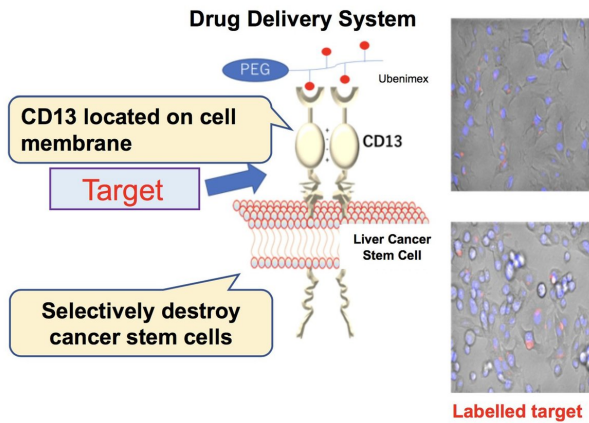


# Anticancer drugs delivered by a new drug delivery system reduce tumor size

8 August 2018



block copolymer-ublenimex conjugate (PEG-b-PLys(Ube)). The use of this DDS has enabled an increase in the concentration of ublenimex in target CSCs. In addition, combined use of standard anticancer drugs significantly decreased CSCs. (Figure 1) Their [research results](#) were published in *Oncogene*.

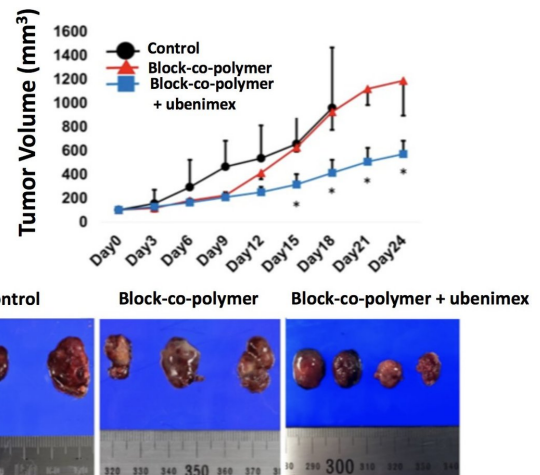
Lead author Masamitsu Konno says, "First, we developed a DDS to deliver highly concentrated ublenimex and then, another DDS in which 20 ublenimex molecules were bound with poly(ethylene glycol)-poly(lysine) block copolymer conjugates."

Outline of the drug delivery system (DDS) created in this study. Credit: Osaka University

Cancer tissue cells are divided into two major groups: cancer cells and cancer stem cells (CSCs). CSCs are related to cancer progression and dissemination, so it's necessary to eradicate CSCs in order to cure cancer. However, because CSCs are resistant to chemotherapy and radiotherapy, cancer is refractory.

A research group from Osaka University, in collaboration with Tokyo Institute of Technology, had found that there were CD13 surface markers in hepatocellular carcinoma (HCC) stem cells. When CD13 inhibitor ublenimex is added to CSCs, HCC stem cells cause apoptosis (programmed cell death), becoming extinct. However, because CSCs only reside in part of tumor tissues, it's imperative to develop a method for delivering drugs in high concentration to target sites.

The researchers created a [drug](#) delivery system (DDS) using a poly(ethylene glycol)-poly(lysine)



Comparative testing: saline solution (control), block copolymer only, block copolymer and ublenimex are administered to mice with hepatic cancer. Days after drug administration and tumor growth in hepatic cancer mice show that hepatic cancer cells significantly reduce in mice that received block copolymer and ublenimex. Credit: Osaka University

Using this method, they performed intraperitoneal

administration and intravenous injection of ubenimex in mice, finding that the tumor size was significantly reduced. (Figure 2) This shows that it has become possible to deliver ubenimex to CSCs in high concentration.

Next, the combined administration of ubenimex and existing anticancer drugs (fluorouracil (5-FU), cisplatin (CDDP), and doxorubicin (DXR)) was performed, enhancing apoptosis in vitro synergistically in CSCs in mice.

Corresponding author Hideshi Ishii says, "Our research results will promote the application of drugs whose medical effects on CSCs were verified but there were challenges in their delivery to target sites, which will promote repositioning, i.e., the drugs will be used to treat different diseases. Block copolymers used in the DDS in this study can be easily produced and exhibit strong effects, allowing them to be used for the application of other drugs as well."

**More information:** Reishi Toshiyama et al, Poly(ethylene glycol)–poly(lysine) block copolymer–ubenimex conjugate targets aminopeptidase N and exerts an antitumor effect in hepatocellular carcinoma stem cells, *Oncogene* (2018). DOI: [10.1038/s41388-018-0406-x](https://doi.org/10.1038/s41388-018-0406-x)

Provided by Osaka University

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