Drug discovery (Gene Therapy by DNA specific recognition) & Biodetection

Recently, gene therapy with genome editing is expected as the novel medical treatment. HiPep Laboratory has been performed Peptide Nucleic Acid (PNA) and Pyrrole-Imidazole Polyamide (PIPA). Both can be performed by the contract syntheses. Moreover the facility of GMP-production is under construction.

PNA is a kind of peptide consisting of base units with amide bonds. PNA can bind complementary with DNA, such as A-T; C-G, and recognize to specific nucleotide sequence. DNA/PNA double-stranded structure is more stable than dsDNA. DNA expression can be blocked by hybridization with PNA and DNA. However, the limitation of PNA is poor membrane permeability. So devised to delivery to pass through the cell membrane and nuclear membrane is required. Especially efficient introduction technology into the nucleus of the target cell is indispensable. In addition, molecules recognition can be applied for biodetection (e.g. FISH etc.). In order to deliver PNA into the cell, we propose a conjugate of module type molecule (designated “Peptide-vehicle” ; “Bio-shuttle”).

Peptide Vehicle; Bio-shuttle module type molecule (Middle Molecular )

Fluorescent Dye | NLS | Cleavage (Enzyme) | PNA | Cleavage (Chemical) | CPP
--- | --- | --- | --- | --- | ---
wire: PIPA | balls: DNA molecule red, blue: recognition part

Advantages of bioconjugate
1. Improvement of drug delivery: Introduced only in target (cancer) cells
2. Cell specific; reduction of side effects: Target cells rather than molecular targets
3. New patent: Drugs out of patent secured new intellectual property right
4. Improve selectivity for cell lines
5. Activity even in cancer-resistant cancer cells (peptide vehicle with anticancer drug)

PIPA is a peptide containing N-methylpyrrole (Py) and N-methylimidazole (Im) as major building units. PIPA can bind to specific nucleotide sequences in the minor groove of double-helical DNA with high affinity and specificity, suggesting that PIPA blocks binding of transcription factors inhibiting gene expression, thus PIPA can be used for gene-control. PIPA is stable in cells or bodies because of nuclease resistance and enters into cell nucleus without any DDS.

Comparison of PNA and PIPA

<table>
<thead>
<tr>
<th>PNA</th>
<th>PIPA</th>
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</thead>
<tbody>
<tr>
<td>Form of recognition DNA</td>
<td>single-stranded DNA</td>
</tr>
<tr>
<td>Bonding mechanism</td>
<td>Bind complementary such as A-T; C-G</td>
</tr>
<tr>
<td>Stability of binding state with DNA</td>
<td>more stable than dsDNA</td>
</tr>
<tr>
<td>Average molecular weight / unite</td>
<td>300/base</td>
</tr>
<tr>
<td>Optional modification</td>
<td>Conjugation with modules to pass into membranes (e.g. CPP, NLS)</td>
</tr>
<tr>
<td>Optional modification Common</td>
<td>Fluorescent label for imaging (selectable fluorescent dye suitable for wavelength to be observed)</td>
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</tbody>
</table>

[ literatures in our activities ] upon requests reprints are available


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