

Antivirus Technology: Inhibition of Virus Replication with Artificial DNA-Binding Proteins

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Various infectious diseases are caused by viruses.

Agricultural Crops

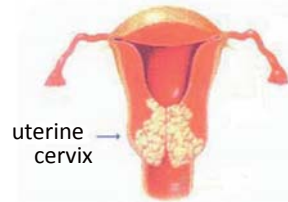


Turnip yellow mosaic virus



Wheat streak mosaic virus

Human



Cervical Cancer

Human papillomavirus



Influenza virus

How to Prevent Virus Infection?

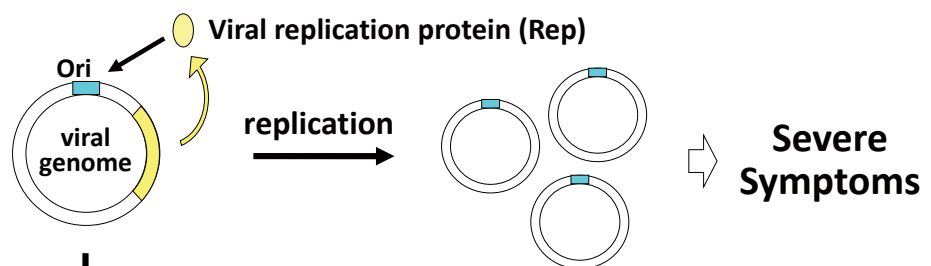
Block virus invasion?

Our Answer: Block virus replication even if viruses invade !

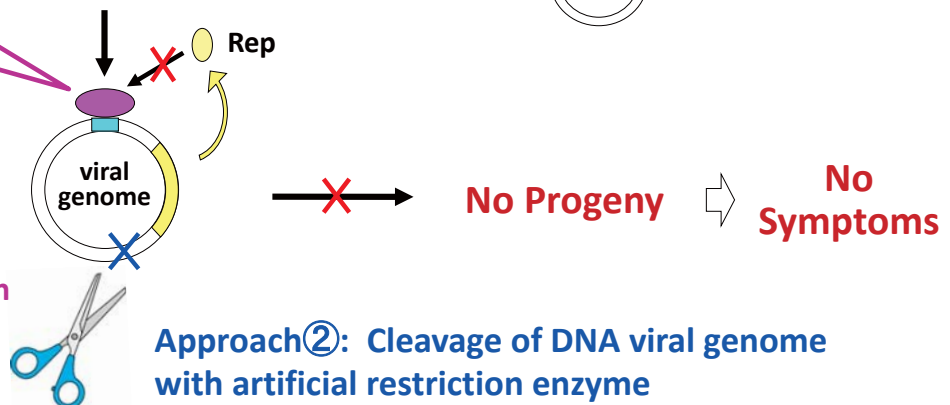
Approach①: Inhibit Rep binding to its replicon

Approach②: Cleave DNA viral genome

Approach①: Inhibition of the binding of a viral replication protein (Rep) to its replicon



Artificial DNA-Binding Protein (AZP)



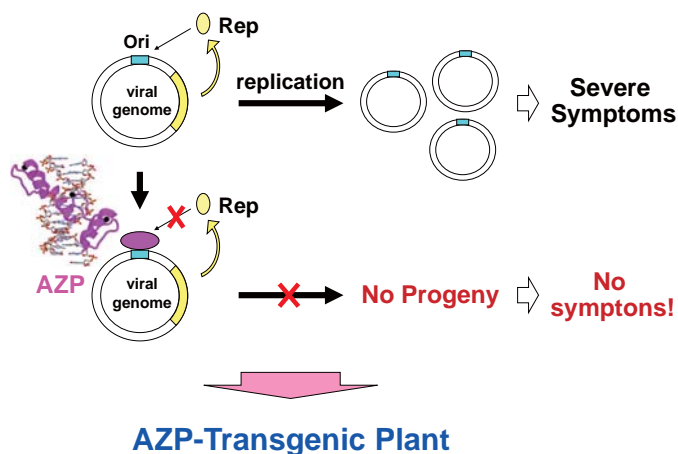
Approach②: Cleavage of DNA viral genome with artificial restriction enzyme

Artificial Restriction Enzyme = AZP+ DNA-cleaving enzyme

Research Examples

1. Development of Virus Resistant Plant using Artificial DNA-binding Protein

Inhibition of Rep Binding with AZP



Creation of Virus-Resistant Plant



Infection to Beet Severe Curly Top Virus (BSCTV)

(4 weeks after inoculation)

- A: Wild Type Plant without Viral Infection
- B: Wild Type Plant
- C: AZP-Transgenic Plant A
- D: AZP-Transgenic Plant B

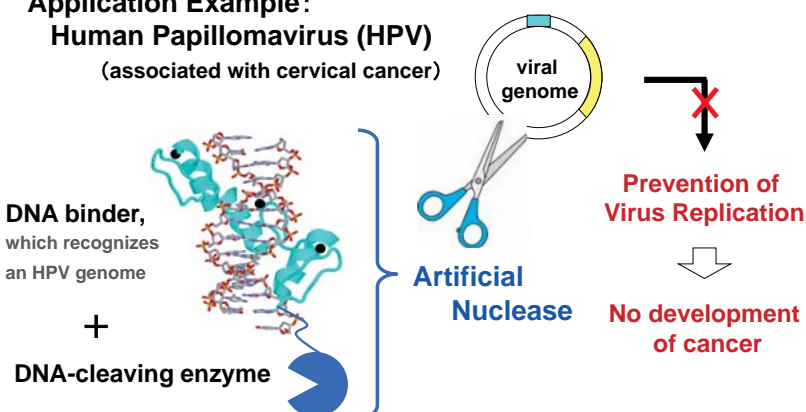
AZP = Artificial DNA-binding Protein

Inoculation of BSCTV

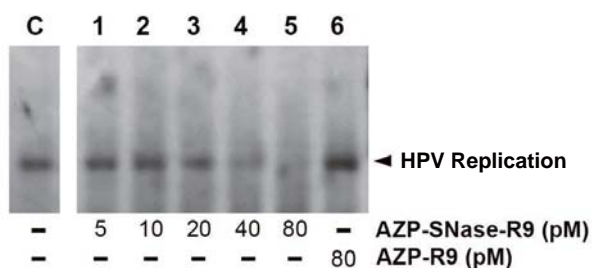
2. Development of Protein-Based Antiviral Drug using Artificial Nuclease

Cleavage Viral Genome with Artificial Nuclease

Application Example:
Human Papillomavirus (HPV)
(associated with cervical cancer)



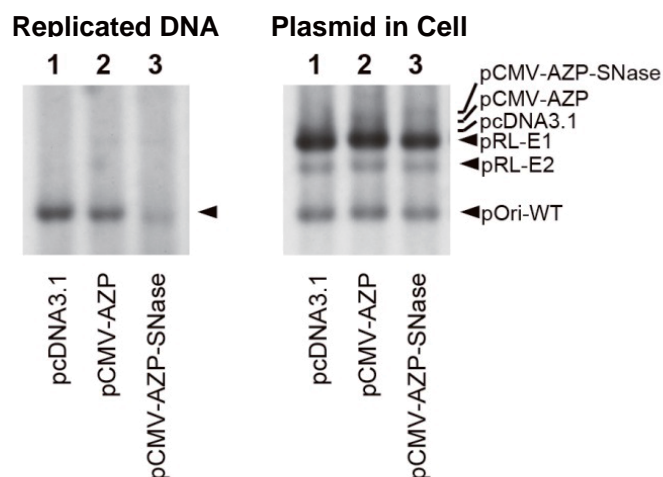
Inhibition of HPV Replication with Cell-Permeable Protein



cell-penetrating peptide

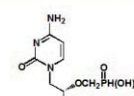
New Protein-Based Antiviral Drug

Inhibition of HPV Replication with Gene Delivery



Comparison with Existing Antiviral Drug

	Cell-Permeable Artificial Nuclease	Cidofovir
EC ₅₀	< 20 pM	63 ~ 159 μM (day 3)* 1.9 ~ 6.3 μM (day 7)*
IC ₅₀	>> 1 μM	—
SI (IC ₅₀ /EC ₅₀)	> 5 × 10 ⁶	15 ~ 42*



(*Oncol. Res. 10, 523-531)

Much more active than Cidofovir !
(10⁵-fold)