T18-508

Tohoku University's Invention

An inhibitor of Influenza A virus: tFIT-DPQ probe

Over 1000 times affinity to bind with RNA virus (vs. DPQ)! Promising diagnostic and inhibitory drug!

Introduction

Influenza prevails broadly every season. Current diagnostic drugs can not be performed until the virus increases quite a lot (ca. 12~24h after infection, symptoms may appear), and if not so, both sensitivity and accuracy of the test will be doubtful. To prevent on-going severe symptoms, new diagnostic tech for influenza at earlier stage becomes so demanded. This invention provides a conjugate of peptide nucleic acid sequence (PNA) and a small molecule, targeting the commonly identical RNA hairpin promoter region of eight kinds of influenza A virus.

Effect & Application

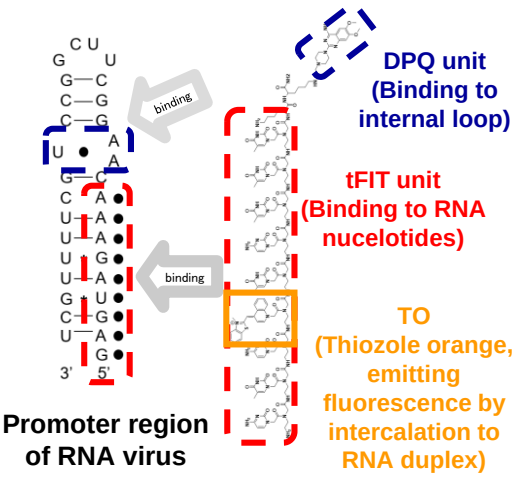
The conjugate (tFIT-DPQ probe) is composed of two parts: tFIT unit for recognition of virus RNA's nucleotides and DPQ* unit for UAA internal loop binding. In tFIT unit, a fluorescent ligand is inserted so as to be capable to emit signals when intercalating to RNA duplex (Fig. 1). The conjugate shows an over 1000 times greater binding affinity than DPQ molecule only (Fig. 2). By simply mixing the virus RNA contained sample and the conjugate together, test result will be obtained within a short time (ca. 2~3 min) and 1nM virus RNA (ca. 10^{10} copies) can be detected. Moreover, the virus inhibition effect by the conjugate in micromolar range was confirmed (Fig. 3).

tFIT-DPQ probe is expected to be applied as diagnostic and inhibitory drugs, as well as a screening tool for influenza drug candidates.

* Chem. Commun., 2014, **50**, 368.

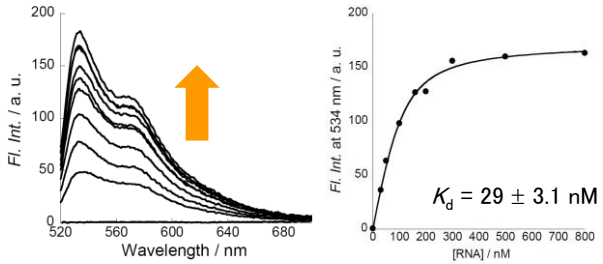
Structure of tFIT-DPQ probe and its virus inhibition effect

Fig. 1. Specific binding to virus RNA



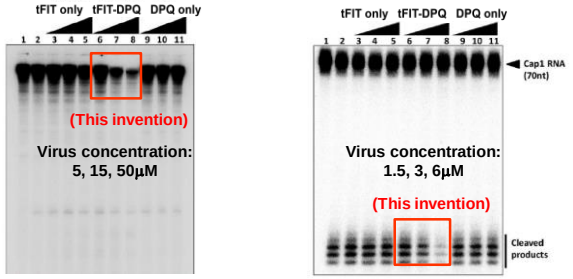
* DPQ: 6,7-Dimethoxy-2-(1-Piperazinyl)-4-Quinozolinamine)
** tFIT: triple-forming Forced Intercalation of Thiozole orange

Fig. 2. Determination of binding affinity



・Fluorescence signal changes sharply at lower concentration of RNA virus (ca. less than 300nM), showing the detection ability of virus for a small amount.
・Dissociation constant (K_d): 50.5μM for DPQ, 29nM for tFIT-DPQ.

Fig. 3. Inhibition of replication and transcription



・*Left*: As tFIT-DPQ probe increases, the full-length genome RNA decreases.
→Inhibition of replication process by virus polymerase
・ *Right*: As tFIT-DPQ probe increases, virus RNA fragment decreases.
→Inhibition of activity of endonuclease

Patent Data Sheet

Application No.(Serial No.): JP2019-141527 (T18-508)
Inventor: SATO Yusuke, NISHIZAWA Seiichi, TANABE Takaaki, KAWAGUCHI Atsushi

Contact

Tohoku Techno Arch Co., LTD
TEL:+81-22-222-3049, FAX:+81-22-222-3419
Click to contact