HiPep Laboratories

# PIPA: a Novel Gene Silencer

## Why don't consider the use of PIPAs over knockout by RNAi or knockdown by genome editing

### Characteristics of PIPA

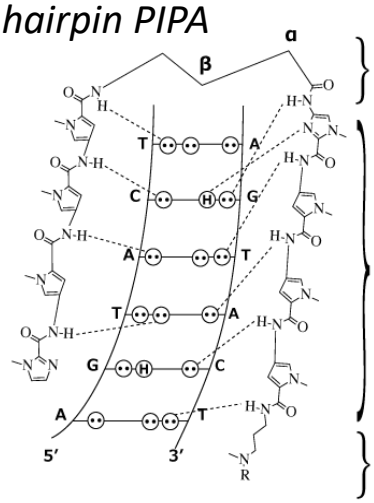
- PIPA is a kind of peptide, masks with an minor groove on the outside of the double stand DNA.
- Recognizing the target double stand DNA in dormant state, the mechanism differs from that of single stranded RNAi.
- PIPA is consisting of all non-proteinogenic amino acids. Stable in cells or bodies because of nuclease resistance.
- Enter into cell nucleus without any DDS.
- Flexible Design against any gene.
- As with RNAi, it is a temporary reduction in expression, its effect is also weakened and restored by passaging.

PIPAs are expected as a novel drugs for gene therapy with a novel mechanism; interfering the transcription of disease-related genes, suppressing expression of diseased proteins, stopping onset and progression of diseases.

[References]
P. B. Dervan et. al., Nature 391 (1998) 468-471; P. B. Dervan and R. W. Burli, Current Opinion in Chemical Biology 3 (1999) 688-693; P. B. Dervan, Bioorganic & Medicinal Chemistry 9 (2001) 2215-2235.

### Principle: double strand DNA recognition by PIPA

*hairpin PIPA*

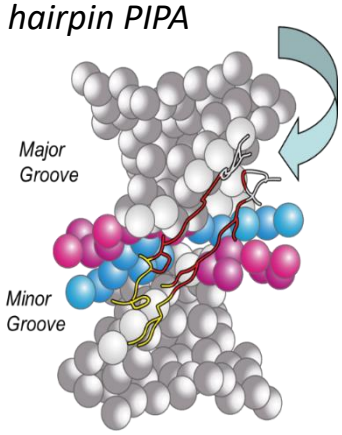



Central gamma aminobutyric acid linker makes the molecule folds into a hairpin type, selectively binds to a specific base sequence.

Adjust the length of the base sequence recognized by introducing beta-alanine at an appropriate position.

At the C terminus, special functional groups are placed to increase affinity for DNA.

*hairpin PIPA*

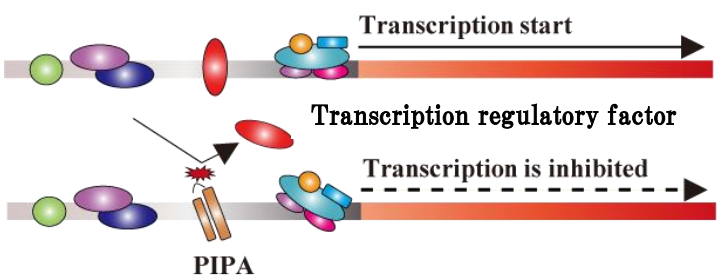



**PIPA binds reversibly to specific nucleotide sequences in the minor groove of double-helical DNA by hydrogen bonding.**

HiPep Laboratory has been performed R&D on industrial application of molecular recognition of living organisms. In addition to biodetection using PepTenChip®, a novel microarrays, drug development are also carried out.

Hence, double-stranded DNA binding using PIPAs, peptides consisting of pyrrole/imidazole rings, control **transcription factors and inhibiting gene transcription**. Academic research on PIPA has been carried out in the past two decades and now clinical applications are reported.

| Method | Target | Cleavage Activity | Gene expression suppression type | Genetic code change | Change in expression level | Necessity of clone isolation |
|---|---|---|---|---|---|---|
| PIPA | Genomic dsDNA | | Knock down gene transcriptional activity | No | ✓ | |
| RNAi | mRNA | ✓ | Knock down gene expression | No | ✓ | |
| CRISPR | Genomic dsDNA | ✓ | Knock out | Yes | ✓ | ✓ |

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