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Antiviral effects of *N*N-DNJ, 2ThO-DNJ and E*O*O-DNJ on dengue-infected monocyte-derived dendritic cells

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Abstract

Dengue virus (DENV) infections range from asymptomatic illnesses to severe haemorrhagic disease and death. Iminosugars are monosaccharide mimics that competitively inhibit α-glucosidases in the host endoplasmic reticulum. *In vitro* studies have demonstrated antiviral effects of iminosugars against dengue in monocyte-derived macrophages. Dendritic cells (DC) are important targets for dengue infection and they play a significant role in the immune response against early dengue infection. Given the important role played by DC in innate immune defence against DENV, it is useful to investigate the antiviral effects of iminosugars in a DENV-infected DC model. We evaluated three deoxynojirimycin (DNJ) derivatives and a deoxygalactonojirimycin (DGJ) control in DENV-infected primary human monocyte-derived DC. *N*-(n-Nonyl)-deoxygalactonojirimycin (*N*N-DNJ), 8-tetrahydrofuranyl-octyl-DNJ (2ThO-DNJ/UV-12) and *N*- (8′-ethoxyoctyl)- deoxynojirimycin (E*O*O-DNJ) were used as DNJ derivatives. *N*-(n-Nonyl)- deoxygalactonojirimycin (*N*N-DGJ), which has galactose stereochemistry was used as the control. Immunofluorescence was used to detect % infection of DENV. Secretion of infectious virus was evaluated with plaque assays while total secreted virus was quantified with qRT-PCR. We demonstrated that iminosugar derivatives of DNJ but not DGJ elicit antiviral activity in DENV-infected monocyte-derived DC. Compounds *N*N-DNJ, E*O*O-DNJ and 2ThO-DNJ reduced the % of infected cells and inhibited the secretion of DENV in a dose dependent manner. In conclusion, we have demonstrated for the first time that the iminosugars *N*N-DNJ, E*O*O-DNJ and 2ThO-DNJ have antiviral effects on DENV-infected DC similar to those seen in DENV-infected macrophages.