**Abstract.** The self-amplifying nature of viral-encoded RNA-dependent RNA polymerases (RdRp) holds promise in the development of a platform for self-amplifying RNA gene delivery. To protect and assist in uptake of mRNA encoding an RdRp (in our case using RNA1 of insect Nodamura virus) coupled to a gene of interest, plant virus-like-particles (VLPs) are a strong candidate. Cowpea chlorotic mottle virus (CCMV) capsid protein has been shown to be able to package in vitro heterologous mRNAs, and also to make the genes available to mammalian cells.

To better characterize the uptake and amplification in mammalian cells of RdRp-associated genes both when naked or encapsidated, reporter genes such as enhanced yellow fluorescent protein (EYFP) or luciferase may be used. This gene delivery system would offer the advantages of avoiding alteration of host genomes, inducing relatively early cytosolic translation and amplification of the gene of interest, and protecting normally vulnerable RNA from degradation.

In collaboration with the German pharmaceutical company Boehringer Ingelheim (B-I), evaluation of possible efficacy of this platform for a cancer vaccine was explored by incorporation of a model antigen (Ovalbumin epitope, SIINFEKL) sequence into the RNA1 (also called a replicon, because of its self-amplifying nature). From in vitro studies involving incubation of OVA-replicon-VLPs, we observed that CCMV VLPs can be taken up by dendritic cells, where replication then occurs to promote increased production of antigen. When these VLPs are injected into mice, there does result a population of SIINFEKL-specific CD8+ (cytotoxic) T cells.

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from

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