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Dual Enzymatic Reaction-Assisted Gemcitabine Delivery Systems for Programmed Pancreatic Cancer Therapy

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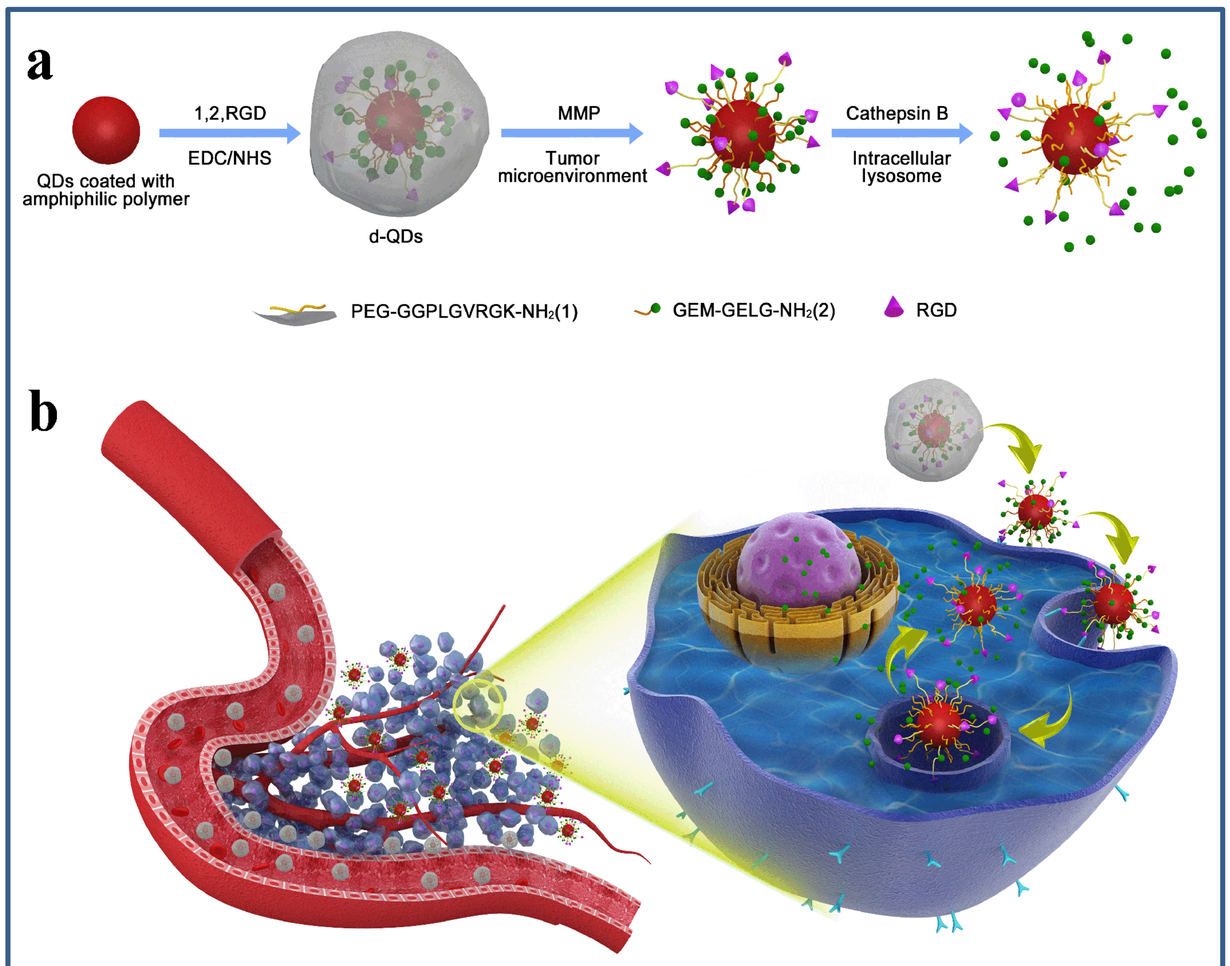
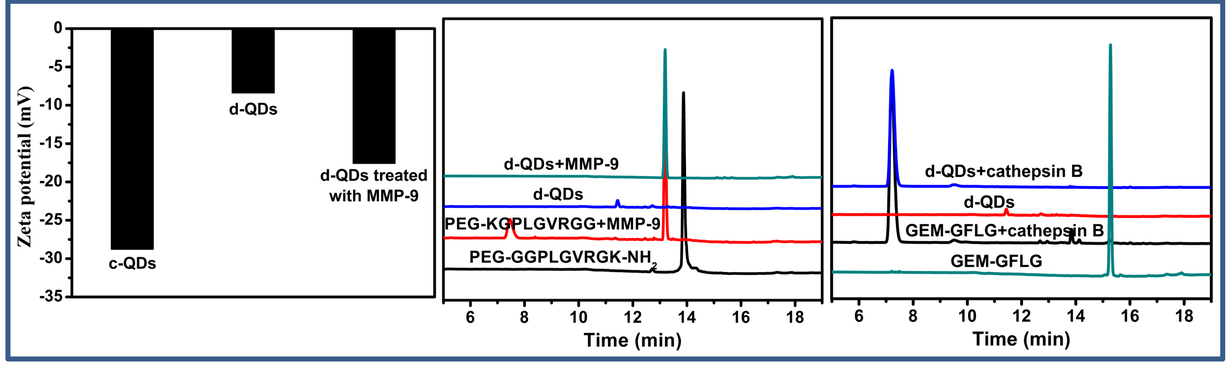
Adstract: Dual enzymatic reactions were introduced to fabricate programmed gemcitabine (GEM) nanovectors for targeted pancreatic cancer therapy. The GEM nanovectors could achieve prolonged circulation time while maintaining enhanced cellular internalization and effective drug release. Meanwhile, compared to free GEM, the deamination of GEM nanovectors into inactive 2',2'-difluorodeoxyuridine (dFdU) could be greatly suppressed, while the concentration of the activated form of GEM (gemcitabine triphosphate, dFdCTP) was significantly increased in tumor tissue, thus exhibiting superior tumor inhibition activity with minimal side effects.

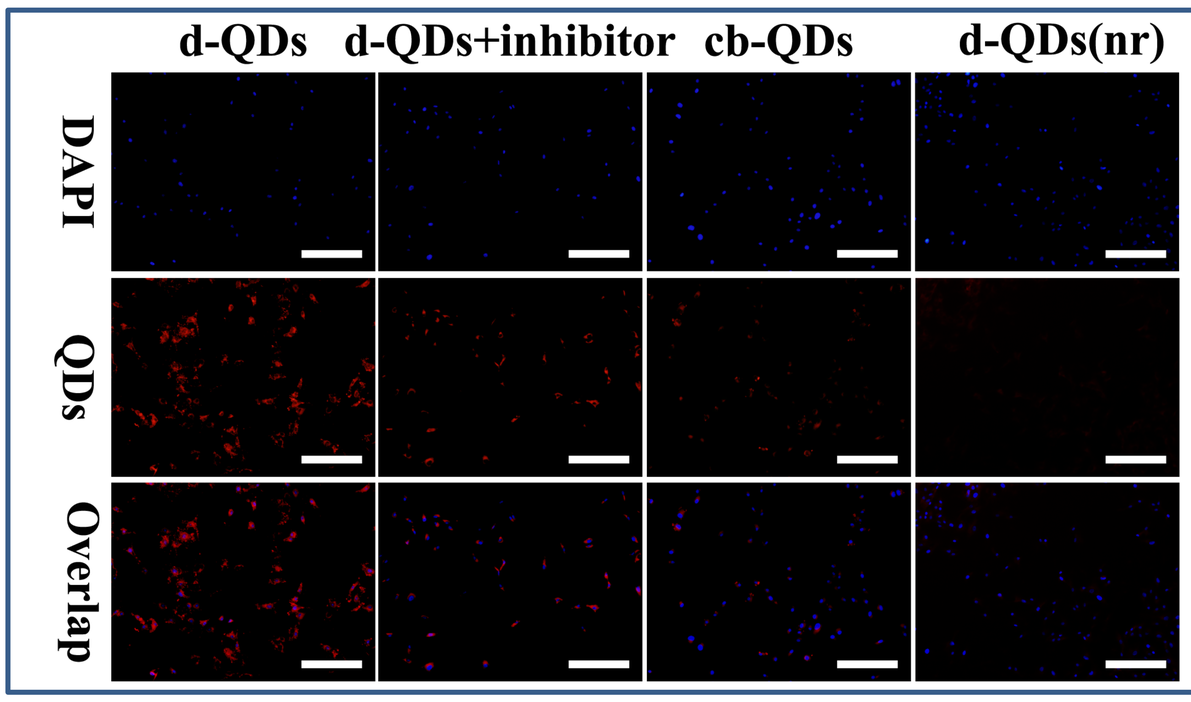


Scheme 1. (a) Schematic illustration of the preparation of nanovectors and their enzyme sensitive behavior; (b) Schematic illustration of the nanovectors delivering GEM to pancreatic cancer cells.

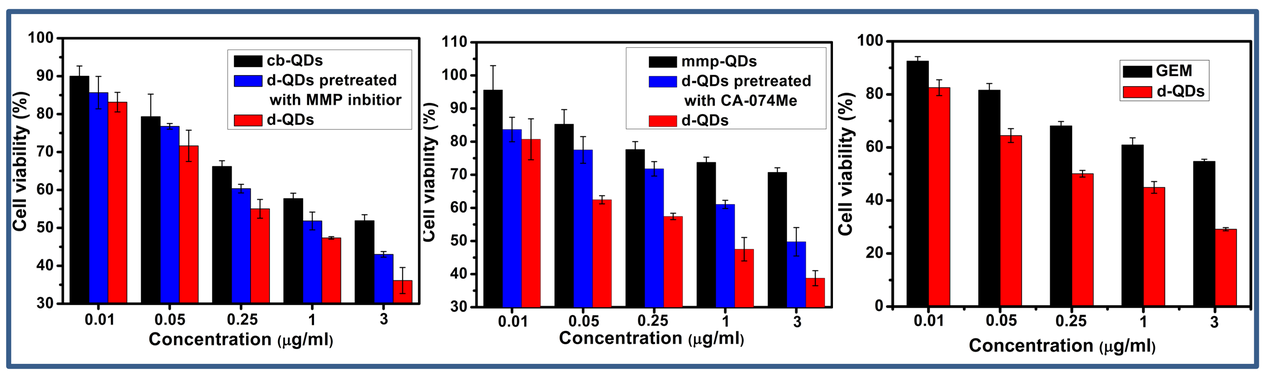
In vitro enzyme response



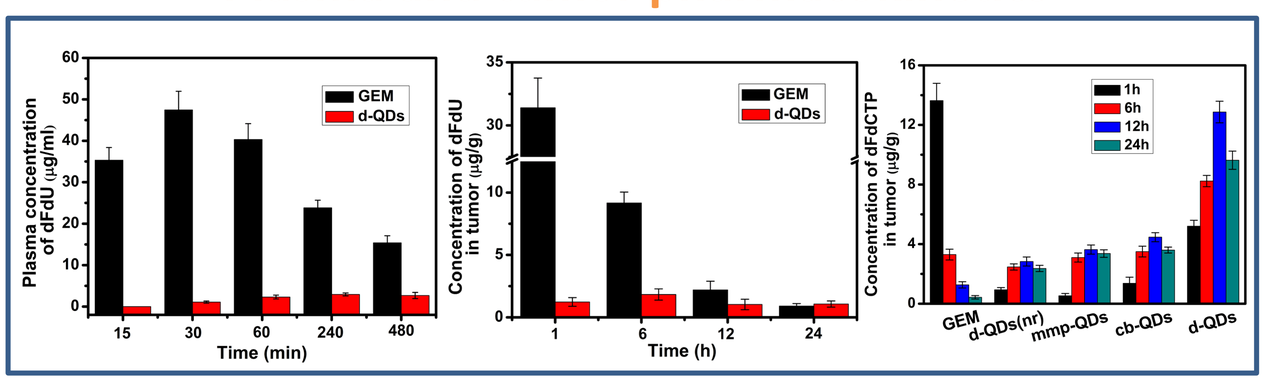
microenvironment activatable targeting ability



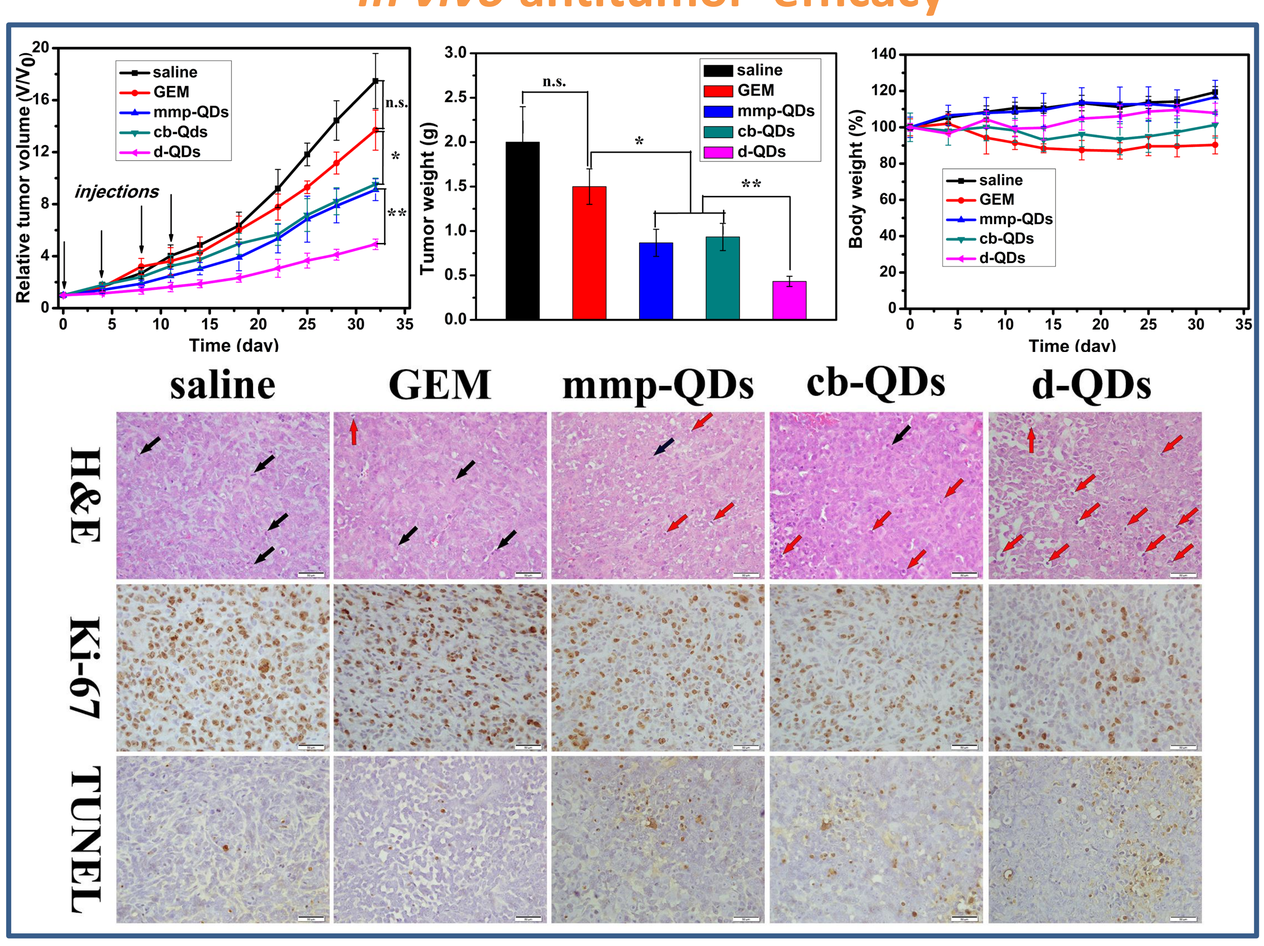
In Vitro Cytotoxicity Assay



Plasma and tumor pharmacokinetics



In vivo antitumor efficacy



Conclusions: In summary, dual enzymatic reaction-assisted GEM nanovectors were successfully fabricated using small-sized CdSe/ZnS QDs as model systems for targeted pancreatic cancer therapy. Reduced GEM deactivation during blood circulation, high accumulation in tumor tissue, enhanced cancer cell internalization, as well as specific intracellular GEM release were achieved owing to the enzyme-triggered programmed targeting strategy, exhibiting superior tumor inhibition activity with minimal side effects.

References:

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2. Lee, G. Y.; Qian, W. P.; Wang, L.; Wang, Y. A.; Staley, C. A.; Satpathy, M.; Nie, S.; Mao, H.; Yang, L. *ACS Nano*, **2013**, *7*, 2078-2089.