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Antiviral immunity in fish – functional analysis using DNA vaccination as a tool

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In fish, DNA vaccines encoding the glycoproteins (G proteins) of the salmonid rhabdoviruses VHSV and IHNV have proved very efficient under experimental conditions. Nano-gram amounts of plasmid DNA can induce long-lasting protective immunity when delivered by intramuscular injection in rainbow trout fingerlings. Vaccination of fish at an early stage appears advantageous, since larger fish require higher doses of vaccine to be protected. Even in fish with an average size of 0.5 g at the time of vaccination, good protection can be obtained. Interestingly, immunity is established already a few days after vaccination and cross-challenge experiments have revealed that protection in the early phase is non-specific. Later on, protection becomes very specific in terms of virus species. The protection in the early non-specific phase is related to interferon induced defence mechanisms whereas specific antibodies and cellular components both play a role in the long lasting protection. The similarity of the functional immune response profile to that induced by a natural virus infection is striking and is most likely one of the major reasons for the efficacy of the rhabdovirus DNA vaccines. Although other elements like CpG motifs in the plasmid backbone sequence might play a role, the viral G protein appears to have an inherent ability to stimulate innate immune mechanisms by receptors and pathways that still remain to be characterized in detail. Immunity to VHS in rainbow trout can be induced by DNA vaccination across a temperature range of at least 5-15°C. Interestingly, the initial non-specific phase is significantly prolonged at lower temperatures, hereby ensuring protection despite a slow activation of adaptive mechanisms. Expression of the rhabdovirus G protein on the surface of transfected muscle cells induces a histologically visible local inflammatory reaction with higher doses of VHSV G DNA vaccine. Cell surface expression may be important for a proper activation of the fish immune system, since blocking of the intracellular trafficking of the expressed glycoprotein G-gene interferes with protection. It may be anticipated that the viral G protein acts like a PAMP (pathogen associated molecular pattern), but it remains to be determined which PRRs (pattern recognition receptors) that may be involved in the recognition of the G protein. Recent data from DNA vaccination trials with variant forms of the G protein gene suggest that the structural requirements for antigenicity are different from the requirements for immunogenicity.

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