

W0255

The Molecular Structure of the Toll-like Receptor 3 Ligand-binding Domain. David Davies, J.K. Bell, I. Botos, P.R. Hall, J. Askins, J. Shiloach, D.M. Segal, NIDDK and NCI, National Institutes of Health, Bethesda, MD 20892-0560.

Innate immunity provides the first line of defense against pathogen attack. Pathogen associated molecular signatures are recognized by the Toll-like receptors which then initiate a rapid host response. The TLRs, of which there are ten human homologs, are of ancient lineage and are germline encoded. We describe the structure of the ectodomain of the first of these TLRs. The molecule forms a large horseshoe consisting of 23 leucine rich repeats together with N- and C-terminal domains. There are 11 N-linked glycans together with two inserts. These results are discussed in terms of potential binding sites for dsRNA, the ligand for TLR3, and models for the mechanism of action.

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