INCREASED PROTECTIVE IMMUNE RESPONSES WHEN COMBINING TLR-AGONISTS IN A WHOLE-VIRUS ANTIGEN VACCINE AGAINST SALMONID ALPHAVIRUS

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CpG oligonucleotides and polyinosinic:polycytidylic acid (poly I:C) are toll-like receptor (TLR) agonists that mimic the immunostimulatory properties of bacterial DNA and double-stranded viral RNA respectively, and which has exhibited potential to serve as vaccine adjuvants in previous experiments. Most studies assessing the immune effects of TLRs have focused on activation of a single TLR, however evidence is accumulating that activation of multiple TLRs can result in complimentary, or synergistic effects, which is also interesting related to the development of adjuvants for fish vaccines. In the current work a combination of CpGs and poly I:C together with water- or oil-formulated *Salmonid Alphavirus* (SAV) antigen preparations has been tested in an SAV challenge trial in Atlantic salmon. The results demonstrate that vaccination with a high dose of the SAV antigen induced protection against challenge with SAV which correlated with production of neutralizing antibodies (NAbs). At the high dose no beneficial effect of the TLR agonist were detected. However the addition of CpG and poly I:C to a low SAV antigen dose formulation significantly enhanced the protection against SAV suggesting that CpG/poly I:C may cause a dose sparing effect. Furthermore, the TLR ligands significantly enhanced the levels of NAbs in serum of vaccinated fish and were the only vaccination group where a significant increase in Nabs was detected prior to challenge. Interestingly, gene expression analysis demonstrated that while addition of oil suppressed the CpG/poly I:C-induced expression of IFN-γ, the upregulation of IFNa1 was substantially enhanced.