Press conference　　Notice of Holding

“Developing a nanomachine which associates with nucleic acid pharmaceuticals in a rendezvous like manner in vivo to target brain tumors”

1. Visit Date:　Tuesday, 23th April, 2019　at　14:00　~　15:00

2. Visit location: Innovation Center of NanoMedicine (iCONM),
KAWASAKI INSTITUTE OF INDUSTRIAL PROMOTION
3rd Floor, 3001 Room
〒210-0821　3-25-14 Tono-machi, Kawasaki-ku , Kawasaki City,
Kanagawa Prefecture (see Appendix)
https://iconm.kawasaki-net.ne.jp/en/contact.html

3. Attendee

・Kazunori KATAOKA
Director General, Innovation Center of NanoMedicine(iCONM) / Professor, The University of Tokyo Institute for Future Initiatives

・Kanjiro MIYATA
Associate Professor, Department of Materials Engineering, Graduate School of Engineering, The University of Tokyo .

4. Point of publication

◆We have successfully developed a nanomachine to stably protect deactivation-prone nucleic acid pharmaceuticals by trapping (rendezvous) and selectively docking them in the bloodstream.
◆ This successfully delivers nucleic acid drugs to refractory cancers such as pancreatic cancer and brain tumors for targeted therapy.
◆This nanomachine has simultaneously realized the protection of nucleic acid pharmaceuticals in the bloodstream, which has been difficult so far, and an ultra-small size (less than 30 nm) that breaks through the biobarrier existing in intractable cancer tissues.

5. Publication overview:

A research group of Kazunori KATAOKA (Director General, Innovation Center of NanoMedicine / Professor, The University of Tokyo Institute for Future Initiatives) and, Kanjiro MIYATA (Associate Professor, Department of Materials Engineering, Graduate School of Engineering, The University of Tokyo), succeeded in developing the Nucleic Acid Medicine-loaded Nanomachine, a technology that can stably protect nucleic acid drugs that are prone to deactivation in the bloodstream and deliver them to intractable cancers such as pancreatic cancer and brain tumors.

Nucleic acid pharmaceuticals such as Small interfering RNA(siRNA) are promising new therapeutic agents for intractable diseases derived from gene mutations such as cancer and Alzheimer's disease, because they can regulate the expression of certain genes according to their base sequence. However, nucleic acid drugs are quickly metabolized in the body, e.g. in the bloodstream. As a result, nucleic acid pharmaceuticals have a low efficiency in reaching diseased tissues, resulting in inadequate therapeutic effect.

We have now developed a nucleic acid pharmaceuticals-loaded nanomachine to solve this problem. The nanomachine is composed of polymers that can be reversibly-docked with nucleic acid pharmaceuticals in a rendezvous like manner in the bloodstream. As a result, the nucleic acid pharmaceuticals are protected from degradation-enzymes by docking with the nanomachine. In addition, this nanomachine can break through various barriers present in living organisms due to its small size comparable to the one of antibodies (~20 nm).

As specific examples, we successfully deliver nucleic acid drugs to cancer cells through a bio-barrier called the blood brain tumor barrier which is present in brain tumors, and through fibrous stromal tissue (mesh structure) which is present in pancreatic cancer tissues.

The shape and length of the constituent polymers are important for the design of such nucleic acid pharmaceuticals-loaded nanomachines. The polymers created in this study incorporate designs that bind nucleic acid pharmaceuticals in blood while suppressing adsorption to other biological components.

Currently, efforts are underway to make this nucleic acid-based nanomachine practical as a drug. There is great promise for emerging new treatments for pancreatic cancer and brain tumors.

6. Published journals:

Journal name: "Nature Communications"
Article titles; In vivo rendezvous of small nucleic acid drugs with charge-matched block catiomers to target cancers:
Authors: Sumiyo Watanabe,Kotaro Hayashi,Kazuko Toh,Hyun Jin Kim,Kanjiro Miyata *, and Kazunori Kataoka *, et al
DOI number: 10.1038/s41467-019-09856-w

7. Precautions :

Publication before April 24, 2019 (Wednesday) 6:00 PM (UK time: 24 (Wednesday) 10:00 AM) is forbidden.

8. Contact:

[Matters related to research content].

Kazunori KATAOKA
Director General of the Innovation Center of NanoMedicine(iCONM), KAWASAKI INSTITUTE OF INDUSTRIAL PROMOTION / Professor, The University of Tokyo Institute for Future Initiatives
TEL: +81-44-589-5700 E-mail: kataoka@ifi.u-tokyo.ac.jp

Kanjiro MIYATA
Associate Professor, Department of Materials Engineering, Graduate School of Engineering, The University of Tokyo
TEL: +81-3-5841-0862 E-mail: miyata@bmw.t.u-tokyo.ac.jp

[Regarding COI programs].

Shigeki SAKAI
Innovation Center Promotion Department, COI Group, Japan Science and Technology Agency (JST)
TEL: +81-3-5214-7997 E-mail: coi@jst.go.jp

[Other matters].

COINS Research Promotion Support Office
Innovation center of NanoMedicine(iCONM),
KAWASAKI INSTITUTE OF INDUSTRIAL PROMOTION
TEL: +81-44-589-5785 E-mail: jimukyoku-coins@kawasaki-net.ne.jp

The University of Tokyo, School of Engineering Public relations office
TEL: +81-3-5841-1790 E-mail: kouhou@pr.t.u-tokyo.ac.jp

9. Attached documents :

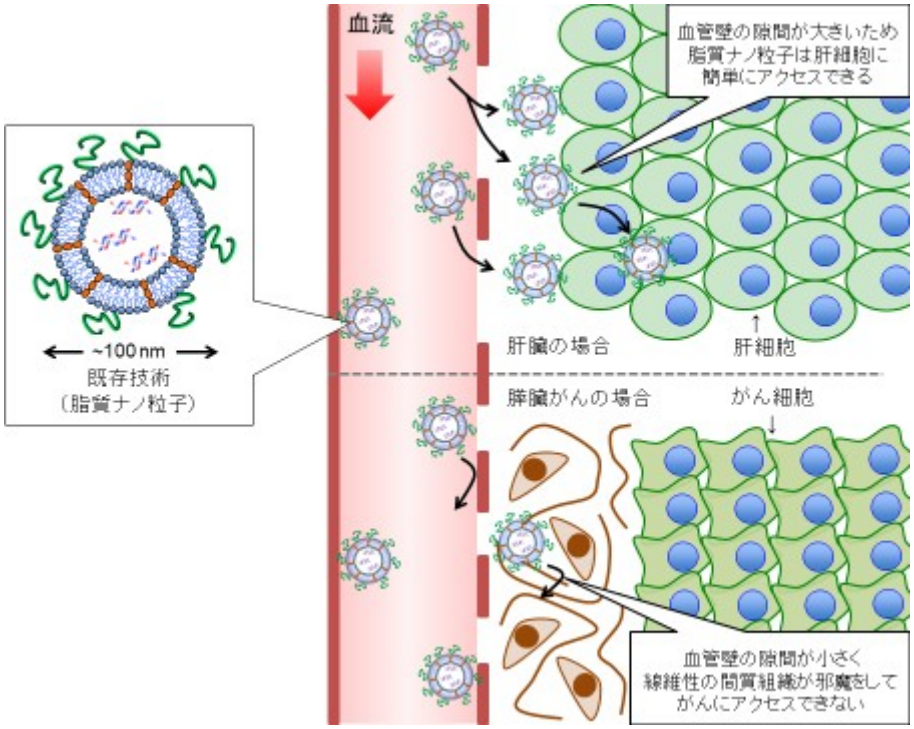

Figure 1. Challenges of Existing Technologies.
Lipid nanoparticles with a particle size of 100 nm are readily accessible to the liver with a large gap in the vessel wall. On the other hand, in the case of pancreatic cancer, cancer cells cannot be accessed because of the small gap in the blood vessel wall and the spread of fibrous stromal tissue outside the blood vessels as a "biobarrier".

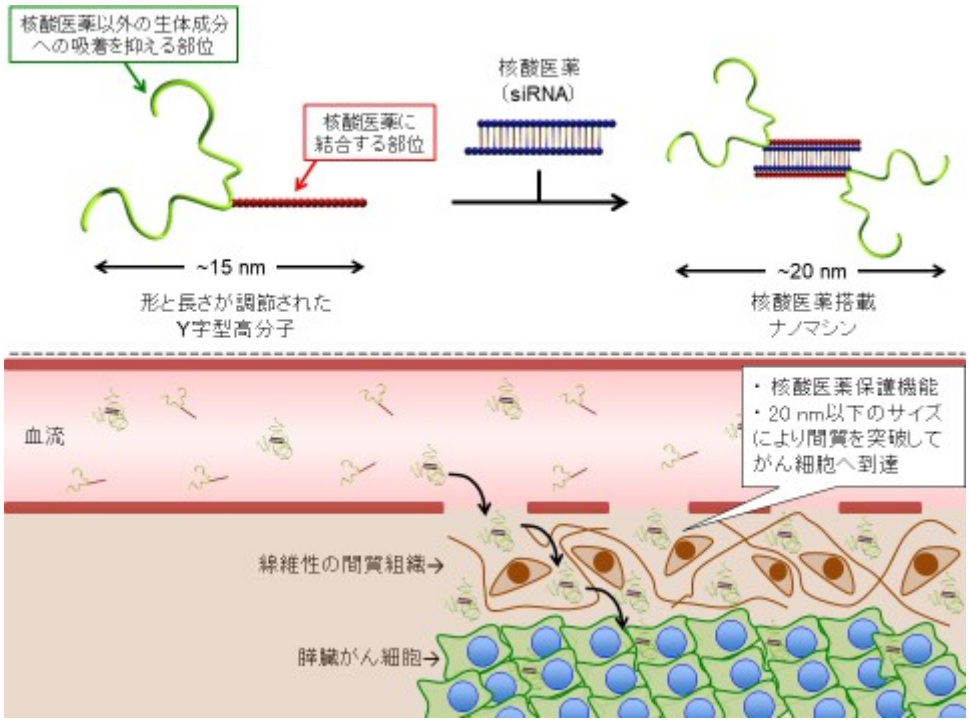

Figure 2. Nucleic Acid Medicine-loaded Nanomachines, a technology that solves the problem
The length-regulated Y-shaped polymers bind one to two molecules to a single nucleic acid drug (siRNA). This allows for significant downsizing compared to existing technologies. Furthermore, this Y-shaped polymer can bind to nucleic acid pharmaceuticals while replacing each other in the bloodstream, dynamically and stably protecting nucleic acid pharmaceuticals due to its high selective binding ability to nucleic acid pharmaceuticals. As a result, the nucleic acid drug-loaded nanomachine can penetrate the interstitial tissue of tumor tissue and reach pancreatic cancer cells.

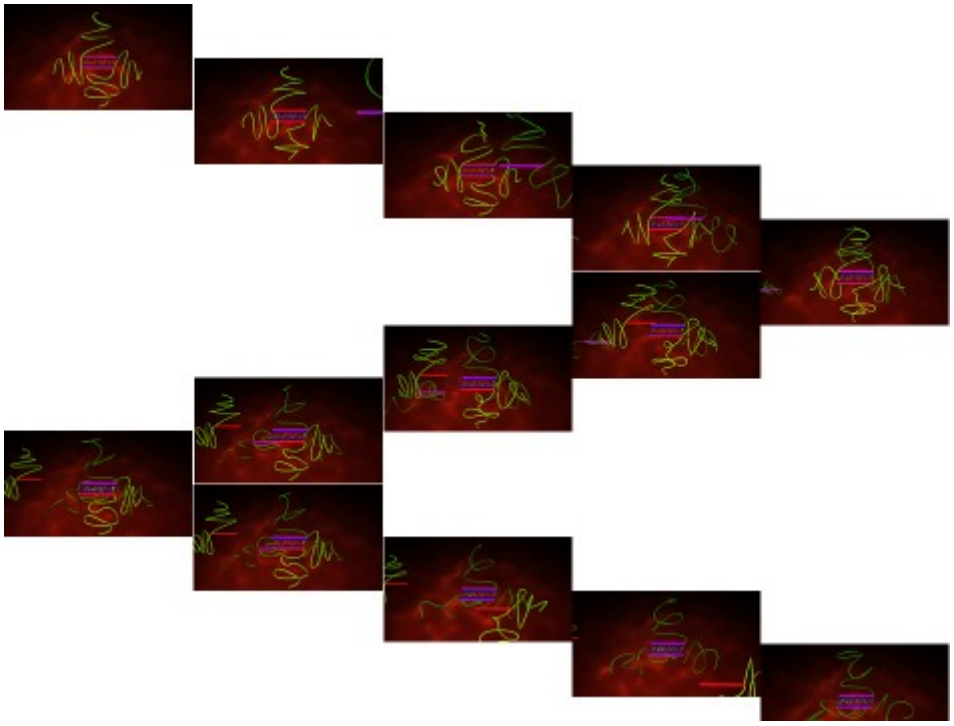

Figure 3. Y Snapshots of in vivo landeviews of shaped polymers and nucleic acid pharmaceuticals
Y Shaped macromolecules protect the siRNA while interchanged with each other in the bloodstream.
The original movie is Nature
Viewable in the Supplementary Movie 1 of the article on the Communications.

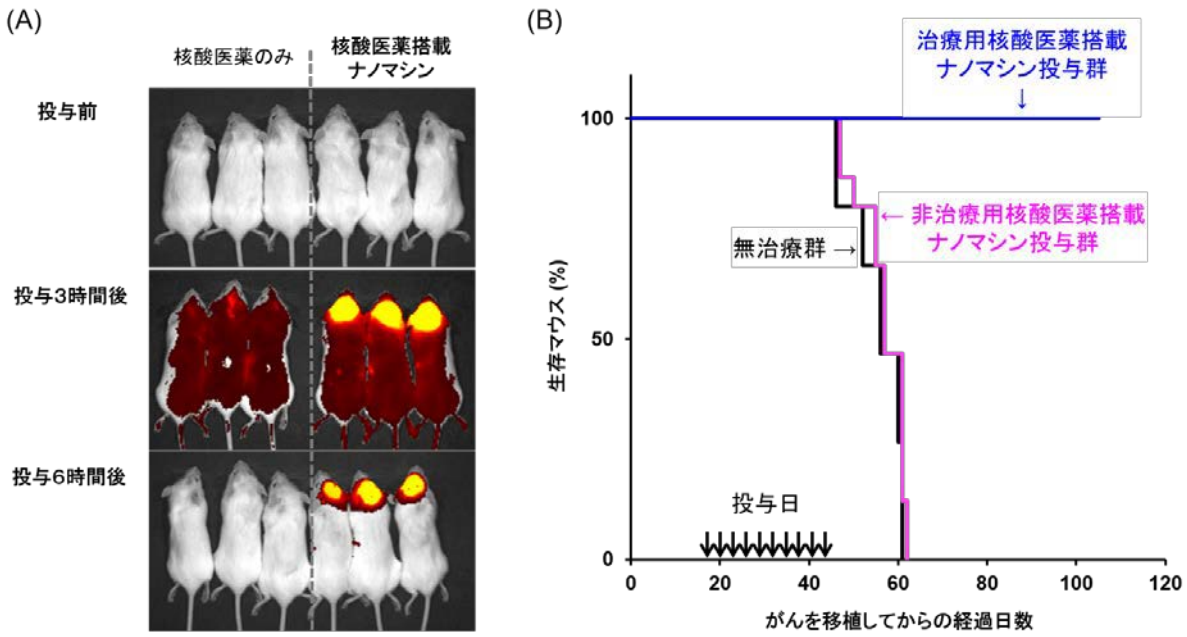

Figure 4. (A) Brain tumor clustering of fluorescently labeled nucleic acid pharmaceuticals in brain tumor orthotopic transplantation model mice.
Six hours after administration, no accumulation of nucleic acid drugs in brain tumors was observed in the group that received the nucleic acid drug only (no nanomachine). On the other hand, the accumulation of nucleic acid pharmaceuticals in brain tumors was clearly observed in the nucleic acid pharmaceuticals-loaded nanomachine administration group.
(B) Survival assessment of brain tumor orthotopic transplantation model mice.
The untreated group and the non-therapeutic nucleic acid drug-loaded nanomachine-treated group all died 60 days after the cancer was transplanted. On the other hand, in the nanomachine administration group with a nucleic acid drug for therapeutic use, an excellent therapeutic effect was observed, in which all cases survived even after 100 days.

Attachment

<Access to venues>

Innovation Center of NanoMedicine (iCONM)

Address: 3-25-14, Tonomachi, Kawasaki-ku, Kawasaki City 210-0821, JAPAN

Tel: +81-44-589-5700

Access by train:

Keikyu-Kawasaki Sta. to Kojima-Shinden Sta. by Keikyu-Daishi Line (ride time about 10 minutes) and Walk about 15 minutes to iCONM (See below access map)

Access by bus

“Bus stop on East Terminal at JR Kawasaki Sta.”

■Bus Stop 20

・川02「King Skyfront East “キングスカイフロント東”」(Rinko Bus) for 30 mins. get off at「King Skyfront West “キングスカイフロント西”」. Walk 2 mins. to iCONM.

・Express「Ukishimabashi “浮島橋”」(Rinko Bus) for 20 mins. get off at 「King Skyfront Entrance “キングスカイフロント入口”」. Walk 5 mins. to iCONM.

■Bus Stop 16

・川03「Ukishima Bus Terminal “浮島バスターミナル”」(Rinko Bus or Kawasaki City Bus) for 30 mins. get off at「King Skyfront Entrance “キングスカイフロント入口”」

Walk 5 mins. to iCONM.

Access by Taxi

■From JR Kawasaki St. Eats Exit: 20 mins. ■From JR Kamata St. East Exit: 20 mins.

Access Map

Go straight between ▲CIEA (the Central Institute for Experimental Animals) and ◆FUJIFILM