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EFdA: An extremely excellent anti-HIV nucleoside from design to the current clinical trial results

EFdA (4'-C-ethynyl-2-fluoro-2'-deoxyadenosine) prevents the emergence of resistant HIV mutants, is over 400 times more active than AZT and several orders of magnitude more active than other clinical reverse-transcriptase inhibitory 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 is presented. Next, the development of EFdA is discussed and then the current clinical trial results by Merck will be presented. For the development of EFdA, four working hypotheses, the way to prevent the emergence of resistant HIV mutants, the way to decrease the toxicity of nucleosides, the way to provide nucleoside with stability for long acting, the difference of the substrate selectivity between human and viral nucleic acid polymerases makes it possible to develop very excellent anti-viral modified nucleosides, were proposed. 4'-C-substituted-2'-deoxy nucleoside (4'SdN) was designed as the nucleoside which could satisfy these hypotheses. The study on 4'SdN has successfully resulted in the development of EFdA.

Biography

Hiroshi Ohrui has completed his PhD in Organic Chemistry at the University of Tokyo and Postdoctoral studies at Sloan-Kettering Institute for Cancer Research and Syntex Research. He has worked at Riken and Tohoku University and received several awards including The Japan Society for Analytical Chemistry Award and Japan Academy Prize.