Title

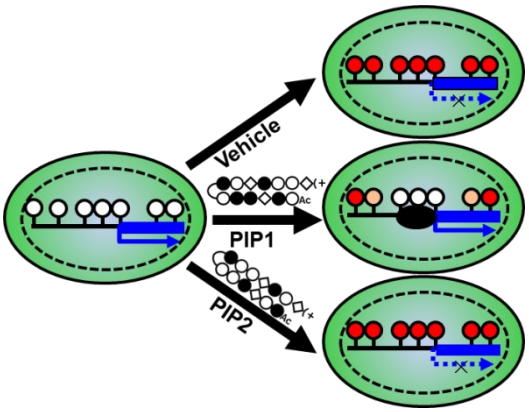
Selective inhibition of DNA methylation based on molecules that bind to DNA

Background and Purpose of Research

Aberrant and hyper DNA methylation of gene promoter regions that regulate the expression of genes affect transcription of genes. Thus, aberrant and hyper DNA methylation of gene promoter regions relative to tumor suppressor genes constitutes significant cause of tumor genesis in colorectal cancer and in many other cancers. From the perspective of cancer therapy, there is need of exploration of means that selectively target the methylated promoter regions with a view of raising the expression of tumor suppressor genes.

Summary of Research Results

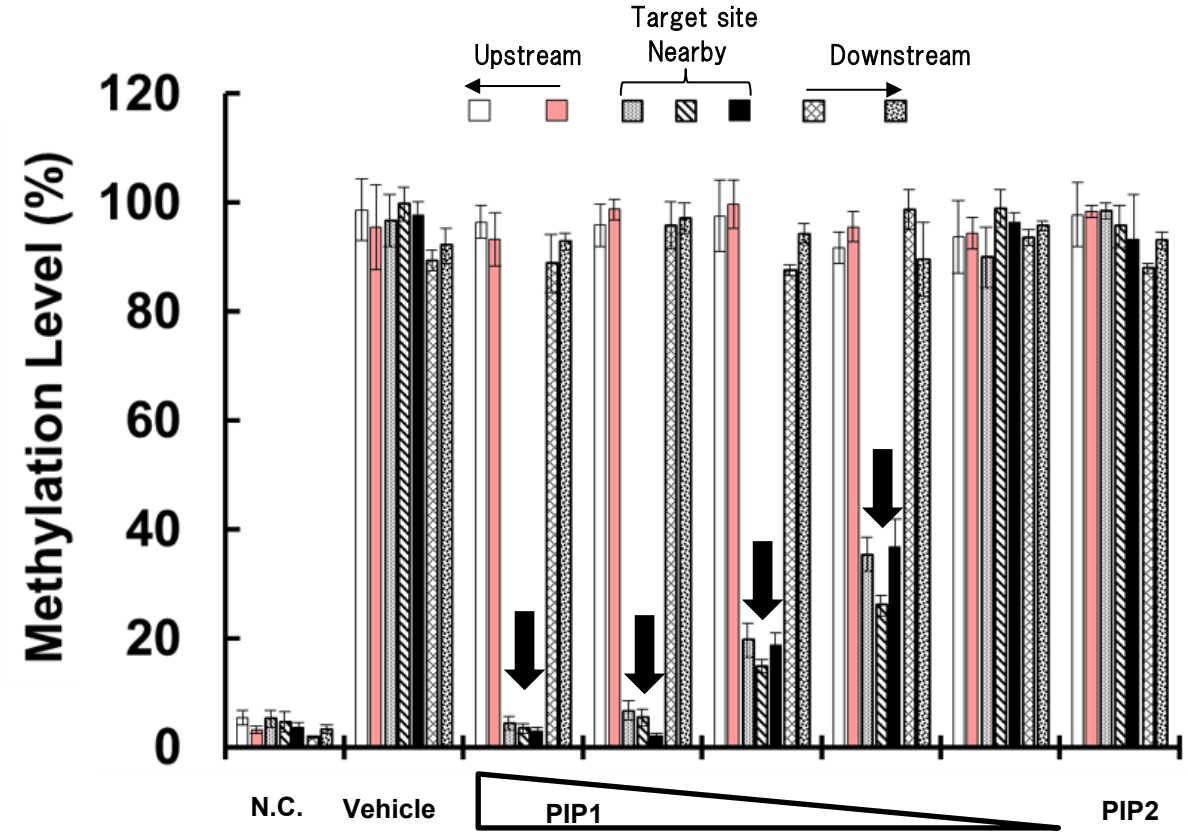
A pyrrole (Py)-imidazole (Im) polyamide (PIP) that selectively binds to target DNA sequence is able to inhibit methylation of target site in living cells.

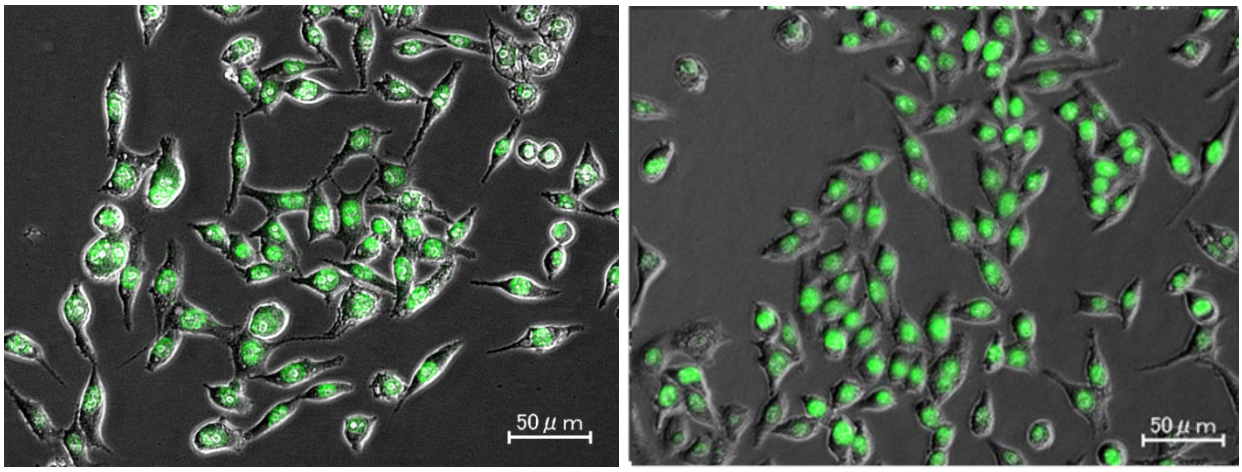


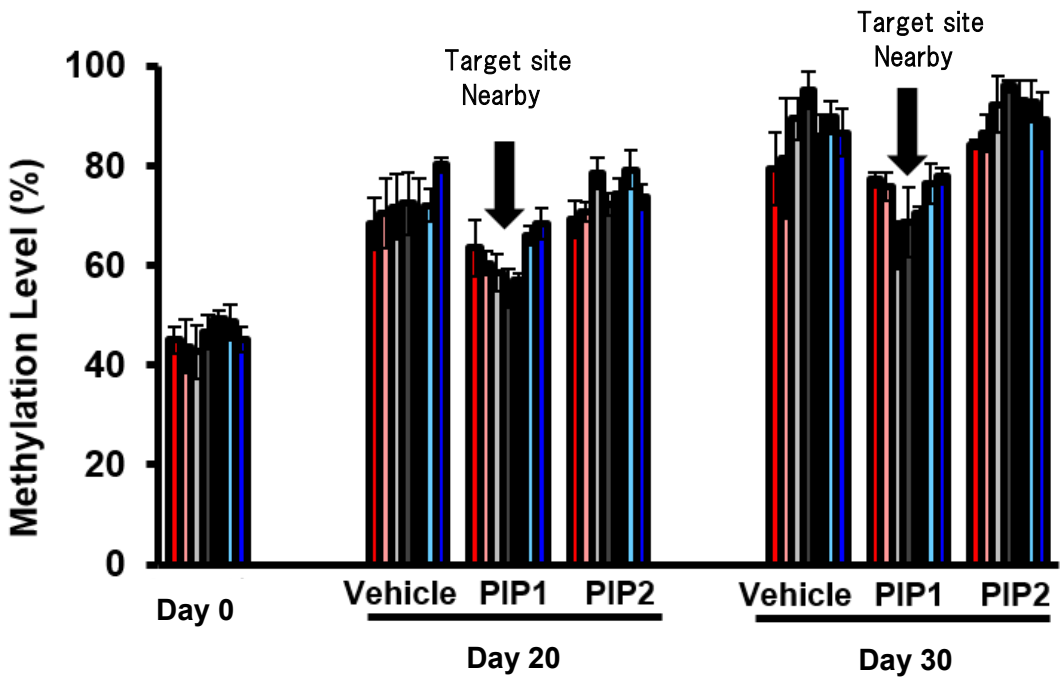
① Investigation into inhibition of plasmid DNA methylation by PIP

Researchers designed and constructed PIP1 that binds to target site (such as gene promoter regions of tumor suppressor gene "X") and investigated its effects on the methylation levels at nearby positions and at positions upstream and downstream of target site For comparison, researchers also designed and constructed PIP2 that does not bind to the site of tumor suppressor gene "X".

PIP1 inhibited methylation of target site concentration-dependently.







②Investigation into inhibition by PIP1 of methylation *in cellulo*

Localization *in cellulo* of PIP1 (See upper Figure above, left) and PIP2 (See upper Figure above, right). Both molecules easily passaged cell membrane and nuclear membrane as they are added on culture medium, and localized to the nucleus.

Lower Figure above demonstrates selective inhibition of methylation of PIP1 target site *in cellulo*.

Patent Status

JP 7030323

Advantages

Capable of site-specific inhibition of perturbation of transcription of tumor suppressor genes, PIP can be therapeutic or preventive agent for cancer.

Applications

Therapy of cancer, prevention of cancer, inhibitor tool of intracellular DNA methylation.

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Licensing Contact

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