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Biography

Hiroshi Ohrui has joined Riken in the year 1966 and moved to Tohoku University (1981) and to Yokohama University of Pharmacy (2006). He worked for Dr J J Fox at Sloan-Kettering Institute for Cancer Research (1972-1973) and Dr J G Moffatt at Syntex Research (1973-1974). He received several awards including The Japan Society for Analytical Chemistry Award (2004), and Japan Academy prize (2010). His research interests cover organic synthesis, chemical biology and chiral discrimination.

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EFDA: A VERY EXCELLENT ANTI-HIV MODIFIED NUCLEOSIDE FROM DESIGN TO THE CURRENT CLINICAL RESULTS

EFdA prevents the emergence of resistant HIV mutants, and is over 400 times more active than AZT and several orders of magnitude more active than the other clinical reverse-transcriptase inhibitor y 2', 3'-dideoxynucleoside drugs, very low toxic, very long acting, and very useful for prophylaxis. EFdA is now under clinical investigation by Merck & Co. as MK-8591. In the beginning, a general idea for the development of anti-viral modified nucleosides will be resented, and next, the development of EFdA is discussed and then the current results of the clinical trials reported by Merck will be presented. For the design of the modified nucleoside which could solve the critical problems that the clinical drugs have (emergence of drug-resistant HIV mutants, adverse effect by drugs, necessity to take considerable amount of drugs), four working hypotheses were proposed. They are the way to prevent the emergence of drug-resistant HIV mutants, the way to decrease the toxicity of modified nucleosides, the way to provide the modified nucleoside with stability to both enzymatic and acidic glycolysis for long acting and it is possible to develop selectively active to HIV and very low toxic to human based on the difference of the substrate selectivity between RT and human nucleic acid polymerases. 4'-C-substituted-2'-deoxy nucleoside (4'SdN) was designed as the nucleoside which could satisfy these hypotheses. The study based on 4'SdN successfully developed EFdA [modified at the two position (2 and 4') of the physiologic 2'-deoxyadenosine] having extremely excellent anti-HIV activity.

Note: