On Saturday, October 19, 2013 5:00 PM, [REDACTED] wrote:

Oh I see. Im sorry as I didnt even think about you not having it and I know you are probably correct about it being cross protective too.

ok. Ill see you in two weeks. :) 

On Saturday, October 19, 2013 4:42 PM, "whalford@siumed.edu" <whalford@siumed.edu> wrote:

Hi [REDACTED]

Regarding the ICP4 in the Genoea vaccine, I do not personally think that ICP4 is a great antigen. If I had to pick one HSV protein to use in my vaccine, this one would be low on my priority list; I can think of at least 20 HSV-2 proteins that are better candidate immunogens / antigens.

Regarding your next immunization, let's stick with HSV-2 for two reasons. First, the HSV-2 vaccine should be very highly cross-protective against HSV-1, so there is really no reason at this juncture to assume that it would not elicit protection against HSV-1. Second, I spent 2008 to now developing a data set that says the particular HSV-2 mutant virus I am using would be safe and highly protective, I simply don't have a HSV-1 ICP0 mutant virus that has been similarly vetted in the same way. It would take me at least a year or two (assuming I had funding) to catch up on the HSV-1 side, so I will be sticking with what I have for now.

See you in a couple of weeks.

- Bill

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Quoting [REDACTED]

> Thanks for the info. Some how I didn't think it would increase 10 fold every time. I couldn't help notice that the Genoea vaccine had a > 10 fold increase in ICP4 antigen without the adjuvent and that got me > thinking about things.
> 
> Anyway, I was also wondering if you'd be interested it testing the > hsv-1 version on me. Maybe get my hsv-2 booster in 1 leg and the
> hsv-1 version in the other. Or I could return later just for the
> hsv-1 if thats better.
> Looks like I will be driving again and thats fine. I wont have to
> worry about getting off work in time to make it to the airport.
> 
> On Saturday, October 19, 2013 10:42 AM, "whalford@siumed.edu"
> <whalford@siumed.edu> wrote:
> 
> October 19, 2013
> Hi
> I am finally out from under my latest grant-writing binge, and
> have a moment
> to breathe before I start into the next writing project.
> 
> I answer your questions below.
> 
> - Bill
> 
> 1. Regarding your first question, a 10-fold increase in T-cells specific for
> HSV-1 would almost certainly be a significant (i.e., real) increase.
> 
> 2. Your second question was....."Would a vaccine capable of doing that
> (eliciting a 10-fold increase in HSV-1-specific T-cells) do that every time?
> 
> No. The most profound change in HSV-specific T-cell number would like happen
> after the first vaccination, where the number of HSV-specific T cells
> that were
> functionally useful (i.e., active, awake, differentiated) would increase from
> somewhere close to 0 (1 per 1 million T cells) to a low, but
> significant number
> like 1 per 100,000 T cells.....that's a 10-fold increase in absolute T-cell
> frequency but is still too few to provide very good protection against HSV-1.
> 
> Perhaps on a secondary booster vaccination (3-6 weeks later) you might get
> another 10-fold increase in HSV-specific T-cell frequency, bring you up to a
> useful number of virus-specific T cells in the bloodstream (about 1
> per 10,000
> T-cells).
Subsequent shots, 3rd, 4th, 5th, etc. would serve to keep these
HSV-specific T
cells active (awake, not in a coma, differentiated, available to
engage in the
game, etc), but the ceiling on the absolute number of HSV-specific T cells
someone could have in their bloodstream would be about 1 per
1,000.....we need
T-cells to do other things than just beat back HSV (e.g., Staph, Strep, CMV,
EBV, gut bacteria, lung bacteria, etc, etc). So, painting broad
brushstrokes,
the goal of a good HSV-vaccine is to get your bloodstream levels of
HSV-specific T-cells into the realm of 1 per 1,000 to 1 per 10,000 (0.1% -
0.01%).

Two vaccinations with a good HSV vaccine is adequate to get you most of
the way
there, and subsequent booster vaccinations would serve only to keep your
HSV-specific T-cells awake / on active duty.

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3. The third important point that you did not ask, but I will bring up
because
it is important relates to the concept of "antigenic breadth." What
this means
is that a given T-cell clone recognizes about 8- to 25-amino acids of
HSV-1 or
HSV-2, but in total these viruses encode 40,000 amino acids worth of viral
proteins. For a vaccine to be effective, I believe that history / the
available evidence says that (1) a good viral vaccine will present close to
100% of the possible viral proteins to the T-cells / immune cells and
then (2)
the T-cells / immune cells can pick and choose their "Top 10 list" of viral
protein pieces-parts they like the best and will make the focal point
of their
subsequent immune attacks on virus-infected cells. This is precisely what a
live HSV vaccine does. In contrast, for the past 30 years scientists in my
field have been trying to use man-made snippets of virus (one protein like
glycoprotein D or a few T-cell targets of HSV like the Agenus vaccine) and
drive T-cell expansion in precisely the way you described in your e-mail. I
generically refer to this as the "subunit vaccine" approach because
people are
cherry-picking their favorite snippet of a virus (i.e., a subunit of
the virus)
and making a "vaccine" out of it. The problem is that we now have 30
years of
data from human clinical trials that tells us that the overall rate
of success
of viral "subunit vaccines" is less than 1%.....Gardasil and the Hep B
vaccine are the exceptions, and there are good reasons why these particular
vaccines worked. The other >200 subunit vaccines that have been proposed and
tested in people have fallen flat on their face.

So, bottom line, it is good to have a ">10-fold T-cell expansion to HSV
proteins" as you suggest, but it is important that those T-cells that are
responding to HSV antigens also be allowed to respond to the full breadth of
HSV's 40,000 amino acids worth of antigens and choose their own "Top 10
list." In contrast, when we vaccinate with a single HSV protein like
glycoprotein D
(300 of HSV's 40,000 amino acids of foreign proteins), it does not matter how
many vaccinations we deliver to the body. Our immune system needs to be able
to recognize a wide variety of HSV proteins if it is going to win
this battle,
and the data clearly says that a single HSV protein or T-cell peptide
approach
is not sufficient to get our immune systems to that level of
"battle-readiness."

Probably more info than you wanted or needed.

See you in a couple of weeks!

- Bill

Quoting:

Hi, I had a question for you.

Would a 10 fold increase in t-cells for a specific hsv-1 antigen/proteinbe fairly significant?

They would have 10 x more t-cells, correct?

Would a vaccine capable of doing that produce a 10 fold increase every time?

In other words, if the same individual received the vaccine every 3
weeks for several months his t-cells would increase 10 fold every
time minus whatever he naturally lost between shots? cumulative?

Sorry that was a lot of questions but I have my reasons for wanting/need to know.

Thanks,