The Drosophila genome encodes nine Toll-related receptors (Toll, 18-Wheeler, Toll-3 to –9). Eight of these molecules are more closely related to each other than to mammalian TLRs, suggesting that Toll receptors evolved independently in Insects and mammals. In keeping with this observation, several members of the family exhibit complex and tissue-specific regulation of expression during embryogenesis, and to date only Toll has been assigned an immune-related function in Drosophila. However, Toll functions as a cytokine receptor, and not as a Pattern Recognition Receptor. The ninth member of the family, Toll-9, is more closely related to mammalian TLRs (TLR-1, -2 and –6 in particular) than to the other Drosophila molecules, both in its ectodomain and its intracytoplasmic part. Toll-9 is the only member of the family other than Toll that interacts with DmMyD88. In addition, overexpression of an active version of Toll-9 in transgenic flies leads to activation of the NF-kB-dependent promoter drosomycin. The IRAK kinase homologue Pelle is required for this activation. Therefore, Toll-9 is structurally and functionally related to mammalian TLRs, and understanding its precise function in Drosophila should shed light on the ancestral function of TLRs. The phenotype of Toll-9 mutant flies will be discussed.