To: jfcrow@facstaff.wisc.edu (James Crow)
Cc:
Fcc: inbox
Subject: Mutagenesis as an invariant rate; HIV in germ

OCT 23 1999

Dear Jim

I recognize there is a lot of empirical evidence to support that invariance (pace exogenous mutagens), and a theoretical framework how it is balanced by evolutionary pressures. But the more we learn about DNA metabolism, the less sense it makes mechanistically. So let's try the exercise of an open mind, can we attribute changes in mutability to the physiological and pathological context of the gametocytes? This is much in the line of pheno-mutators that Ninio and others have been pushing.

Why shouldn't DNA repair be more or less accidentally contigent on say virus infection, as well as toxic insults and direct chemical attack on DNA? I don't know of any direct measurement of DNA repair efficiency as function of developmental stage, and of miscellaneous pathologies.

your comment?
Jsh.

I do come to believe that the germ line is remarkably well insulated from run of the mill infectious agents; or is it just lack of search? Gerry Weissman has passed on some references on HIV entry into germ cells, but mainly mature gametes as far as the asbtracts imply. (There has to be a route for retroviruses to get in: there are so many integrated segments.)

Joshua.

Authors
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Title
The debate on the presence of HIV-1 in human gametes. [Review] [48 refs]
Source
Journal of Reproductive Immunology. 41(1-2):41-67, 1998 Dec.
Abstract
The debate about the presence of HIV-1 particles in human gametes and recent experimental results are reported in detail. Using immunocytochemistry, in situ hybridization at electron microscopy level, polymerase chain reaction and in vitro fertilization, it has been demonstrated that human spermatozoa can incorporate HIV-1 using special receptors, different from the usual CD4, and that they remain active and able to vehicle the viral particles into the oocyte, which is regularly fertilized. Moreover, by transmission electron microscopy (TEM),

immunocytochemistry and PCR, we demonstrated that cell-free HIV-1 is not able to bind and penetrate the human oocyte in vitro. We attribute this behaviour to the fact that the oocyte and cumulus cells are devoid both of GalAAG and of CD4 receptors. PCR analysis indicated that mRNAs specific for CD4, CXCR4 and CCR5 proteins were absent, too. [References: 48]