TAIPEI MEDICAL UNIVERSITY

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Development of Hybrid Cell Membrane Nanovesicles for Enhanced Pancreatic Cancer Treatment

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International Ph.D. Program for Cell Therapy and Regeneration Medicine

CRS 2025 ANNUAL MEETING & EXPOSITION

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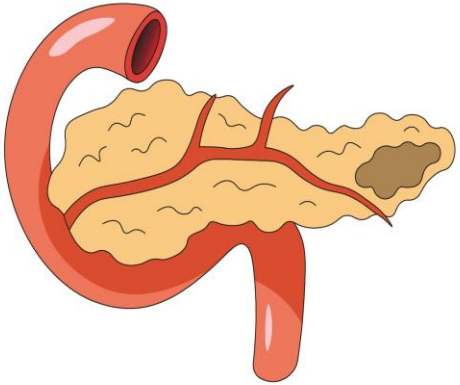
NEXT-GENERATION DELIVERY INNOVATIONS

The burden of pancreatic cancer

- 5% of all Cancer fatalities
- 5-year survival rate 12.8%
- 12th most common Cancer

Pancreatic Cancer (PC)



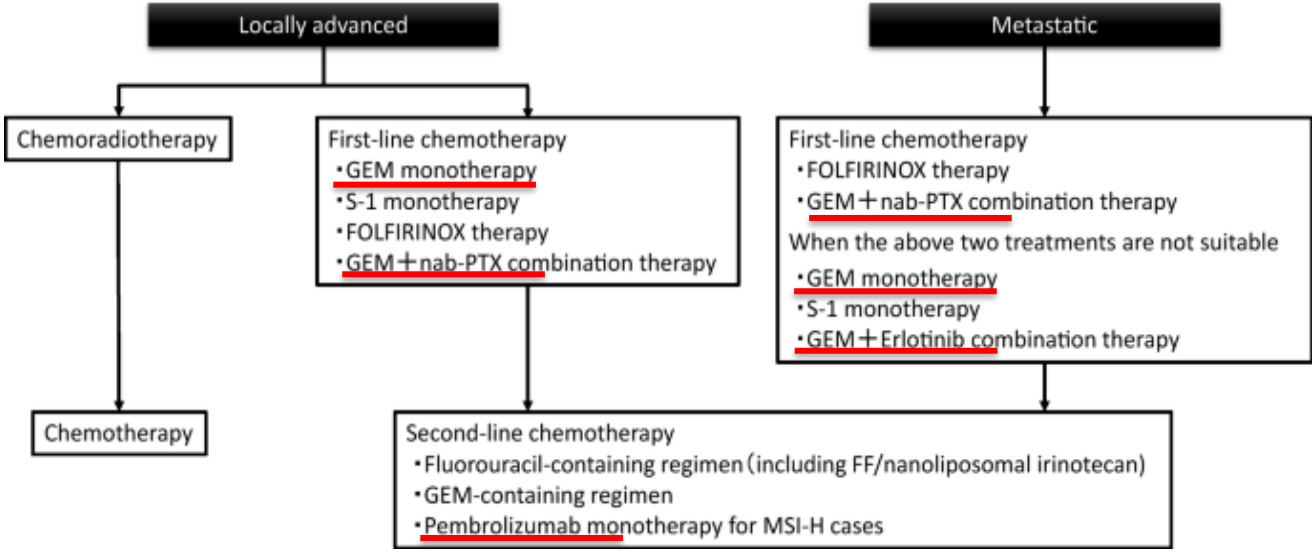
1990 — 2021

- ↑ 8.9% Global Incidence of PC
- Especially in higher SDI regions
- ↑ Early onset PC cases
- Particularly younger women

Zottl et al., Unraveling the Burden of Pancreatic Cancer in the 21st Century: Trends in Incidence, Mortality, Survival, and Key Contributing Factors, 2025

Pancreatic cancer treatment

Gemcitabine monotherapy/combination is still the first-line chemotherapy for pancreatic cancer



Resistance to **gemcitabine** and other chemotherapeutic drugs is one of main factors causing the failure of treatment of pancreatic cancer

Okusaka, et al., 2020. J Gastroentero

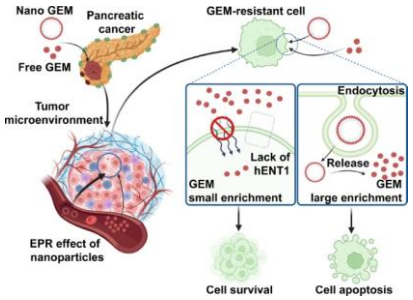
Strategies for addressing chemoresistance in pancreatic cancer

The cause of Gemcitabine resistance

- **Reduced Uptake of Gemcitabine:** Lor Altered Function of Nucleoside Transporters (hENT1)
- **Increased Efflux of Gemcitabine**
- **Role of Cell Membrane-Related Factors:** Epithelial-to-Mesenchymal Transition (EMT), CD44

The strategies to overcome Gemcitabine resistance

- **Targeting NTs**: Enhancing hENT1 expression or preventing its degradation
- Inhibiting Efflux Pumps, Blocking IGF1R Signaling
- **Nanoparticle-Based Drug Delivery**



Hong, et al., Nano Research, 2024

Development of new drug delivery systems

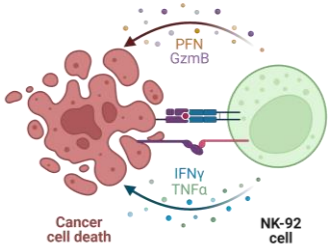
Have tumor-specific GEM delivery

Enhance intracellular uptake of GEM

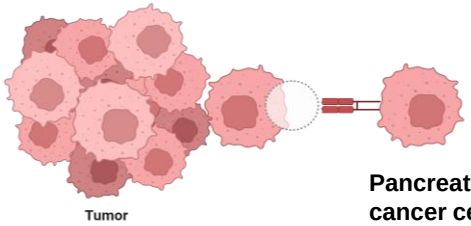
hENT1: human equilibrative nucleoside transporter 1

Purpose

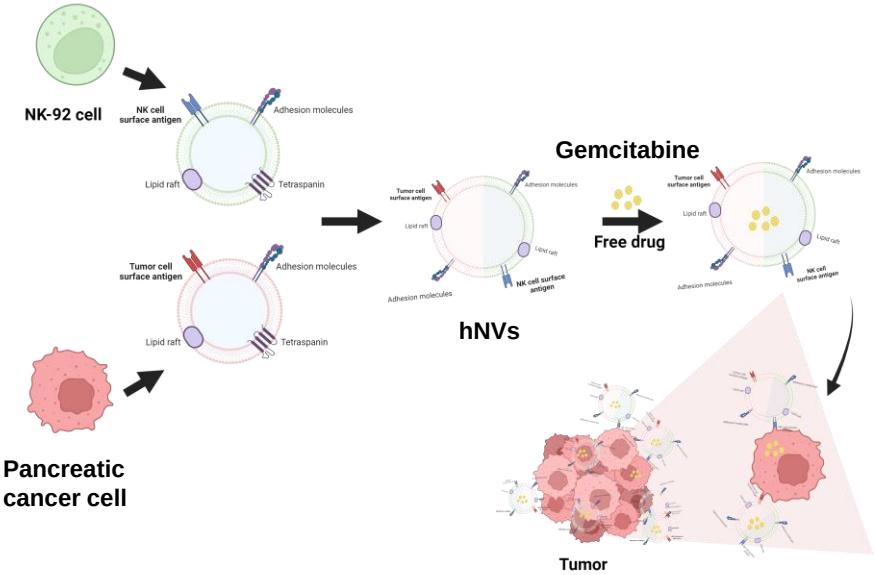
Development of Hybrid cell membrane-derived nanovesicles (hNVs) as potential drugs delivery system



Tumor recognition



Homologous targeting ability



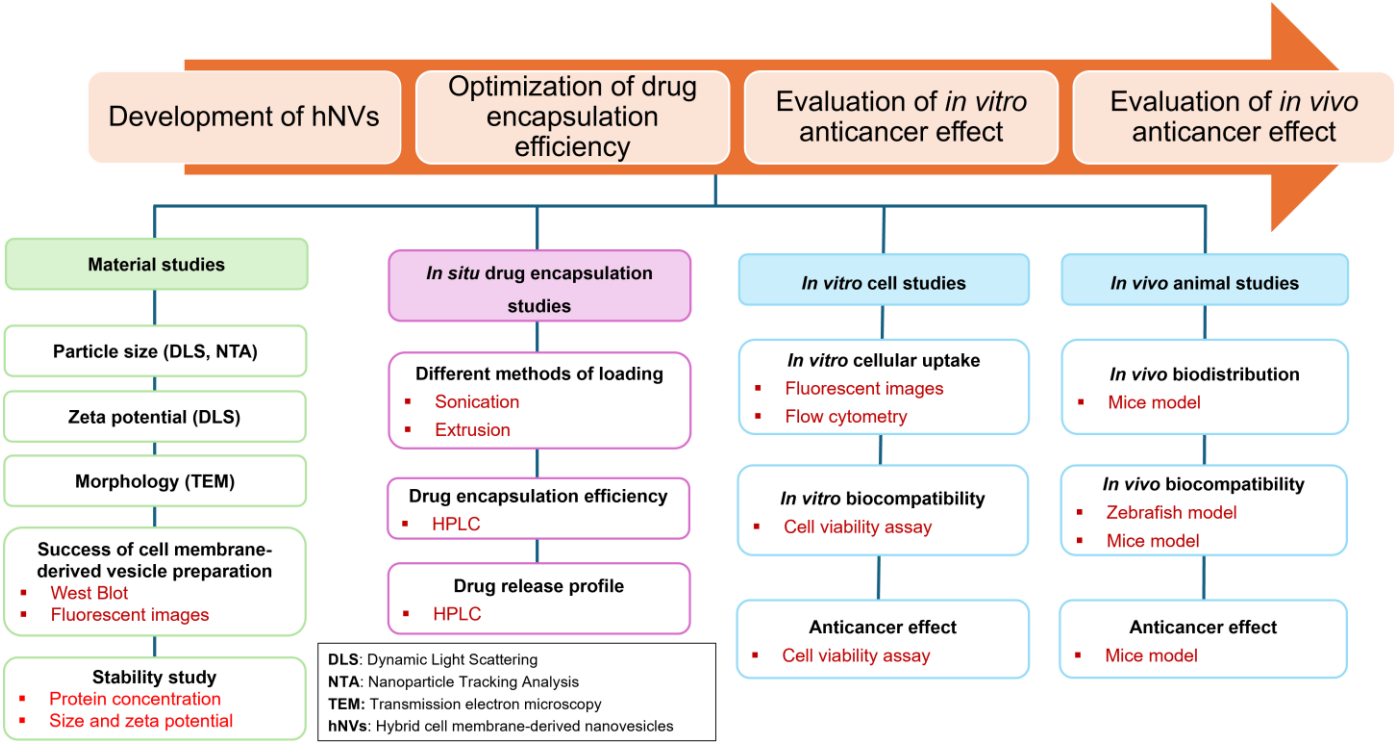
Enhance the specific tumor target

Avoid off-target

Reduce drug resistance

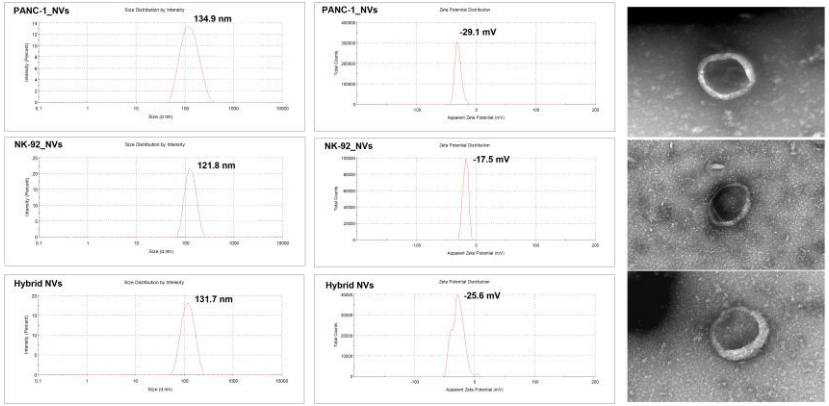
Aims

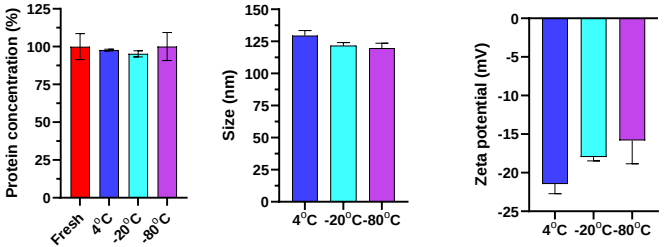
Development of Hybrid cell membrane-derived nanovesicles (hNVs) as potential drugs delivery system



Development of Hybrid cell membrane-derived nanovesicles (hNVs)

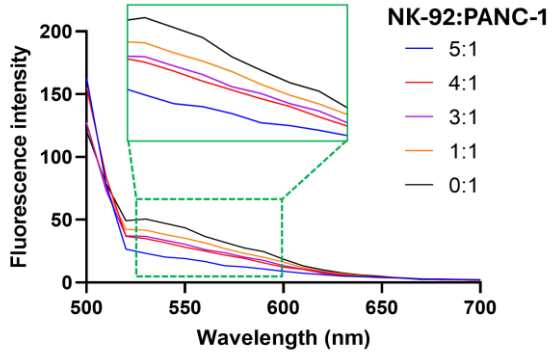
Characterization of nanovesicles

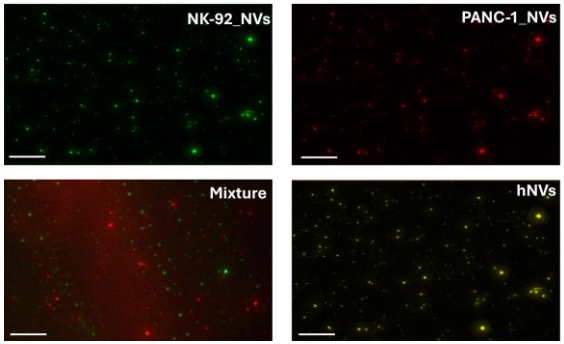




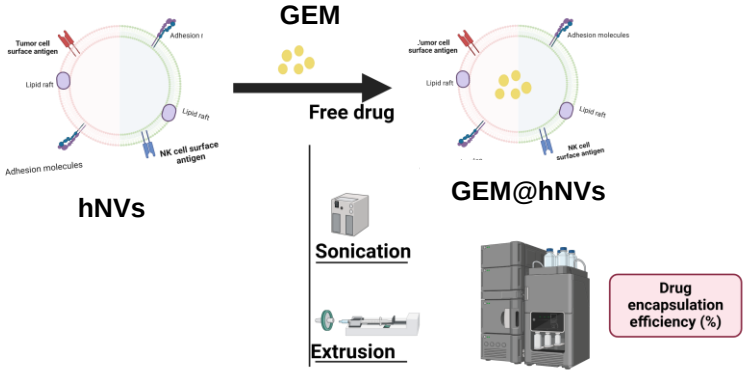
Protein concentration, size, and zeta potential of hybrid NVs under different storage conditions after 7 days.

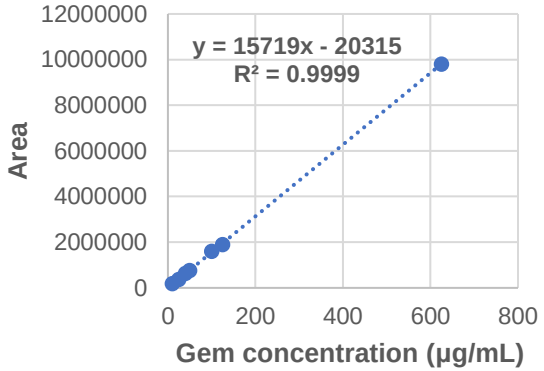
Successful preparation



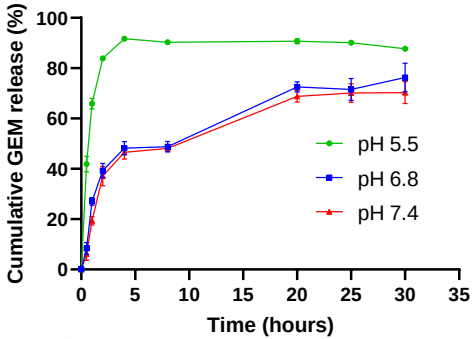


Drug encapsulation efficiency and release profiles

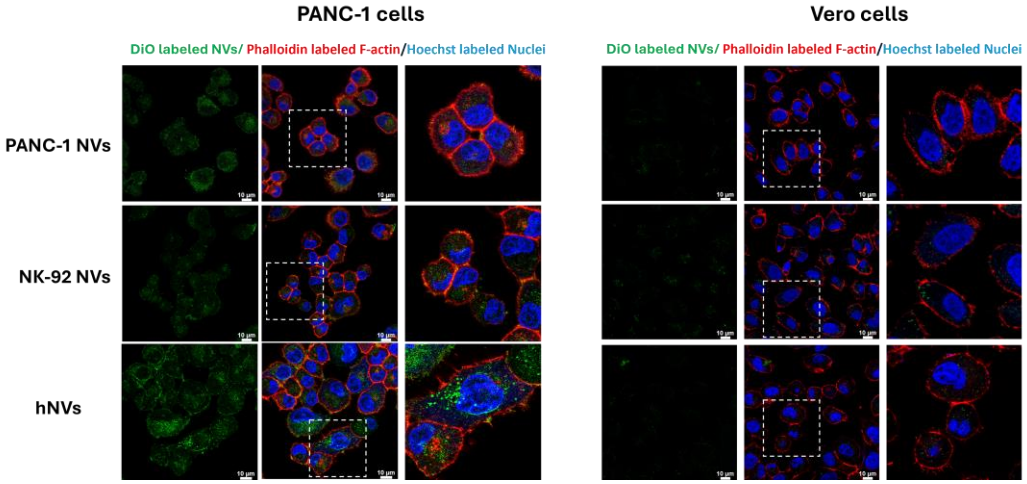


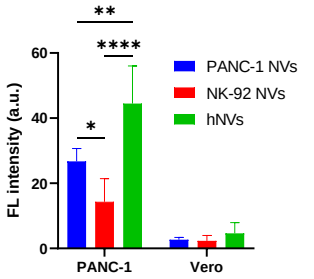


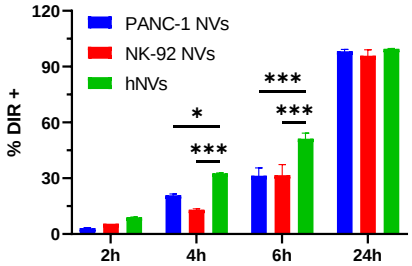
Methods	Encapsulation efficacy (EE%)
Sonication	32.51±0.58
Extrusion	51.97±1.75

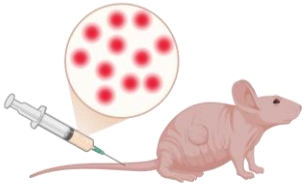


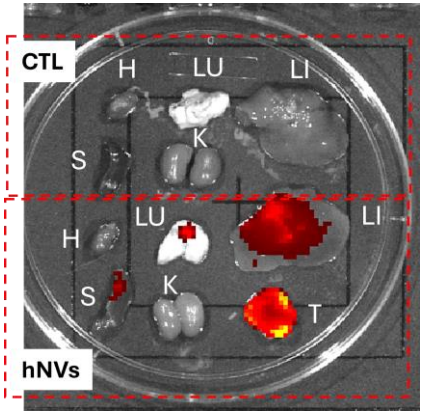
The high specific cancer target of hNVs





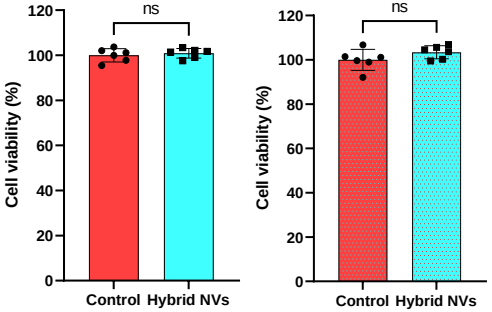




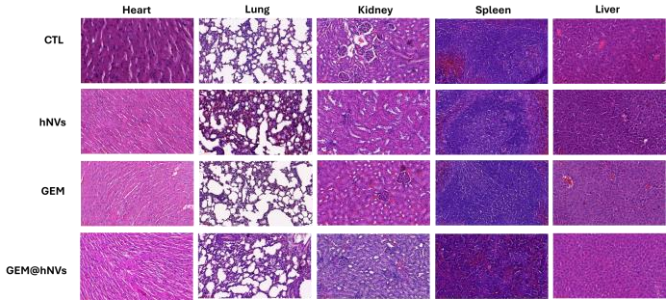


Representative fluorescence images of different organs after injection of of hNVs

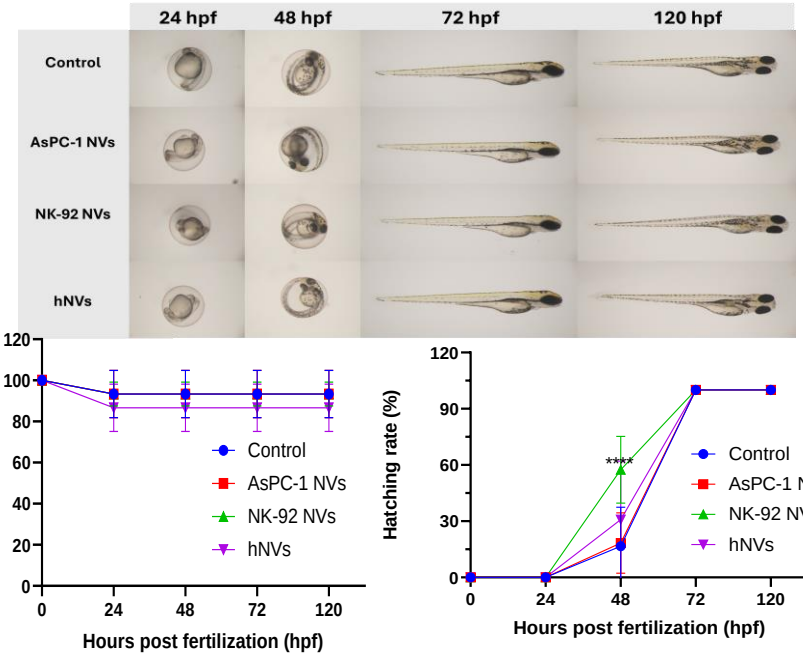
hNVs showed the high biocompatibility and safety



Cell viability of CCD-966SK normal cells and PANC-1 cancer cells after treatment of 50 μg protein of hNVs for 48h

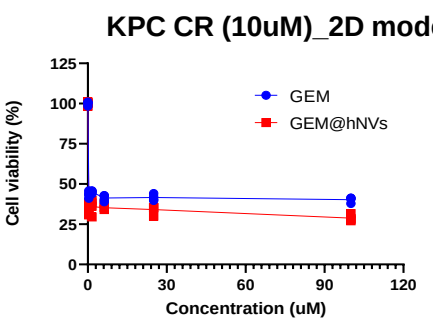


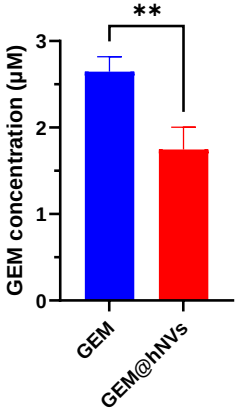
Representative H&E staining of organs after treatment for 4 weeks, Gem: 5mg/kg

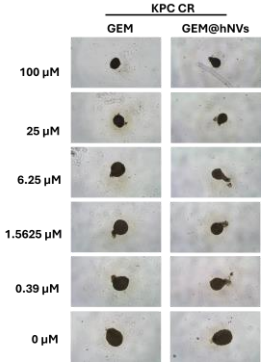


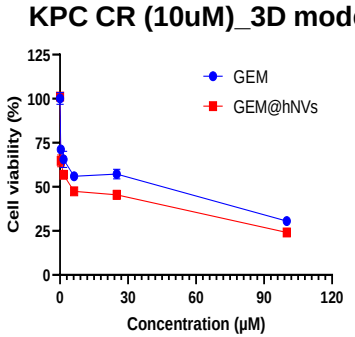
Representative morphology, Survival rate (%) and Hatching rate (%) of the development of zebrafish embryo to larval stage from the control group and after being exposed to 50 ug protein of AsPC-1 NVs, NK-92 NVs and hNVs groups

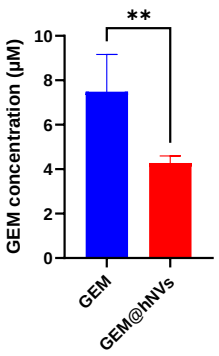
The high in vitro anti-cancer effect of GEM@hNVs

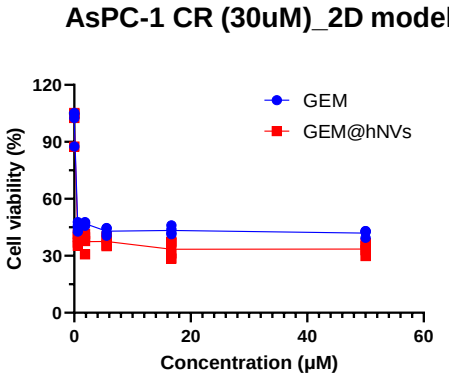


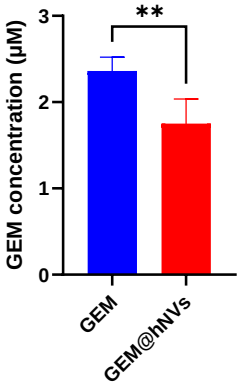


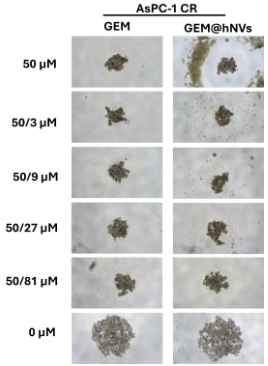


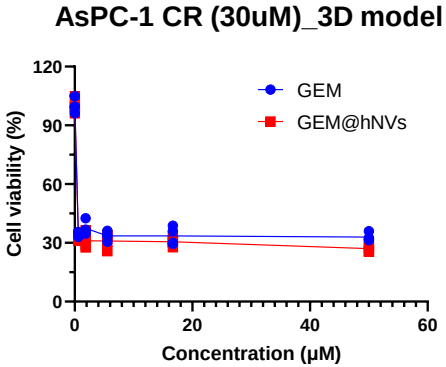


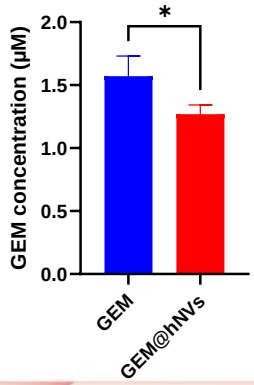




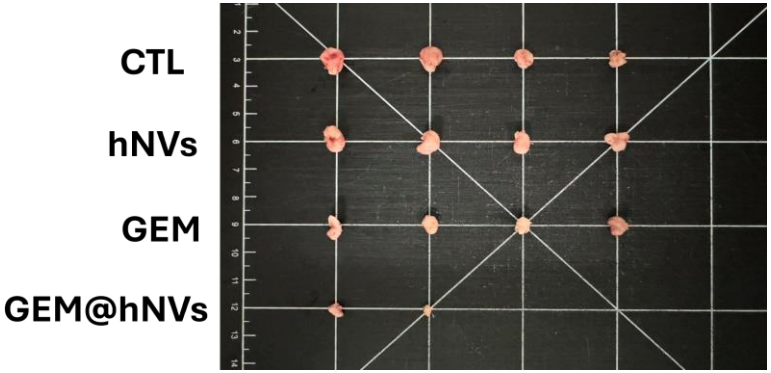


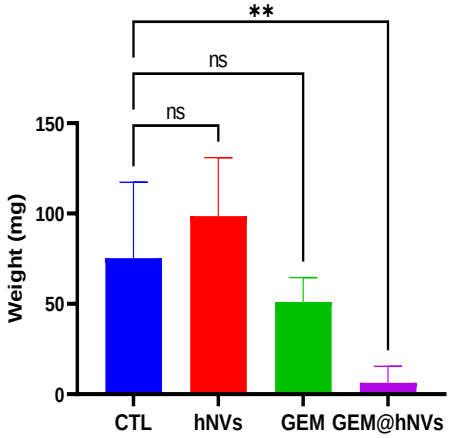






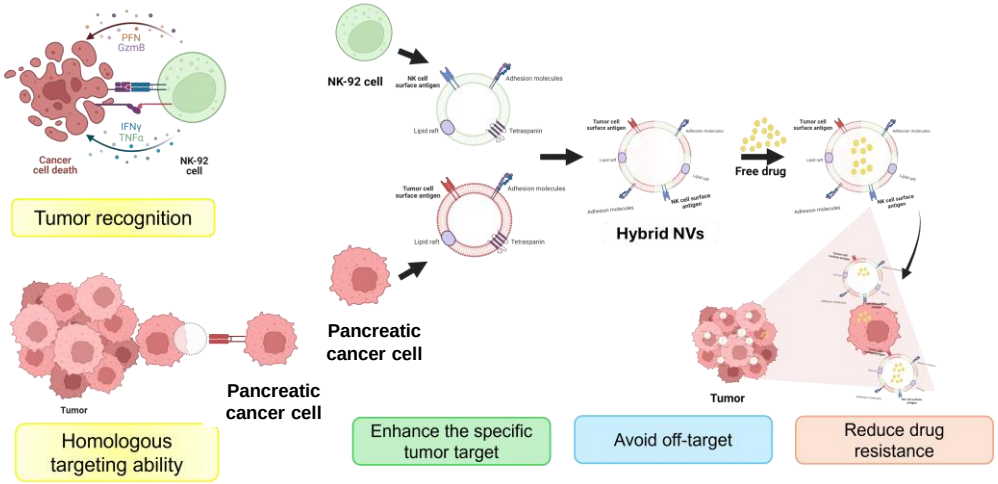
The high in vivo anti-cancer effect





Conclusion

By harnessing the complementary properties of immune cells with innate tumor-recognition capabilities and pancreatic cancer cells with inherent homing abilities, our hNVs offer a highly effective and selective drug delivery platform



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THANK YOU FOR YOUR ATTENTION!