

We release supplementary information to the release on May 25, 2009
**“Signing of Exclusive Licensing Agreement Concerning
Cationic Polyamino Acids with The University of Tokyo and TODAI TLO, Ltd.”**

Contact:
President's office, NanoCarrier Co., Ltd.
TEL: 81-3-3548-0213
E-mail: info@nanocarrier.co.jp

Supplement to the release on May 25, 2009

“Signing of Exclusive Licensing Agreement Concerning Cationic Polyamino Acids with The University of Tokyo and TODAI TLO, Ltd.”

The license agreement gives NanoCarrier the opportunity to expand R&D activities by introducing new technology.

NanoCarrier obtained two delivery technologies for siRNA medicine

➤ **New delivery technology using cationic polyamino acid**
(Non micelle*)

- Release siRNA into cytoplasm by forming macromolecular ionic complex with siRNA

➤ **Conventional delivery technology using micellar nano-particle.**

- Form siRNA micelles stable in the body with pegulated cationic polymers

*possible to bind siRNA to hydrophilic polymers and form siRNA micelles

Application and Issue of siRNA Micelle

siRNA (small interfering RNA)

Found through the mechanism which cells utilize to prevent virus infection

Small molecular double-strand RNA with 21 to 23 base pairs interferes with expression of the specific gene



Applied to siRNA pharmaceuticals

Inhibit the production of the specific protein causing the disease → Therapeutic effects

Target disease of siRNA pharmaceuticals

Cancer, AMD¹⁾, CNV²⁾, RSV³⁾, DME⁴⁾, ARF⁵⁾, Asthma, Hyper-lipidemia, etc.

- 1) age-related macular degeneration, 2) choroidal neovascularization, 3) respiratory syncytial virus,
4) diabetic macular edema, 5) acute renal failure

Problem of developing of siRNA as drug candidate

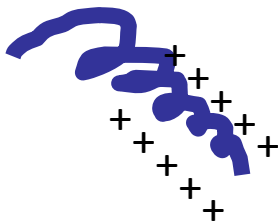
1. **Rapidly excreted from kidney** if dosed intravenously
2. **Unstable** in the body and **easily degraded**
3. **Difficult to be transported into cells** due to large molecular size and hydrophilicity

Cationic Polyamino Acid and siRNA

~ New Technology ~

Break-through for the development of siRNA pharmaceuticals

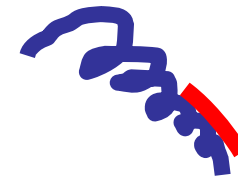
- Form macromolecular ionic complex and **stabilize siRNA**
- Design of polymer to **transport siRNA into cytoplasm**
- Delivery system suitable for local administration
- **Sustained release in the blood** by PEG-bound micellar nanoparticles



Positively charged polyamino acid



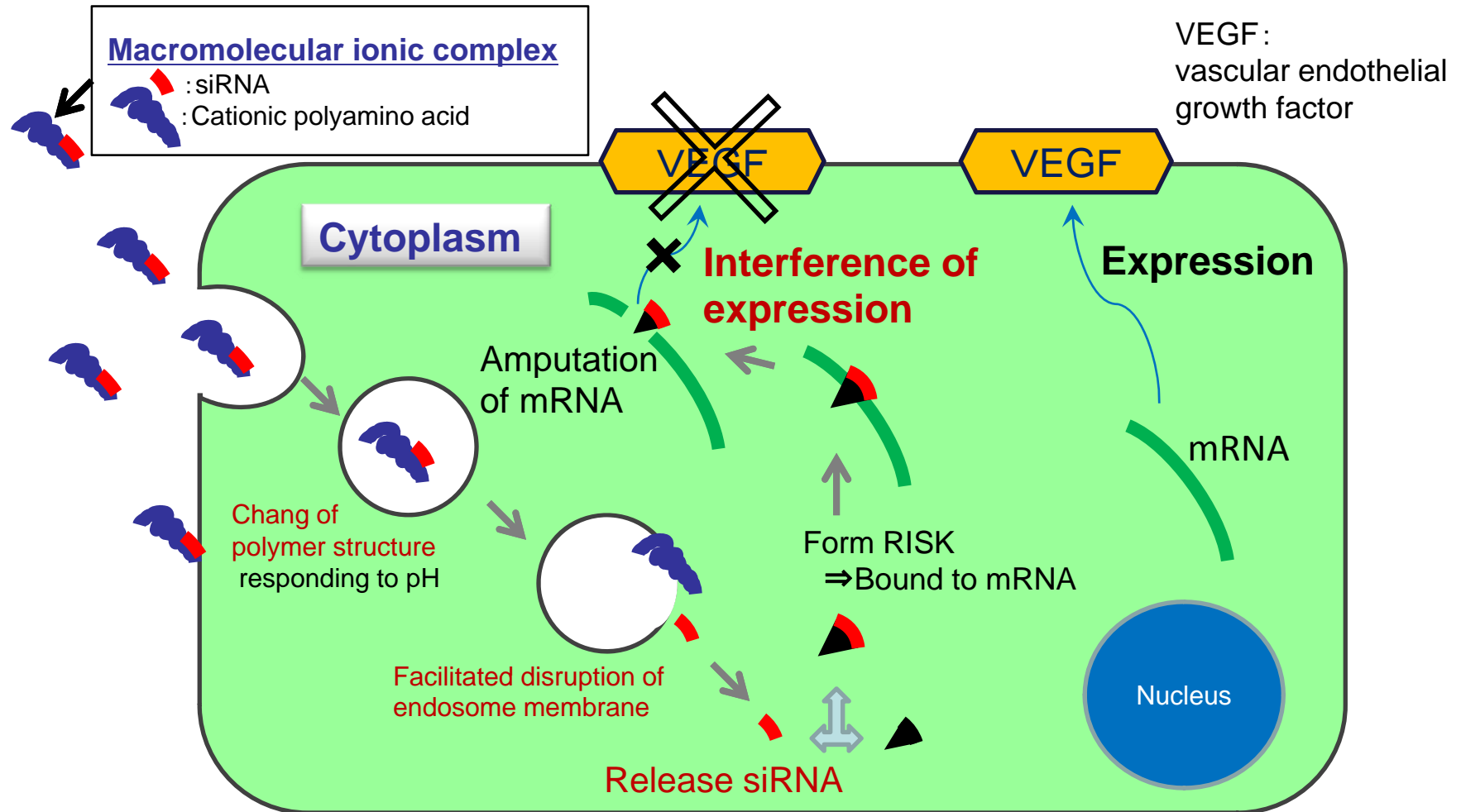
Negatively charged siRNA



Macromolecular ionic complex

Expected Intra-Cellular Mode of Action

~ Case of Macromolecular ionic complex ~



mRNA (messenger RNA): RNA having information of base sequence necessary for protein synthesis

RISC: RNA-induced silencing complex

siRNA is bound to homologous mRNA,
 amputates its specific site and interferes with the expression of target gene