Novel SN-38 Derivatives

~ A Nano Carrier-free Prodrug for High Anti-Tumor Activity and Safety ~

KEY INVENTION

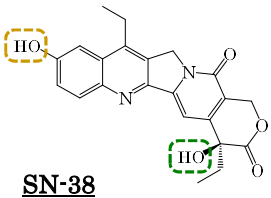
- A prodrug utilizing SS bond reduction by glutathione (GSH) localized in tumors
- A nano carrier-free DDS designed by making the drug itself into nanoparticles

➡ *For development of a novel drug showing a high anti-tumor activity and safety!*

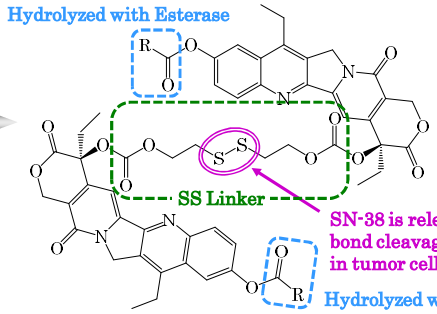
(A medical doctor-led clinical trial is expected to be carried out.)

[Disadvantage of Current Nano Carriers and Prodrugs]		[Advantage of SN-38 Derivatives]
◎ Nano Carriers (LNP, etc.)		
• High Liver Accumulation (>90%)	➡	• High Target Cell Accumulation
• Low API Loading (<10%)	➡	• High API Loading
• Side Effects by Carriers (other than API)	➡	• Nanoparticles by Drug Itself (No Carrier)
◎ Prodrug		
• Low efficacy and side effect by metabolism before delivery to the target cells	➡	• Poorly metabolized before delivery to the target cell (metabolized by GSH)

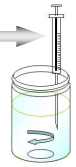
SUMMARY of INVENTION



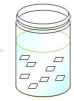
Dimerization



A DMSO Solution of SN-38 Derivatives

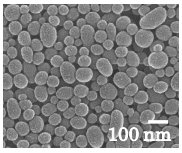


Reprecipitation



Ultrapure Water

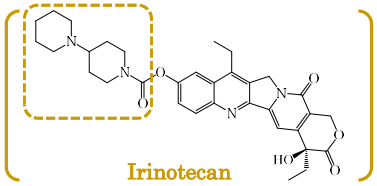
Water Dispersion (Nanoparticles)



High Dispersion Stability

SN-38

- Topoisomerase Inhibitor
- Low Water Solubility (<5 ppm)
- Prodrug (Irinotecan) is commercialized.



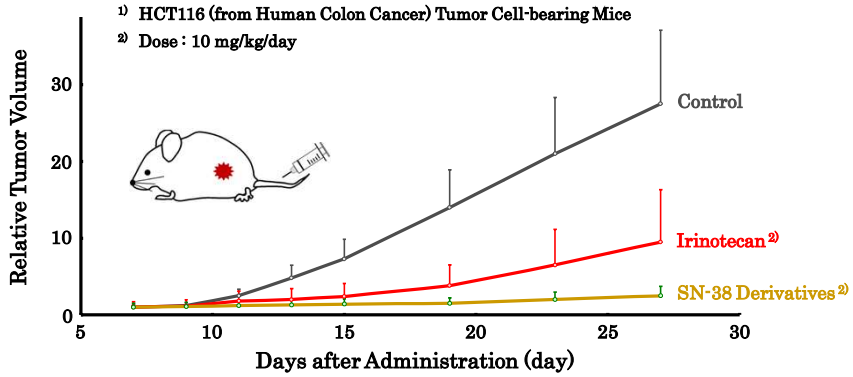
SN-38 Derivatives (SN-38 SS Linker Dimers)

- SN-38 Dimers through SS Linker including an SS Bond
- Prodrug utilizing SS Bond Cleavage (Reduction) by GSH
- Less impact on normal cells due to less GSH in the cells

COMPARISON with and ADVANTAGE over CURRENT TECHNOLOGY

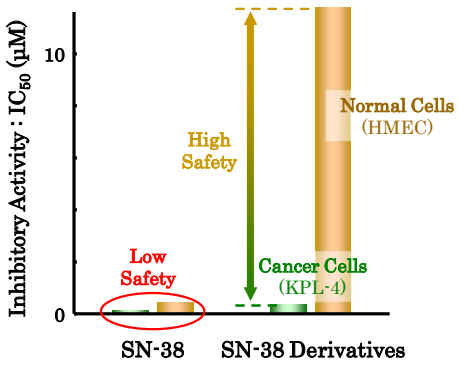
[Efficacy and Safety Comparisons of this Technology with Current Technology]

a. *in vivo* Trial (Mice [1], i.v.)



The anti-tumor activity of SN-38 derivatives is higher than that of Irinotecan.

b. Safety (SN-38 vs. SN-38 Derivatives)



The safety of SN-38 derivatives is higher than that of SN-38.

APPLICATION expected

◎ Development of Novel Anti-Cancer Drugs such as for Lung, Breast, Colorectal, Cervical or Stomach Cancers

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Licensable Patent

Title of Invention : SN-38 Derivatives, Nanoparticles including the Derivatives, Medicines and Production Methods of the Nanoparticles

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