Retrovirology

Poster presentation

P12-07. Novel HIV vaccines using chimeric influenza HA vectors

DA Steinhauer*, WA Langley, G Talekar and Z Li

Address: Microbiology and Immunology, Emory University School of Medicine, Atlanta, GA, USA
* Corresponding author

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Background

Influenza viruses containing chimeric hemagglutinin (HA) glycoproteins with large foreign polypeptide insertions are being examined as a novel vaccine vectors. Our initial studies involved polypeptide insertions derived from the *Bacillus anthracis* protective antigen (PA), and showed that the entire140 amino acid receptor binding domain of PA could be incorporated into functional chimeric PA/HA proteins. These were engineered into infectious influenza viruses by reverse genetics, and the resulting viruses displayed replication properties similar to WT influenza virus. Using a mouse model, we examined the induction of antibody responses using heterologous prime/boost strategies with a variety of PA vectors (influenza, vaccinia, rabies, cDNA), and we found that strategies involving initial priming with the influenza vector resulted in anti-PA serum antibody titers that were 10-fold higher than alternative regimes. These sera displayed *in vitro* neutralization titers against anthrax toxin that were remarkably high, >10-fold greater than values considered to be neutralization positive, and animal protection experiments are currently underway.

Methods

Using similar strategies, chimeric HIV Env/influenza HA proteins have been generated, functionally characterized, incorporated into influenza viruses by reverse genetics, analyzed for replication properties, and used as immunogens.

Results

We have generated functional chimeric HA proteins with insertions of the Env protein as large as 250 amino acids. ELISA data suggest that some of these expressed chimeric Env/HA glycoproteins can be recognized by the anti-Env neutralizing antibodies 2G12 and 447-52D, and the chimeric proteins have been incorporated into influenza viruses that replicate to titers within one log of WT influenza. Inserts are stable upon passage, and will initially be evaluated as immunogens in mice.

Conclusion

It is possible to generate efficiently replicating influenza viruses with chimeric hemagglutinin proteins that contain insertions of up to 250 residues of HIV Env proteins to evaluate as vaccine candidates.