

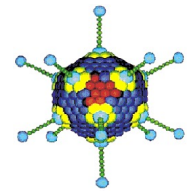
A Novel Vaccine against Capsular Group B Meningococcal Disease Based on an Adenoviral Vector: Preclinical Development, Evaluation and Optimization for Clinical Development

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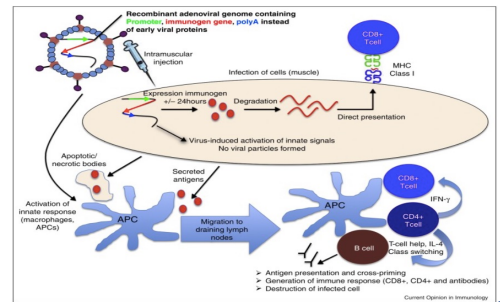
1. Introduction: Replication-deficient adenoviral vectors

- Expression of target protein in host cells
- Induction of antibody and cellular responses (three COVID-19 vaccines)
- Supports functional antibody responses (intrinsic adjuvant effect)
- Potential for expression of a bacterial antigen? Group B meningococcal vaccine?



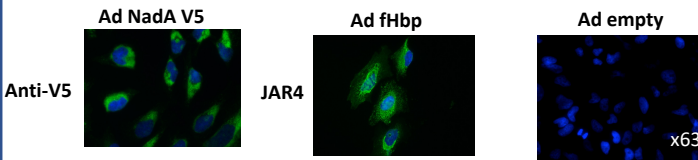
2. Methods: Construction and evaluation of vaccines

- Insertion of group B meningococcal target antigens NadA or fHbp, package into Adenovirus → antigen expression ?
- Point mutations in fHbp gene (2 versions, M1 and M2) → abrogate binding to human factor H ?
- Immunogenicity in mouse → Serum bactericidal antibody responses in presence of human fH ?



3. Results: Confirm antigen expression

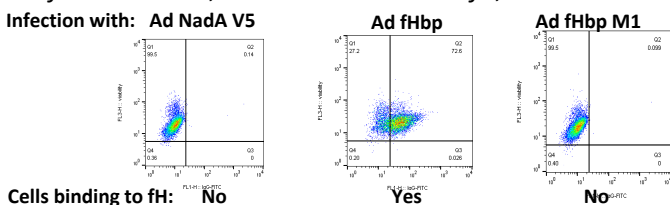
Infect HeLa cells – detection with monoclonal antibody



NadA and fHbp are expressed in target cells

4. Results: mutated fHbp does not bind fH

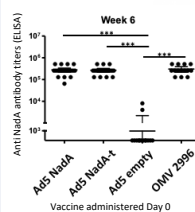
Infect HeLa cells, Incubate with human fH, detect bound hfH



Mutation in fHbp abrogates binding to fH
Same result with mutation M2 (not shown)

5. Results: Immunogenicity in mice

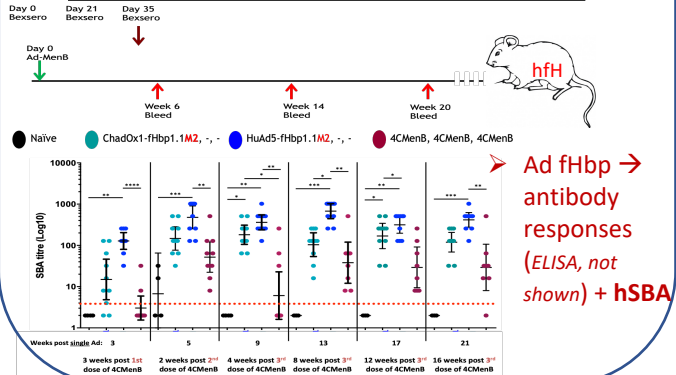
Antibody responses?
ELISA, hSBA



Immunization with Ad NadA

- Ad NadA induces antibody responses (ELISA) but **NO** hSBA (<1:4, data not shown)

Immunization with Ad fHbp M1 or Ad fHbp M2



➤ Ad fHbp → antibody responses (ELISA, not shown) + hSBA

6. Conclusions

- fHbp can be incorporated in Ad, resulting in immunogenic vaccine with functional antibodies → clinical development

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