Retrovirology



Poster presentation



# Genomic instability induced by AZT in cultured normal human mammary epithelial cells (NHMECs) generates aneuploidy

Ofelia A Olivero*[1], Jennifer P Borojerdi[1], Cristina Semino-Mora[2], Yvonna Ward[1] and Miriam C Poirier[1]

Address: [1]National Cancer Institute, National Institutes of Health, Bethesda, Maryland, 20892, USA and [2]Uniformed Services University of the Health Sciences, Bethesda, Maryland, 20814, USA

* Corresponding author

*from* 2006 International Meeting of The Institute of Human Virology
Baltimore, USA. 17–21 November, 2006

Published: 21 December 2006

*Retrovirology* 2006, **3**(Suppl 1):P48 doi:10.1186/1742-4690-3-S1-P48



The antiretroviral drug Zidovudine (AZT), a transplacental carcinogen in mice, becomes incorporated into DNA of eukaryotic cells and acts as a chain terminator. Previously we reported that NHMECs exposed to AZT exhibit S-phase arrest, alterations in cell cycle gene expression, micronuclei, sister chromatid exchanges and shortened telomeres. A predicted consequence of these events is genomic instability. Aneuploidy, a direct consequence of genomic instability, was explored in NHMECs exposed to 200 : M AZT for 24 hours. A pericentrin antibody was used to identify centrosome amplification, which was confirmed by electron microscopy. In an NHMEC strain that was shown previously to incorporate AZT into DNA, centrosomal amplification, measured by scoring centrosomal positive bodies, occurred in 31.7% of the exposed cells compared to 5.83% in the unexposed cells. A second cell strain analyzed, which did not incorporate AZT into DNA, showed an increase of 20% in pericentrin positive bodies in exposed cells vs 7.83% in the unexposed cells. Additionally, ~25% of the AZT-exposed cells exhibited differences in size and shape and alterations in the distribution of tubulin, a critical component of the mitotic spindle. Chromosomal losses were inferred from the presence of micronuclei containing centromeric positive signals in AZT exposed cells. Because aberrations in centrosome morphology are associated with chromosomal mis-segregation, the evidence presented here suggests that AZT-induced genomic instability may play a role in AZT-induced carcinogenicity