

RNA INTERFERENCE

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What is RNA interference

- biological process in which RNA molecules inhibit gene expression or translation
- It is abbreviated as RNAi
- It needs siRNA or miRNA

siRNA

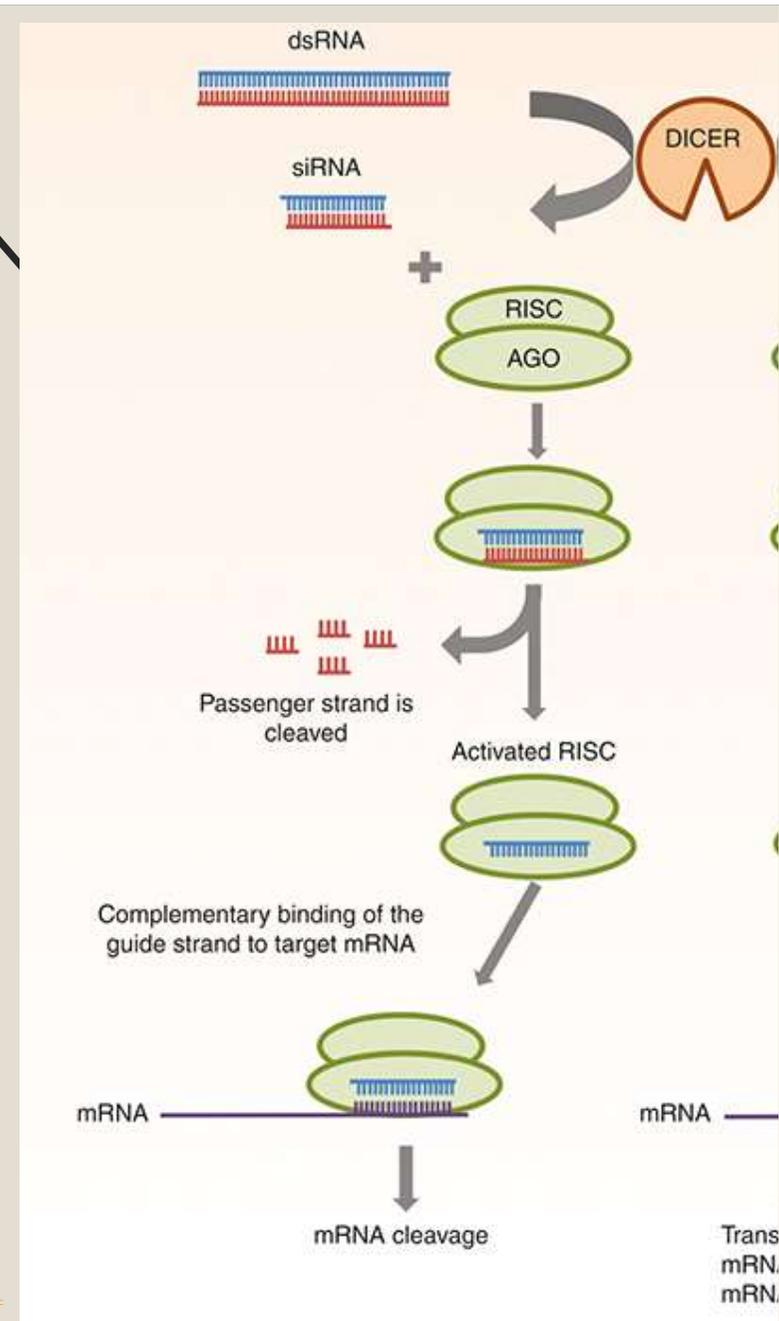
- Small interfering RNA
- 21-25bp (base pair)
- duplex
- perfectly same as mRNA
- degrades mRNA
- exogenous

miRNA

- microRNA
- About 22 bp
- Partially different from mRNA
- Represses mRNA
- endogenous

Mechanism of siRNA

- Dicer make dsRNA smaller
- RISC binds siRNA
- It cleaves passenger strand
- RISC-guide strand complex recognize and cleave mRNA



RISC

- RNA-induced silencing complex
- The complete structure of RISC is still unsolved.

AGO

- Argonaute
- Essential component of RISC
- Active site of RISC

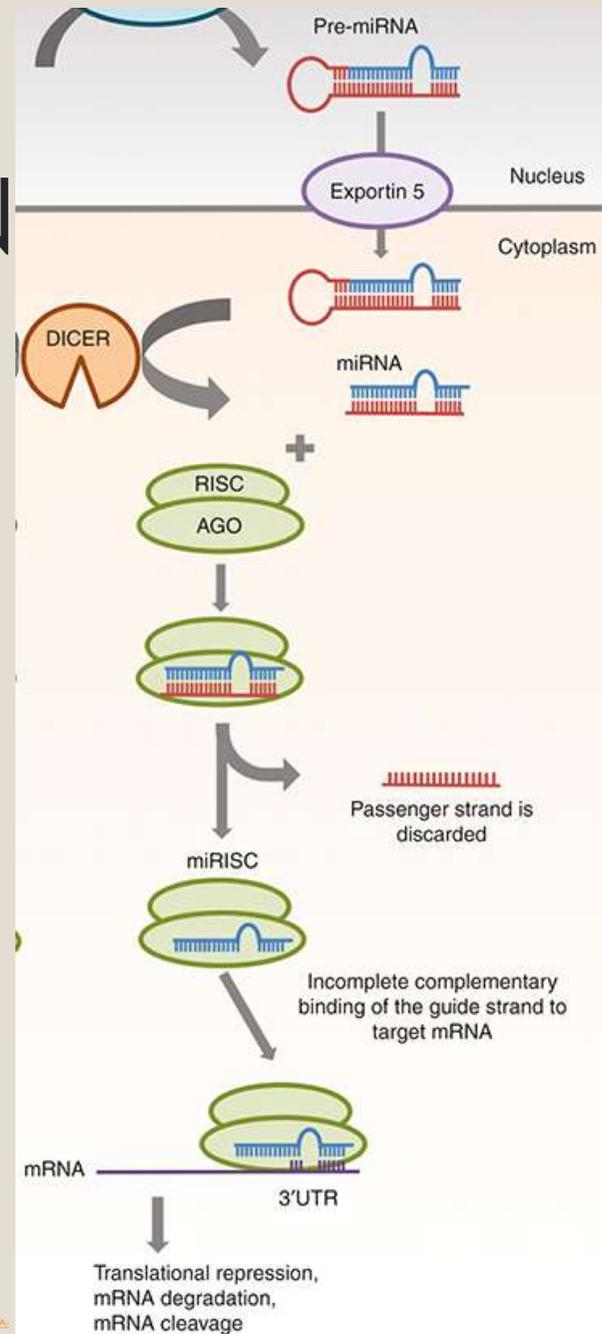
Mechanism of miRNA

- miRNA is made from DNA
- miRNA forms hairpin structure
- miRNA is cut by Drosha

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Mechanism of miRNA

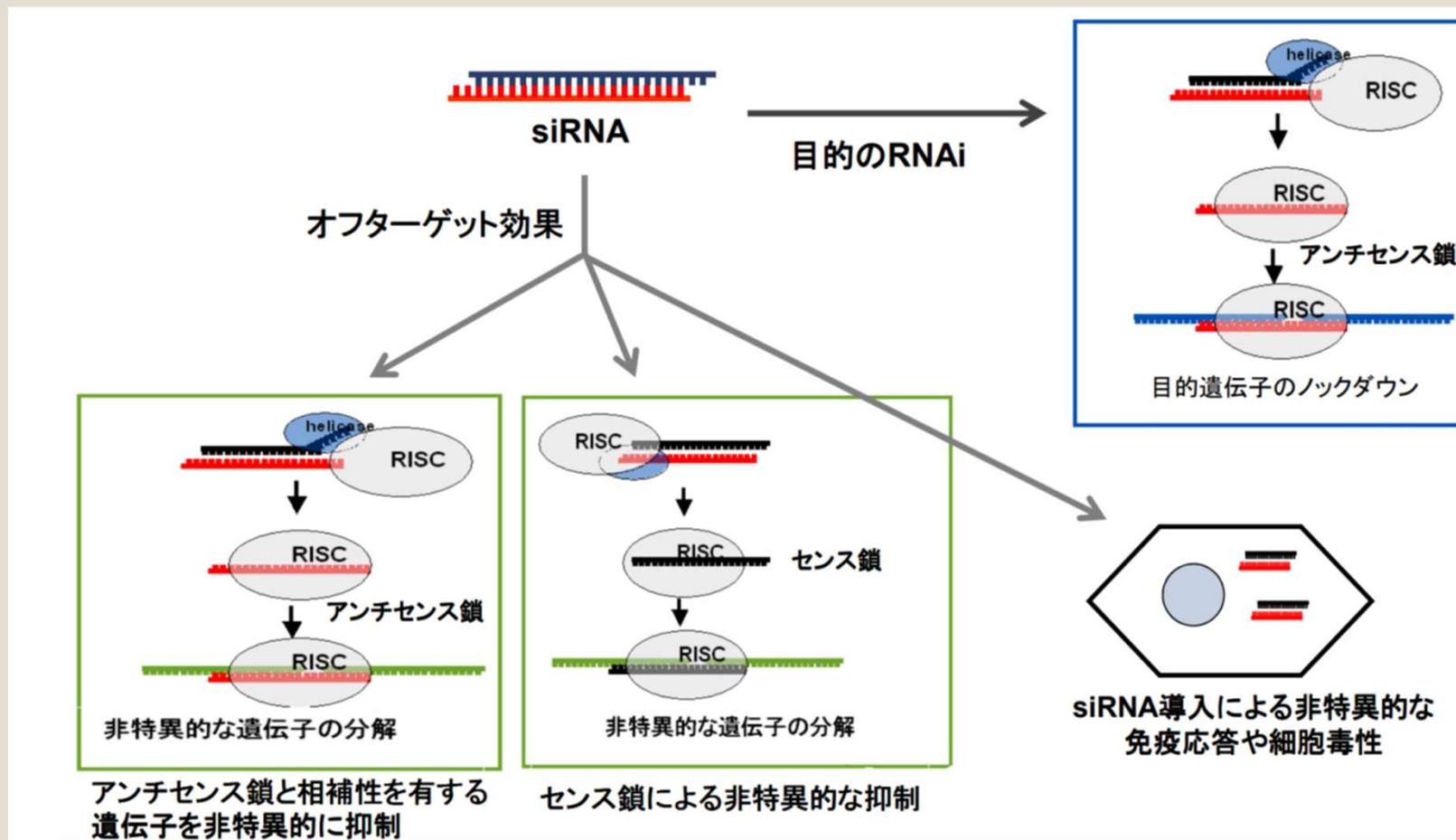
- mRNA is transported Nucleus to Cytoplasm by Exportin
- Almost same process as mechanism of siRNA



Off-target effect

- mRNA which is not target mRNA is also repressed

Off-target effect

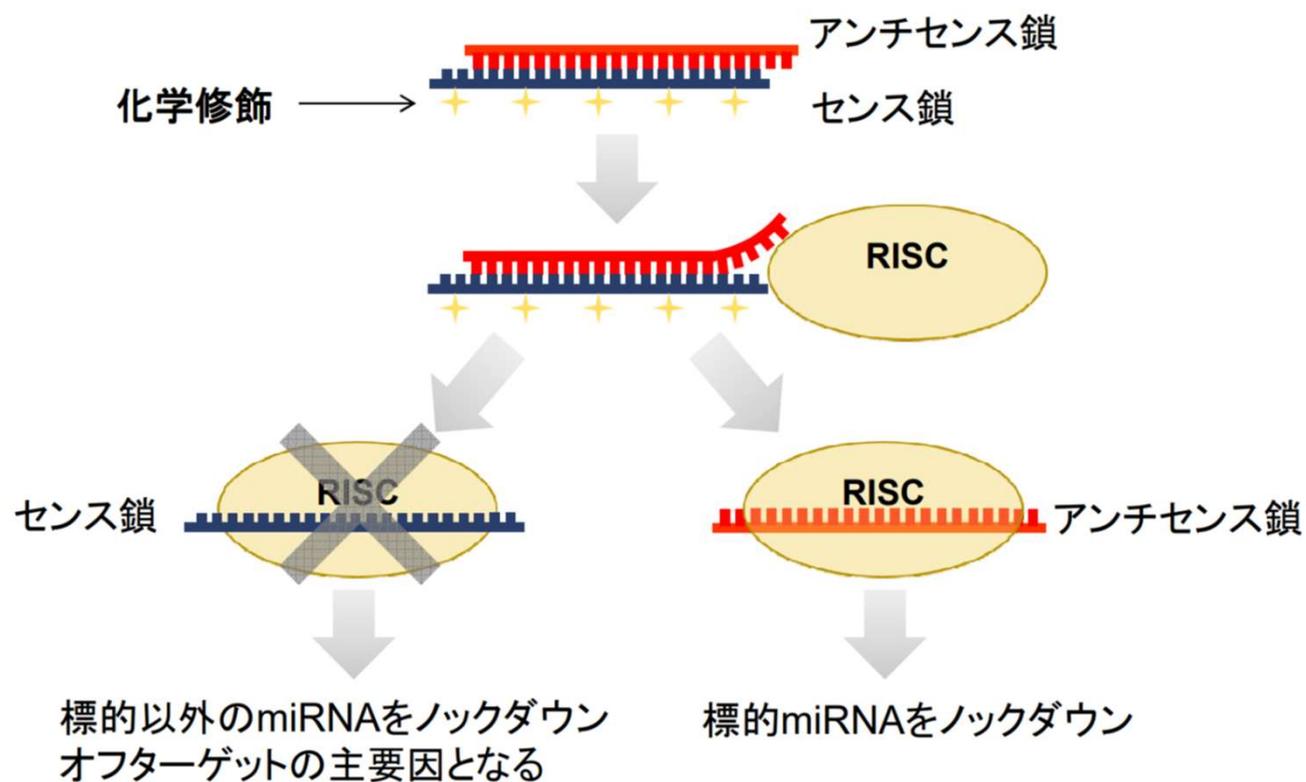


Off-target effect

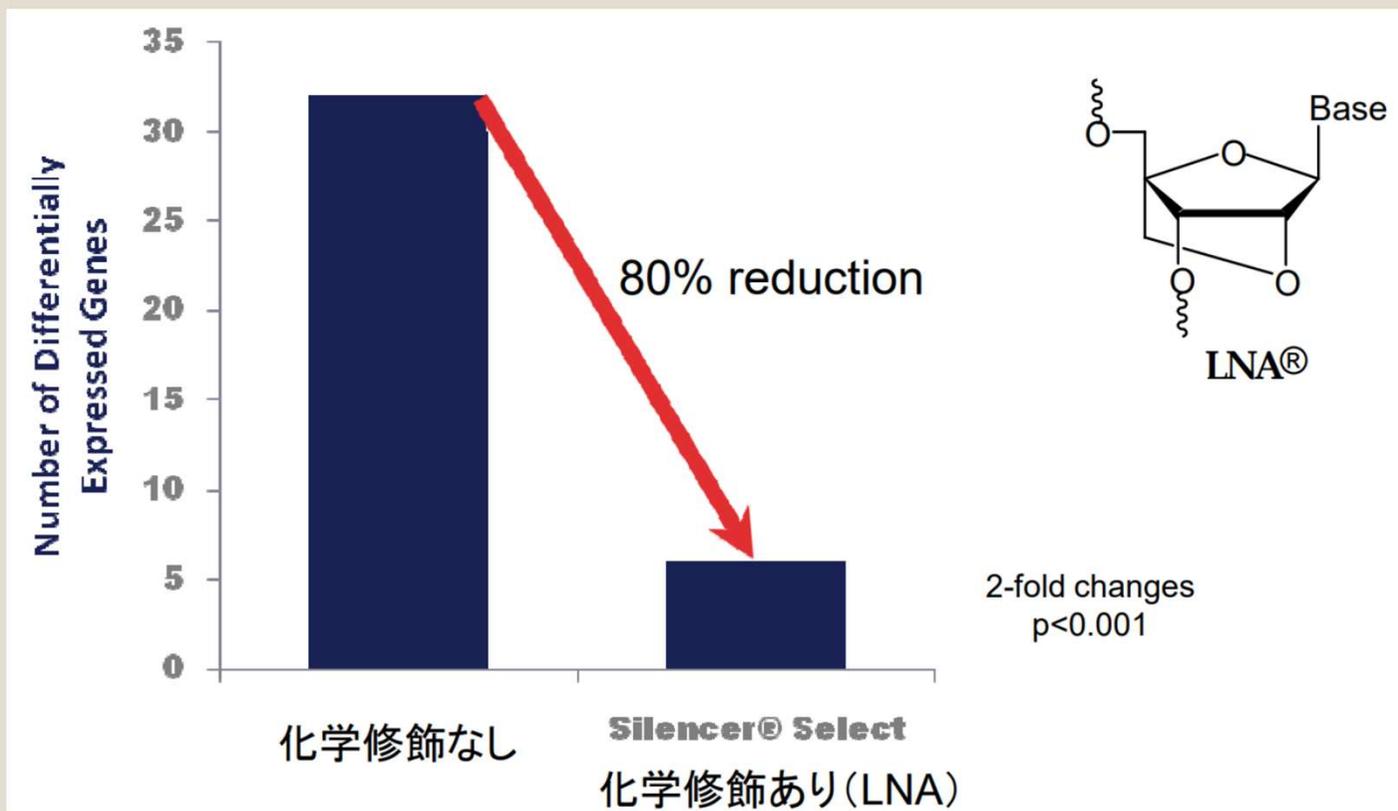
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To repress off-target effect

- Low concentration
- Chemical modification



センス鎖を化学修飾により非活性化することで、センス鎖がRISCに取り込まれるのを防ぐことが可能



Application

- Gene knockdown
- Functional genomics
- Medicine
- Biotechnology

Patisiran

- the first small interfering RNA-based drug
- medication for the treatment of polyneuropathy
- C₄₁H₅₂O₂₉N₁₄P₄
- 21 bp

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参考文献

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