

P025 Identification of the regions of MD-2 and TLR4 that are required for activation of the horse receptor complex by lipid IVA

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There is species variation in the response of TLR4/MD-2 to lipid IVA. A transient transfection system was used to show that horse TLR4/MD-2 signalled in response to lipid IVA, whilst human TLR4/MD-2 did not. TLR4/MD-2 from both species signalled in response to lipid A. Transfection of horse MD-2 with human TLR4, or human MD-2 with horse TLR4, resulted in signalling in response to lipid A, but not lipid IVA, suggesting neither MD-2 nor TLR4 is solely responsible for ligand discrimination. A chimera in which amino acids 59-107 of human MD-2 were replaced by the horse residues signalled in response to lipid IVA with horse, but not human, TLR4. A chimera in which amino acids 57-66 of human MD-2 were replaced by the horse residues was also able to signal in response to lipid IVA with horse TLR4. A TLR4 chimera with leucine rich repeats 14-18 of horse TLR4 replacing the equivalent region of human TLR4 could signal to lipid IVA in association with horse, but not human MD-2. These data suggest that both TLR4 and MD-2 contribute to signalling in response to lipid IVA.