Fusion of HCV non-structural antigen to MHC Class II associated invariant chain enhances T cell responses induced by vectored vaccines in non-human primates

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Developing a vaccine against hepatitis C virus (HCV) infection is an important medical priority. Induction of robust T cell responses could provide effective immune control. We have previously shown that adenovirus-vaccine encoding non-structural (NS) HCV proteins induce potent T-cell responses and efficacy studies in chimpanzees demonstrate that these responses can be protective against challenge. Our phase I trial based on prime/boost with a simian Adenoviral (ChAd3) and MVA expressing the HCV-NS antigen has demonstrated that this vaccine strategy is safe and highly immunogenic. However, even higher T cell responses might be required to achieve efficacy in at risk populations and to exert a therapeutic effect in chronically infected HCV patients.

In this study we assessed fusion of the HCV NS antigen to murine and human MHC Class II associated invariant chain (li) expressed by viral vaccine vectors for its ability to increase the induced T cell response in mice and non-human primates (NHP). A dramatic increase was observed in CD1 outbred mice where vaccination with ChAd3 expressing the fusion antigen resulted in a 10-fold increase in IFN-γ producing CD8⁺ T cells. In NHP CD8⁺ T cell responses were enhanced and accelerated with vectors encoding the antigen fused to the human or murine li. Further experiments are underway to elucidate the adjuvant mechanism of li.

These data showed for the first time that the enhancement induced by vector vaccines encoding antigen fused to li was not species-specific and translated from mice to non-human primates opening the way for testing in humans.