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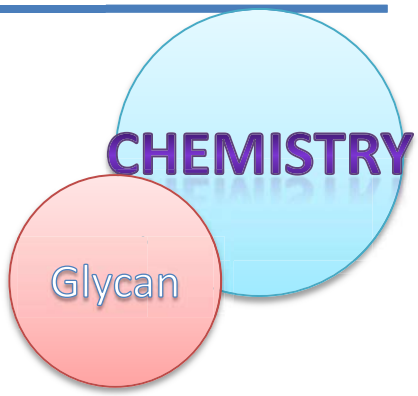
http://www.sci.ocha.ac.jp/chemHP/labos/ogawaHP/index.files/Page660.htm



■ **Researcher information**

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Major

Biochemistry, Glycoscience, Glycobiology and Medicine

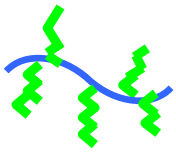
■ **Research topics**

Novel anti-HIV-1 compound, pseudoproteoglycan, produced by conjugating unsulfated glycan with backbone amino group-having polymer

Keywords

Glycan, Unsulfated sugar, Amino group-having polymer, Conjugate, Anti-HIV-1 activity

Contents



Dex-PLL pseudoproteoglycan

■ Overview (background, goal, detail)

A proteoglycan (PG) consists of a core protein combined with more than one glycosaminoglycan chain. We synthesized unique pseudoproteoglycans (pseudoPGs) that simulate PG macromolecular structure with combinations of different sizes and different types of glycans and core polymers to elucidate the biological activities of pseudoPGs. Novel pseudoPGs synthesized using poly-L-lysine (PLL) with unsulfated dextran (Dex) by reductive amination exhibited remarkable anti-HIV-1 activity, although neither PLL nor Dex has such activity. The pseudoPG will enable the development of a potential anti-HIV-1 agent.

■ Process, case study

Conjugation with Dex was found to expose the antiviral effect of PLL, and the pseudoPG synthesized using 6–10 kDa PLL and 10 kDa dextran showed IC50 16–80 times lower than that of sulfated dextran or heparin against BaL viral strains and equal to that of sulfated dextran or heparin against IIIB, indicating that Dex-PLL was markedly more effective against R5 virus than sulfated polysaccharides. The expression of anti-HIV-1 activity and selectivity for a virus depend on the structure of the glycan moiety and backbone poymer.The mechanism by which Dex-PLL prevents HIV-1 infection is still unclear.

■ Potential (applications, future goals)

Recently, the number of AIDS patients are gradually decreasing in advanced countries, whereas those in Japan and developing countries are still increasing and the drugs having novel prevention mechanisms are strongly required. In the proliferation cycle of HIV-1, Dex-PLL is considered to interact with both the virus and the cell surface at the stage of adsorption to the cell, and to inhibit virus invasion of the cell, suggesting the unique preventive mechanism of PLL-Dex against HIV-1. moreover, pseudoPG also interacts with virus internal proteins. Therefore, studies on anti-HIV-1 activity of pseudoPG by synthesizing conjugates of various glycans and backbone molecules will open insights into the development for a potential anti-HIV-1 agent.

Intellectual properties (Patents, computer programs), productization, publications and social/industrial contributions

Japanese Patent No.4759736 “Pseudoproteoglycan and its utility”
Japanese Unexamined Patent Application Publication No. 2010-126471 “Antiviral reagent”
Japanese Unexamined Patent Application Publication No. 2010-31002 “Preventive and therapeutic reagent to pancreatitis”

Potential of social/industrial contribution

■ Joint research to develop anti-HIV-1 drug utilizing pseudoPG (ointment for skin or mucous membrane, or spreading material for medical tools)
■ Joint research/ licensing / technical consulting / knowledge sharing (open courses, workshops, publications) in the field of glycobiology, utilizing glycan or derivatives.