Over-stimulated

July 17, 2008 By Paul Dalton

Stop the world! I don?t want to get off, I just want to take a slow, deep breath.

As far as problems go, this is a good one to have. There is just too much to write about. Possible genetic explanation for high rates of HIV infection among people of African ancestry? Senate passing a PEPFAR bill that not only increases funding, but seeks to overturn the draconian travel restrictions aimed at HIVers in the US? Elizabeth Dole lobbying to have Jess Helms? name attached to an HIV bill? The PAVE trail decision? Genetic resistance to HIV? Oy.

As one of those, ?both-and people, in an either-or world,? so I will give my quick takes on each.

Genetic link explains higher rates of HIV among people of African descent.

Researchers working in both Texas and London examined whether a small genetic variation could help explain the higher rates of HIV infection found both in Africa and among people around the world with African ancestry. The thought that a component of red blood cells called a buffy protein might have a role.

This protein has a number of distinct functions, including absorbing a chemokine (chemicals that allow cells of the immune system to communicate with each other), called CCL5. CCL5 also has anti-HIV activity, although it isn?t clear why.

CCL5 used to be a major player is malaria. A form of the parasite, called plasmodium vivax, which used to be very common in sub-Saharan Africa, used CCL5 to gain entry into red blood cells. Therefore people who harbored a genetic variant causing CCL5 to be absent were resistant to infection by plasmodium vivax, which gave them a powerful survival benefit over people who did not have it.

This genetic trait became widespread in Africa. According to the New York Times story on this finding, ?More than 90 percent of people in Africa now lack the receptor on their red blood cells, as do about 60 percent of African-Americans.?

The authors propose that this finding might explain the high rates of HIV in both Africa and among, for example African-Americans. Agreeing, Phil Wilson, founder of the Black AIDS Institute, quoted in the San Francisco Chronicle, said ?Gay black men do not engage in riskier behavior than gay white men, for example. African people with this gene might have a higher vulnerability.?

The data suggest this is a possibility. The researchers probed a database of African Americans from the US military, and found that people with the CCL5 deletion had 50% higher rates of HIV infection that those without it. Interestingly, they also found that disease progression was somewhat slower in people with the CCL5 deletion.

While this finding is intriguing, it is far from definitive. These findings must be confirmed by others before much can be made of them. Even if confirmed this finding is unlikely to fully explain the disproportionate impact of HIV on Africa and Africans.

PEPFAR

In what is being called a ?landmark piece of legislation,? both the House and Senate have passed a bill which would both greatly increase funds for the PEPFAR program- which, among other things bring ARVs to developing countries- and will make it easier for HIVers to both visit and seek residence in the US.

The travel and immigration ban an people living with HIV is draconian, unfair and puts the US in some pretty dubious company, including Iraq, China, Saudi Arabia, Libya, Sudan, Qatar, Brunei, Oman, Moldova, Russia, Armenia, and South Korea.

How could it be that over a quarter of a century into this epidemic, a country which leads the world in HIV science and research can have such a archaic and discriminatory policy? F-E-A-R, or in 12 step parlance False Evidence Appearing Real. As with the Texas spitting case, many folks still remain terrified of people with HIV. Lest we forget, to many we are still diseased pariahs.

Sen. Kerry- yeah that one- introduced an amendment to the PEPFAR bill to reverse this policy, and the Senate passed the modified bill. The House and Senate will conference to resolve the differences between the bills, which Bush has indicated he will sign.

F-U Elizabeth

In what can only be seen as a full frontal attack on people with HIV, Senator Elizabeth Dole is trying to get the late-and-not-great Jesse Helm?s name attached to the above-mentioned PEPFAR bill. As my 15 year old daughter would no doubt say, ?WTF!?

Jesse Helms was an arch enemy of all people with HIV/AIDS, in the US and around the world. He was an arch reactionary and an unrequited bigot. He literally hated people with HIV. As Peter recounted in his post recently, Helms was more dangerous than a virus.

I should confess I forgot Dole was even a Senator anymore. I won?t soon forget now. Grrrr.

unPAVEd

Rumored for weeks now, the official decision not go forward with the planned PAVE 100 HIV

vaccine trial can down the proverbial wire this morning. The PAVE 100 trial was a large efficacy trial of a vaccine developed by the National Institute of Allergy and Infectious Diseases (NIAID)?s Vaccine Research Center.

It was the right decision, which follows and flows from the failure of the Merck vaccine earlier this year. As Martin Delaney wrote about, the Merck vaccine?s failure was not simply a major set back for that candidate, but for most, or maybe all of the vaccines in development.

The decision was made not to do a large trail, like PAVE 100- as the chances of success were considered too low for the investment in resources, not to mention the risks for the participants. The vaccine?s developers think that their vaccine is ?different enough? to merit more research however. They are working on designing a smaller, proof-of-concept trial in place of PAVE 100.

The whole field of HIV vaccine research is floundering right now. It would have been folly to move ahead with a large, expensive trial like PAVE 100 that had little real chance of payoff. The smaller scale study idea might have some merit- we?ll see.

Genes and HIV Resistance

The last story to come across my desk yesterday- thank you Diane- was about research suggesting that a combination of two genetic traits might make some people highly resistant to HIV infection. The genes in question are HLA-B57 and KIR3DL1. A group of Canadian scientists compared the genetic profiles of one group of people who were recently HIV infected to a group of repeatedly exposed, but uninfected people. They found that a particular combination of the two genes was 4.5 times more common in the uninfected group.

KIR3DL1 makes a protein which activates a type of immune system cell called a natural killer cell. HLA-B57 makes a protein that can attach to KIR3DL1, and reduce natural killer cell activity. The theory goes that if HLA-B57 isn?t binding to KIR3DL1, the natural killer cells might retain higher levels of activity and might more effectively combat HIV infection.

If confirmed and expanded by other research this finding has the potential to advance both the treatment and prevention of HIV infection. One of the most vexing problems for both HIV treatment and vaccine research has been the lack of a clear understanding of what kind of immune response is necessary and adequate to prevent and control HIV infection- something called the correlate of immunity. This finding might help in that endeavor.

Deep Breath

Days like this are rare. It will take some time to fully appreciate each of these stories, particularly those that require more research, like the genetics stories. Working in HIV is rarely dull, but today I could have used a little less stimulation.