Royal Perth Hospital
Wellington Street Perth Western Australia

DEPARTMENT OF MEDICAL PHYSICS

28TH MAY, 1991

EE:JB

Dr. Anthony S. Fauci
Director
National Institute of Allergy & Infectious Diseases
National Institute of Health
Bethesda, MD 20892
U.S.A.

Dear Dr. Fauci,

My colleagues and I read with great interest your paper "Suppression of human immunodeficiency virus expression in chronically infected monocytic cells by glutathione, glutathione ester and N-acetylcysteine", published in the Proc. Natl. Acad. Sci., February 1991.

Although your findings were no surprise to us, we were suitably impressed by your well executed experimental work. You and your colleagues are apparently unaware of work published by us in which we, in addition to predicting your experimental results, advocate the use of antioxidants in the prevention and treatment of AIDS and also, based on well known facts, hypothesise:-

(a) the mechanism which "produces a striking decrease in the level of a major cellular antioxidant" in AIDS patients and those at risk of developing it,

(b) the mechanism of retroviral induction.

Please find enclosed our published work and a letter, which my colleagues, Dr. V.F. Turner, Prof. J.M. Papadimitriou and I submitted for publication in Lancet, February 1990 which was rejected. In it we give the causes and a mechanism for the decrease in cellular sulphydryl groups, GSH and total glutathione in AIDS patients and those at risk of AIDS.

We would be very grateful if, after reading our papers, you could find the extra time to give us your comments and criticism.

Yours sincerely,

ELENI ELEOPULOS
PHYSICIST
CLINICAL PHYSICS DIVISION

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August 2, 1991

Dr. Eleni Eleopulos
Royal Perth Hospital
Department of Medical Physics
Clinical Physics Division
Wellington Street
Perth Western Australia

Dear Dr. Eleopulos:

I have read with interest your manuscript on the role of oxidation in the pathogenesis of HIV infection. I certainly agree with your general hypothesis that oxidation and anti-oxidation may be critical factors in the control of virus expression as well as in determining certain systemic dysfunctions associated with HIV infection. However, I suggest that you modify your penultimate sentence ". . . HIV cannot be detected unless strong oxidants . . . are added to the culture . . ." because it is an overstatement. First, it is not demonstrated that the mechanism through which 5-iodo-2-deoxyuridine and PHA are increasing the expression or replication of HIV is oxidation. At least for PHA, the most important functional explanation is its ability to induce IL-2 receptor expression on the target cells. Second, HIV expression or replication can be easily obtained in different cell types (for example, macrophages) in the absence of oxidants or PHA. In general, without underemphasizing the potential role of oxidation in HIV infection in vitro and in vivo, I think that much more needs to be understood in terms of the actual mechanism of action of these agents. As you have certainly noted, in our manuscript published in PNAS, we underscore the fact that NAC has a different, more profound suppressive effect than glutathione or glutathione monoester on HIV expression in our cell systems, suggesting that the most important component of NAC effect may not be, as postulated, just increasing the intracellular levels of glutathione.

I certainly appreciate your interest in our research and I will be available for further discussion on this important matter. Thank you and best regards.

Sincerely,

Anthony S. Fauci, M.D.
Director
National Institute of Allergy
and Infectious Diseases

ASF:lr