Many of our readers have been curious about the status of Dr. Harvey Friedman's (University of Pennsylvania) trivalent sub-unit herpes vaccine, given the recent disappointment of Genocea's GEN-003 vaccine candidate (1).

In my interview with him, Dr. Friedman addresses many of these questions:

JB: This past January you published a paper [2] in PLOS Pathogens which discussed the immunological response of rhesus monkeys and guinea pigs to your trivalent HSV vaccine. At the time you said, “I really do think this is more promising than other vaccine research out there. I've never seen anything published that comes close to our efficacy.”

Has anything happened since that would lead you to change your mind? What can you tell us?

HF: We have continued to evaluate our subunit trivalent herpes vaccine (THV) in animal models, and I am pleased with what we've seen. There are some technological hurdles that we are addressing, but I am confident that the THV will elicit a sufficient immune response in animals to warrant clinical trials in uninfected people to prevent genital herpes infection.

JB: Can you tell us about the animal models of the infection? What are their strengths and weaknesses? Are they predictive of efficacy in humans?

HF: The primary animal models of herpes simplex virus (HSV) infection, mice, and guinea pigs, are a useful guide as to what to expect in people, but vaccines that have looked effective in animal models have failed in humans. These animal models can, depending on the particular animal, give
us information about the type and magnitude of immune response to a given vaccine, which makes them useful in fine tuning the vaccine, but this may or may not be effective in humans, I would say that the models are not great.

**JB:** Genocea suspended development of its GEN-003 last month. Were you surprised? Do you have any thoughts on why 003 didn’t work? Is a subunit vaccine a feasible approach?

**HF:** GEN-003 did work, but not well enough. This may be due to the company’s choice of proteins in the vaccine. There are many proteins involved in eliciting an immune response. GEN-003 possibly failed because they chose the wrong proteins or not enough different ones. I do believe that a subunit [synthetic vaccine] vaccine is a viable option, but its success depends entirely upon the choice of proteins in the vaccine. The failure of 003 does not mean that a subunit vaccine cannot work. On the contrary, I believe that ours in combination with a strategy “Prime and Pull” will perform better because of the approach we have chosen.

**JB:** Can you compare, if only qualitatively, the difference in the efficacy of 003 and your trivalent vaccine in animal models?

**HF:** In guinea pigs the two perform similarly.

**JB:** Can you comment on the advantages and disadvantages of subunit vs. live attenuated vaccines?

**HF:** Live attenuated vaccines contain many more proteins than subunit vaccines, so they are perhaps more likely to be effective. But, this can be at the expense of safety. Live attenuated vaccines can (rarely) cause infection. Subunit vaccines cannot.

**JB:** What is your strategy going forward? Will you be looking for a therapeutic vaccine or one that is prophylactic?

**HF:** Our [THV] is intended for prevention, not treatment, of herpes simplex. Our goal is to attain what we call "sterilizing immunity," which means that the vaccine would prevent lesions and any indication of infection, including silent or subclinical shedding of virus and latency in vaccinating individuals.

**JB:** Why not try [THV] as a therapy as well?

**HF:** Right now, I don't believe that the vaccine would work well enough to be therapeutic. However, we are addressing this. My colleague and collaborator at Yale, Dr. Akiko Iwasaki, is working on an approach we call "Prime and Pull". This research, which is funded by the NIH, would make it possible for the vaccine to also be therapeutic, which is a higher bar to attain. Dr. Iwasaki's approach is to draw out the immune cells to the genital tissues to make the T-cell [one of the components of the immune system] response stronger.

**JB:** Can you describe your timing to get your vaccine into human volunteers for safety studies?

**HF:** We are expecting to begin human safety trials in about 18 months.

**JB:** Can you provide details?

**HF:** Not really. The University of Pennsylvania is in negotiations with a biotechnology company
that we hope will lead to funding for human trials. Recently, negotiations fell through with another major drug company; however, the company may be able to proceed without my lab’s or Penn’s involvement. This is personally disappointing, but it is more important to get the vaccine into people. If I have to step aside to allow this to happen, so be it.

JB: Rational Vaccines has recently been involved in a controversy about its decision to bypass the FDA and run trials in the Caribbean and Mexico. Depending on who you speak to, the company's strategy is either innovative or reckless and dangerous. Can you comment on Rational's plans?

HF: I can understand why Dr. Halford wanted to take this route since it is quick and he was dying. There are obviously concerns about such a strategy, especially safety. But in this case, the major concern, that people would become infected with herpes, is a moot point, since all of the volunteers were already infected. That said, I still believe that it is better for drug and vaccine developers to stay within the system. It is safer for our subjects that way.

Impression: I’m sorry to report that those of you who are infected and have been awaiting a therapeutic vaccine to treat your genital herpes will not find relief from Friedman's group right away. However, there is ongoing work looking to make it possible for the vaccine to treat, as well as prevent, herpes. If all goes well in guinea pig experiments the vaccine could be in humans in 18 months.

Notes:

(1) See "Bombs Away: Genocea's Herpes Vaccine Goes Down In Flames" [3]."