

TOPIC #3: Status of HIV Vaccine Development

Background:

For over 20 years, attempts to develop an efficacious vaccine against HIV have largely failed. While a number of these vaccine candidates have induced antibody responses against HIV proteins, and some have induced T-cell responses, these have not been demonstrated to be protective in human clinical trials. Two recent attempts, the “Thai Trial” and the “STEP Trial” (see starter refs below) highlight some of the difficulties.

Discuss the strategies used in both the Thailand Trial and the STEP trial. How did the vaccine approaches differ? Describe the levels (and type) of immunity produced by each vaccine. What are the encouraging and discouraging messages from these studies? What do you think are the key hurdles to be overcome in developing an effective prophylactic vaccine against HIV?

Starter References

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<http://www.nature.com/nm/journal/v17/n3/full/nm.2316.html>

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<http://www.nejm.org/doi/full/10.1056/NEJMoa0908492>

Margaret I. Johnston, Ph.D., and Anthony S. Fauci, M.D. An HIV Vaccine — Challenges and Prospects. *N Engl J Med* 2008; 359:888-890. August 28, 2008

<http://www.nejm.org/doi/full/10.1056/NEJMp0806162>

<http://www.twiv.tv/2009/09/27/alvac-hiv-and-aidsvox-be/>

Review Points:

Because of the nature of small group discussions, we expect (and hope) that each group will cover slightly different aspects of each topic. In order to make sure that key aspects of each topic are covered by all groups, please make sure that the discussions in your group includes the following points. It is from these points that exam questions will be drawn.

- Know the composition of the vaccines and the difference in the two strategies used.

What is a “prime-boost” vaccine?

- Why was the STEP trial halted? What was the unexpected genetic outcome observed in the viruses isolated from the STEP trial participants?

- Why is simply inducing an antibody response against HIV proteins not protective? What is a neutralizing antibody? Are there any neutralizing antibodies against HIV?

Discuss the role of inflammatory responses in potentially promoting HIV infection. Specifically, evidence relating to why HSV-2 infections increase the risk of contracting HIV.