# New Drug Combination for the Treatment of Viral Diseases

## Background

Genetic heterogeneity is a major obstacle in the pharmacologic treatment of HIV infection. Current antiretroviral therapies such as AZT offer only limited benefits against HIV infection due to the emergence of resistant variants. However, the emergence of variants cannot completely explain certain phenomena such as the inability of viral isolates to replicate *in vitro* in tissue culture in the presence of AZT. By contrast, resistance to non-nucleoside inhibitors develops readily in both tissue culture and in patients. The resistance to non-nucleoside inhibitors arises, presumably, due to the selection of genetic variants because these inhibitors are not metabolized.

Resistance to AZT develops over months as opposed to resistance to nonnucleoside reverse transcriptase inhibitors, which develops rapidly. These differences can be attributed a) to the inherent differences in the ability of individual cells in a cell population to uptake and metabolize drugs and also b) to pre-existing viral-encoded drug resistance mutations in the initial viral population prior to their exposure to antiretroviral drugs. These differences could allow the selective replication of viral variants sensitive to drugs in cells that do not readily uptake and metabolize antiretrovirals such as AZT. Thus, the metabolic factors involved in the metabolism of AZT represent potential opportunities to modulate the clinical effectiveness of this drug.

## Description of the Invention

Previous studies have demonstrated that the emergence of HIV variants in the presence of Stavudine is a result of infection of cells refractory to the drug. In an effort to overcome the ineffectiveness of AZT, UMDNJ investigators have used a novel approach to modulate the effects of AZT. This approach involves manipulating the biochemical pools of phosphorylated thymidine. By co-administering a thymidine analog, which is a reverse transcriptase inhibitor, and an antimetabolite that is a thymidylate synthase inhibitor, the viral burden was reduced significantly. The use of thymidylate synthase inhibitor augments antiviral effect of the thymidine analog.

Further, it was found that the antiviral effects of thymidine analog can be enhanced when administered with thymidylate synthase inhibitor and a folate antagonist.

## Application

- For the treatment of HIV infection

## Patent Status

- US Patent granted on June 10, 2003. Patent No.: 6,576,622 B1.

## Licensing Opportunity

- Available for exclusive license.

## Contact

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File CINJ 94-41/Strair