have found that Nod1 is involved in clearance of intracellular bacteria through mechanisms that do not involve nitric oxide or oxygen reactive species. Additionally, cells isolated from Nod1 knock-out mice do not activate NF-κB and secrete significantly less pro-inflammatory cytokines in response to bacterial infections when compared to cells isolated from wild-type mice. In contrast, following bacterial infection, Nod1-deficient cells maintain a sustained activation of the MAP kinases Erk, p38 and JNK and produce more IFN-β which, together with the lack of activation of PI3K, is responsible for significantly higher levels of apoptosis in these cells when compared with the type controls. In summary, our results show that Nod1 is a crucial intracellular sensor that detects specifically Gram-negative bacterial peptidoglycan and is involved in the elimination of invading bacteria and protection of the host cells against apoptosis.