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Targeting TLR9 and TLR21 to develop vaccine adjuvant for different species

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CpG-oligodeoxynucleotides (CpG-ODN) contain potent immune stimulatory activity and are being investigated as vaccine adjuvant and immune modulator in different species. Toll like receptor (TLR) 9 and TLR21 are the cellular receptors of CpG-ODN in mammals and avian species, respectively; whereas fish contain both of these two genes. We comparatively investigated zebrafish zebTLR9 and zebTLR21. They were responding to CpG-ODN but not to ligands for other TLRs. These two TLRs have distinct CpG-ODN recognition profile, which was determined by their ectodomain. The zebTLR9 broadly recognized CpG-ODN with different CpG motifs but CpG-ODN with GACGTT or AACGTT had better activity. In contrast, zebTLR21 responded more preferentially to CpG-ODN with GTCGTT motifs. We also investigated the ligand recognition of rabbit TLR9 (rabTLR9). The CpG-ODN with 18-24 deoxynucleotides that are in current use for human and mouse cells have low activity with rabbit TLR9. We developed a type of CpG-ODN containing a GACGTT or AACGTT motif in 12 phosphorothioate modified deoxynucleotides with potent stimulatory activity for rabTLR9. The developed CpG-ODN has higher activities than other current developed CpG-ODN in eliciting antigen non specific immune responses in rabbit cells. In addition, they are more potent as an adjuvant in boosting antigen-specific immune responses in rabbits. The results of this study suggest that TLR9 and TLR21 have different CpG-ODN sequence recognition profile. Moreover, both the choice of CpG-motif and its length are important factors for CpG-ODN to effectively activate immune responses in different species.

Biography

Tsung-Hsien Chuang has obtained his PhD degree from Iowa State University and Postdoctoral studies from the Scripps Research in La Jolla, California. His research interest is mainly focused on the molecular mechanism for control of TLR activations and targeting TLRs and their signaling for development of immune modulator. He has published more than 50 papers in reputed journals.

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