

HIV AND APOPTOSIS OF CANCER CELLS: THE KILLER'S PROMISES



M. Ruggiero*, T. Punzi°, G. Morucci°, S. Pacini°



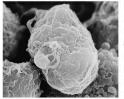
*Department of Experimental Pathology and Oncology,

*Department of Anatomy, Histology and Forensic Medicine, University of Firenze, Italy.



Corresponding Author: Professor M. Ruggiero, marco.ruggiero@unifi.it

HIV and AIDS. For more than 25 years it was assumed that HIV was the sole cause of AIDS. Although there have been a few voices of dissent since the early days (Science 1988; 241:514-17. J Biosci 2003; 28:383-412. See also: Bauer HH, "The Origin, Persistence and Failings of HIV/AIDS Theory"), in the past three years definitive evidence has accumulated demonstrating that HIV cannot be considered the (sole) cause of AIDS. In 2006, a large meta-analysis of ten years of highly active antiretroviral therapy (HAART) demonstrated that "the virological response after starting HAART has improved steadily since 1996. However, there was no corresponding decrease in the rates of AIDS, or death" (Lancet 2006; 368:451-8). In 2008, Professor Luc Montagnier, after having been awarded the Nobel Prize, stated: "We can be exposed to HIV many times without being chronically infected. Our immune system will get rid of the virus within a few weeks, if you have a good immune system" (quoted in the documentary "House of Numbers", 2009. URL: http://liamscheff.com/daily/2009/04/01/house-of-numbers/), thus reversing the long-assumed cause-effect relationship between HIV and AIDS whereby HIV inevitably brings on AIDS. Therefore, HIV infection itself reflects an already

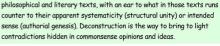


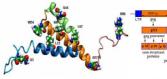
deficient immune system; it is the immunodeficiency that causes chronic HIV infection and not vice versa, as commonly believed. Finally, a review in 2009 demonstrated that HIV has been present in humans since at least the early 1900s, thus definitely ruling out the possibility that it could have been responsible for a syndrome that appeared only at the beginning of the 1980s (Curr Opin HIV AIDS 2009; 4:247-52). Quite obviously, if HIV caused AIDS, then AIDS should have been observed in earlier periods, when the hygienic and nutritional conditions of human populations were much worse than in the 1980s (i.e. during the two world wars and the depression in between). The very fact that AIDS was never described before the 1980s despite the persistent presence of HIV in humans, clearly demonstrates that HIV cannot be the cause of AIDS.

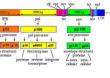
HIV and cancer. Many different strains and hybrids of HIV have been described, all of them apparently infective, yet it seems that few of these strains have been actively epidemic since "...despite the potential for different divergent viruses to spread, surprisingly few viruses successfully expanded to cause the global epidemic. In approximately 80% of cases, productive infection is the result of infection with only a single virus..." (Curr Opin HIV AIDS 2009; 4:247-52). This suggests the establishment of a symbiotic relationship between HIV and humans leading to a delicate survival balance.

We hypothesize that HIV-induced apoptosis of human cancer cells might have contributed to this symbiotic relationship. In fact, there exists a HIV protein termed viral protein R (Vpr) (a 14kD, 96 aminoacid, auxiliary protein of HIV) that induces selective killing of rapidly dividing cancer cells, arrests the cell cycle, inhibits inflammation and provokes p53-independent apoptosis (Curr Drug Deliv 2004; 1:335-44).

The deconstructive approach. It is easy for any reader to realize that most articles on HIV and AIDS demonstrate that HIV is not the cause of AIDS, if the articles are read using the deconstructive approach proposed by the philosopher Jacques Derrida. Derrida's approach consisted in conducting thorough, careful, sensitive, and yet transformational readings of







Vpr-mediated apoptosis was observed in all tumour-cell lines tested (Cancer Cell Int 2009; 12:9-20), and, in vivo, Vpr induced inhibition of melanoma growth and the induction of complete tumour regression coupled with long-term survival of mice in a highly aggressive and metastatic solid tumour model (Mol Ther 2006; 14:647-55). Free Vpr is detectable in the serum of HIV patients, and in vitro studies implicate extracellular Vpr as an effector of cellular responses mediated through its ability to transduce through intact cytoplasmic membranes (DNA Cell Biol 2002; 21:679-88). These results suggest that HIV infection could be associated with reduced risk of developing neoplasms in humans and, in fact, epidemiologic data from Western countries and Africa demonstrate that HIV infection is not permissive for breast cancer (J Womens Health 2003; 12:227-32). However, in humans the anti-tumour properties of HIV could be masked by widespread use of HAART; thus, HAART increases the risk of developing cancer (Curr Opin Oncol 2006; 18:469-78) and there was statistically a larger proportion of non-AIDS-defining cancer cases in the post-HAART period compared to the pre-HAART period (J Natl Med Assoc 2008; 100:817-20). Also in Italy a significant excess of liver cancer emerged in 1997-2004, i.e. after the introduction of HAART in 1996 (Br J Cancer 2009; 100:840-7). The potential oncogenicity of HAART is currently under investigation (Curr HIV/AIDS Rep 2008; 5:140-9. Curr Opin Oncol 2008; 20:534-40).



Conclusions. HIV, rather than being a harmless passenger virus (J Biosci 2003; 28:383-412), might provide the long-sought-after "magic" bullet that selectively kills cancer cells by inducing p53-independent apoptosis.

We thank Professor Henry Bauer for constructive, helpful discussions. This study was supported by grants of the University of Firenze.