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Novel oleanoic acid-derived HIV entry inhibitor: Design, synthesis and bioevaluation

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Naturally occurring pentacyclic triterpenoid derivatives, such as betulinic acid derivatives, have been shown to exhibit various biological activities including anti-HIV activity. IC9564 and RPR103611 are statin derivatives of betulinic acid tethered by 8-aminooctanoic acid linker, which was reported as a novel class of HIV-1 entry inhibitors. Although those betulinic acid derivatives show nanomolar order potency against diverse HIV-1 strains, relatively high cytotoxicity is one of the drawbacks of them. In this study, the structure-activity relationship study of a series of triterpenoid derivatives was conducted to identify the potential triterpenoid-based HIV entry inhibitors with lower cytotoxicity than betulinic acid derivatives. Significant potency gains were made by replacing the betulinic acid moiety with the oleanoic acid, resulting in the discovery of several potent compounds. This study identified a novel lead compound OKS3-019 with significant anti-HIV activity against 89.6 strain of HIV-1 and lower cytotoxicity than those of known betulinic acid derivatives. Design, syntheses, bioevaluation and docking models of the newly identified oleanoic acid derivatives will be discussed.

Biography

Tetsuo Narumi studied Organometallic Chemistry at Waseda University in Shinjuku, Tokyo, where he worked in the research group of Prof. Isao Shimizu. After PhD studies at Waseda University with Prof. Shimizu followed by Kyoto University with Prof. Nobutaka Fujii, he spent a year in US as a JSPS Postdoctoral Fellow with Prof. Jeffrey W Bode at the University of Pennsylvania. In 2009, he began his academic career in Japan, at Tokyo Medical and Dental University with Prof. Hirokazu Tamamura. In 2013, he began his independent career at Shizuoka University in Japan, as an Associate Professor in Bioorganic Chemistry.

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