

Collagenase-loading pH-sensitive nanocarriers efficiently remodeled tumor stroma matrix and improved enrichment of nanomedicines

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Table S1 The selection of the most suitable molecular weight DEX. Four kinds of molecular weight (1w,7w,50w,100w) DEX were reacted for three times(2min,3min,4min) to obtain 12 kinds of products, whose degradation time at PH6.5 are shown in the table(the “*” represent nanoparticles that cannot be manufactured).

□	1w	7w	50w	100w
2min	*	*	*	*
3min	9h	6h	*	*
4min	17h	13h	*	*

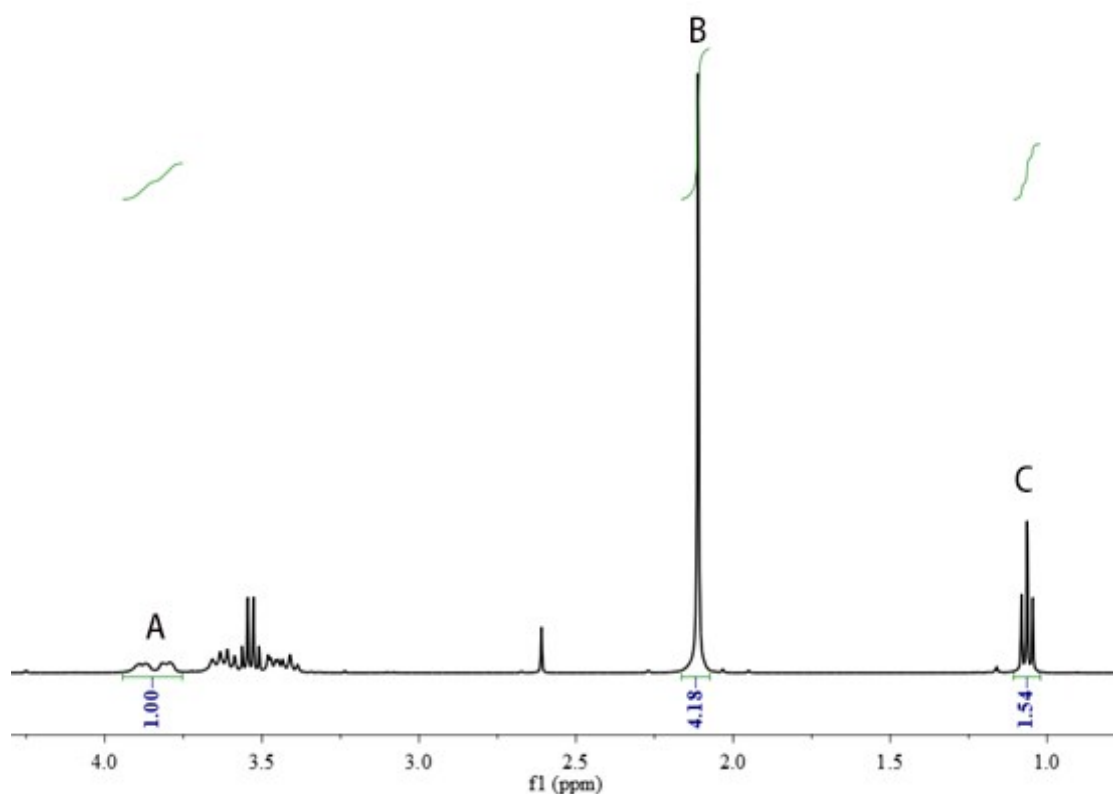


Figure S1 The NMR spectrum of the product obtained from 7w molecular weight DEX reaction for 3 minutes.

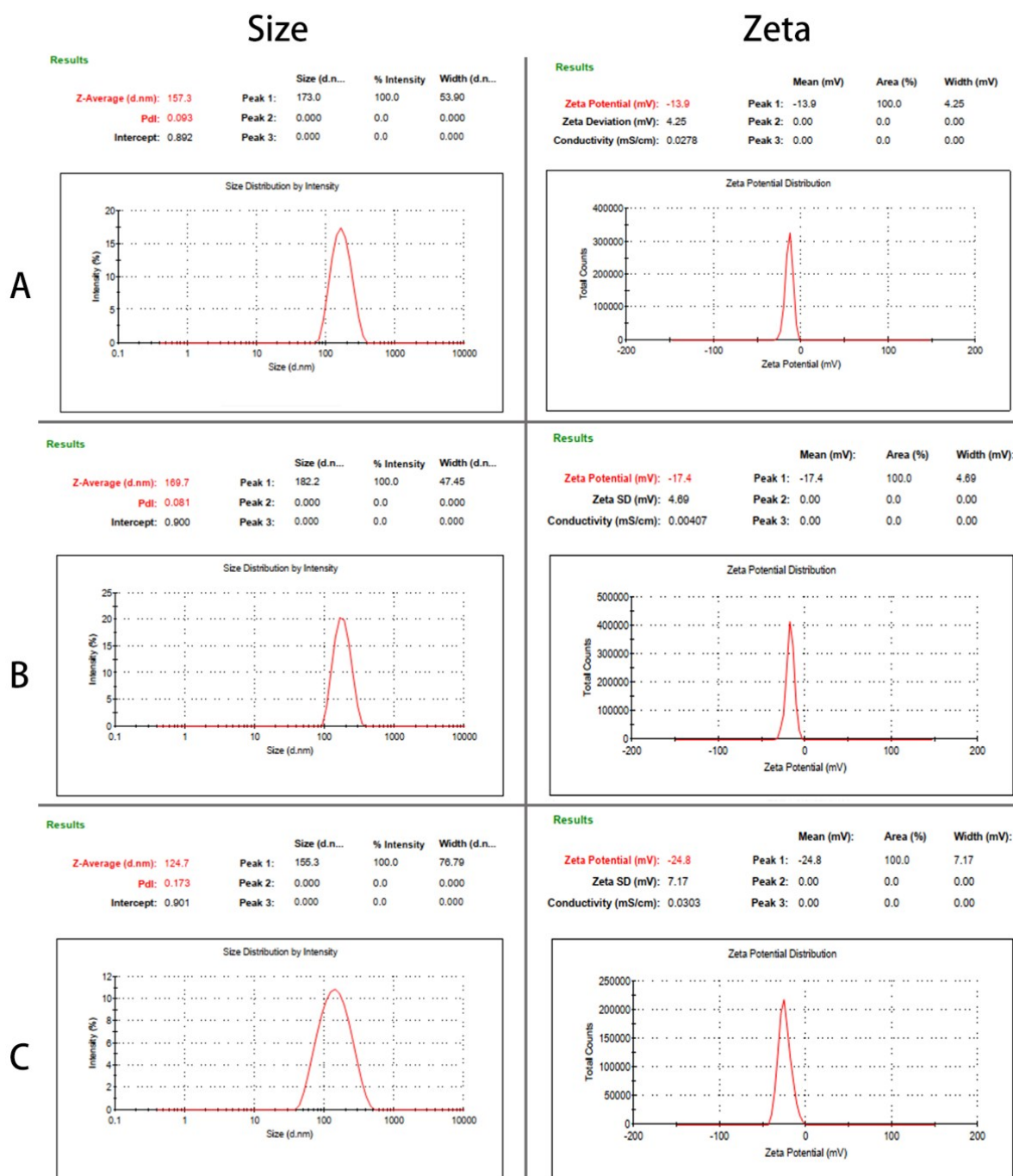


Table S2 Loading capacity (LC) and encapsulation efficiency (EE) of Col-NPs to collagenase, residual activation (RA) of collagenase and total residual mass (RM) of nanoparticle after Col-NPs preparation. LC = (weight of collagenase measured in Col-NP/total weight of Col-NP) \times 100%. EE = (weight of collagenase measured in Col-NP/weight of the feeding collagenase) \times 100%.

LC of optimized preparation method	4.62% \pm 0.35%
LC of traditional preparation method	2.21% \pm 0.41%
EE	21.05% \pm 1.35%
RA	91.03% \pm 1.21%
RR	90.69% \pm 1.42%

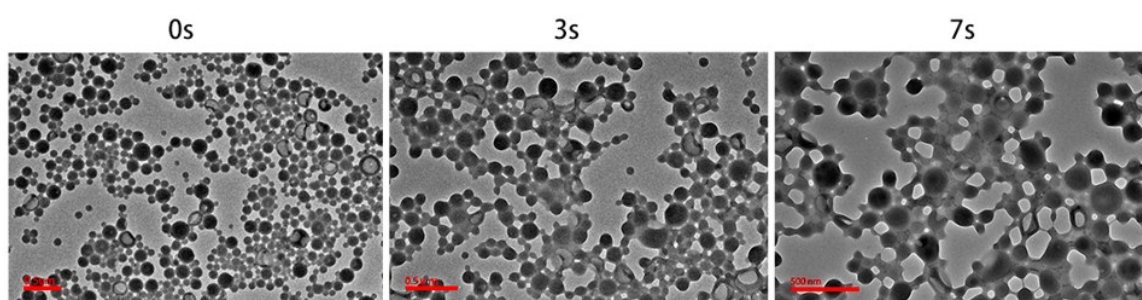
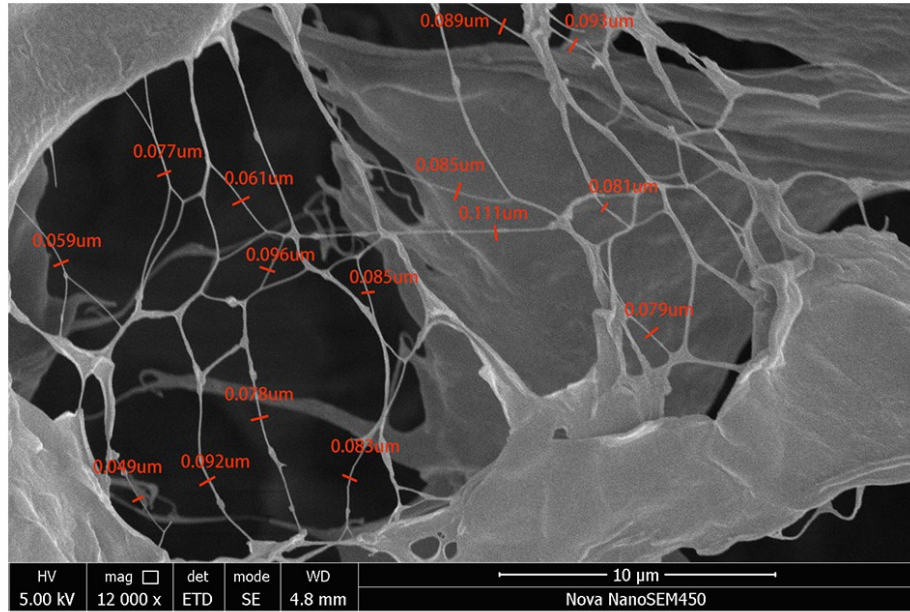


Figure S3 The Col-NPs collapse rapidly under the bombardment of TEM electron beams.

Blank



Col-NP

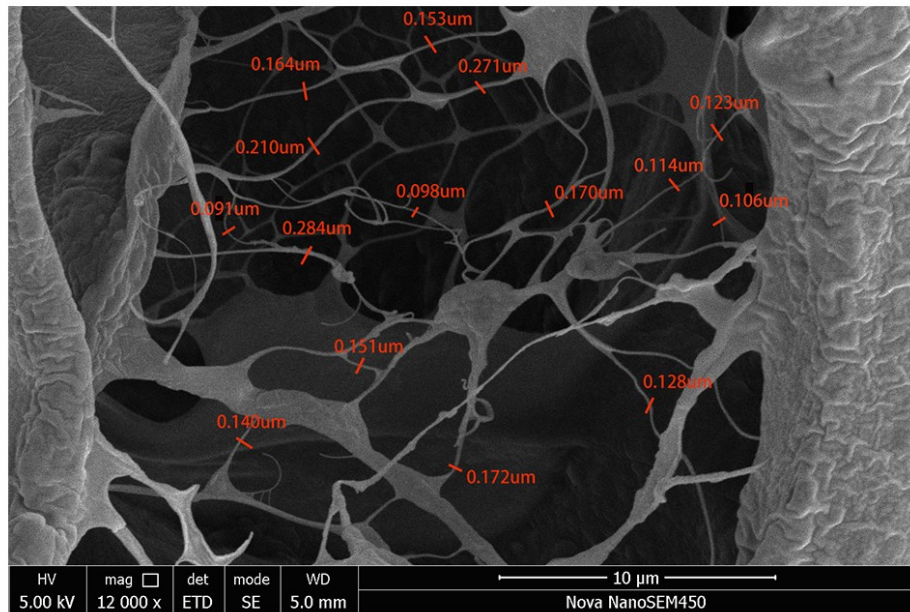


Figure S4 The thickness measurement of the main fibers in collagen network before and after Col-NP treatment by software ImageJ 1.48v. There are little thin(thickness<0.1um) fibers left in network after Col-NPs treatment. (There are three layers of collapsed networks under the view of Group C, so we take the clearest and most complete network as a sample)

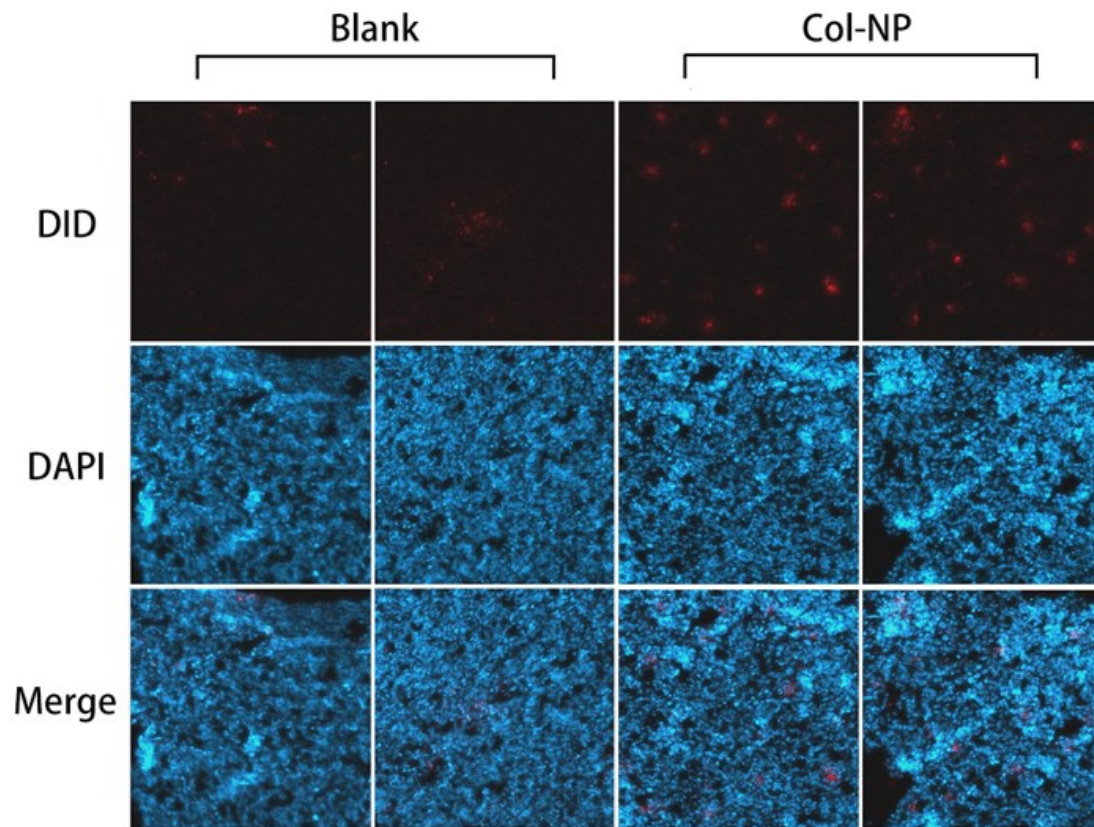


Figure S5 The tumor section photos by laser confocal microscopy after Col-NPs+DID-Lipo or saline+DID-Lipo treatment.

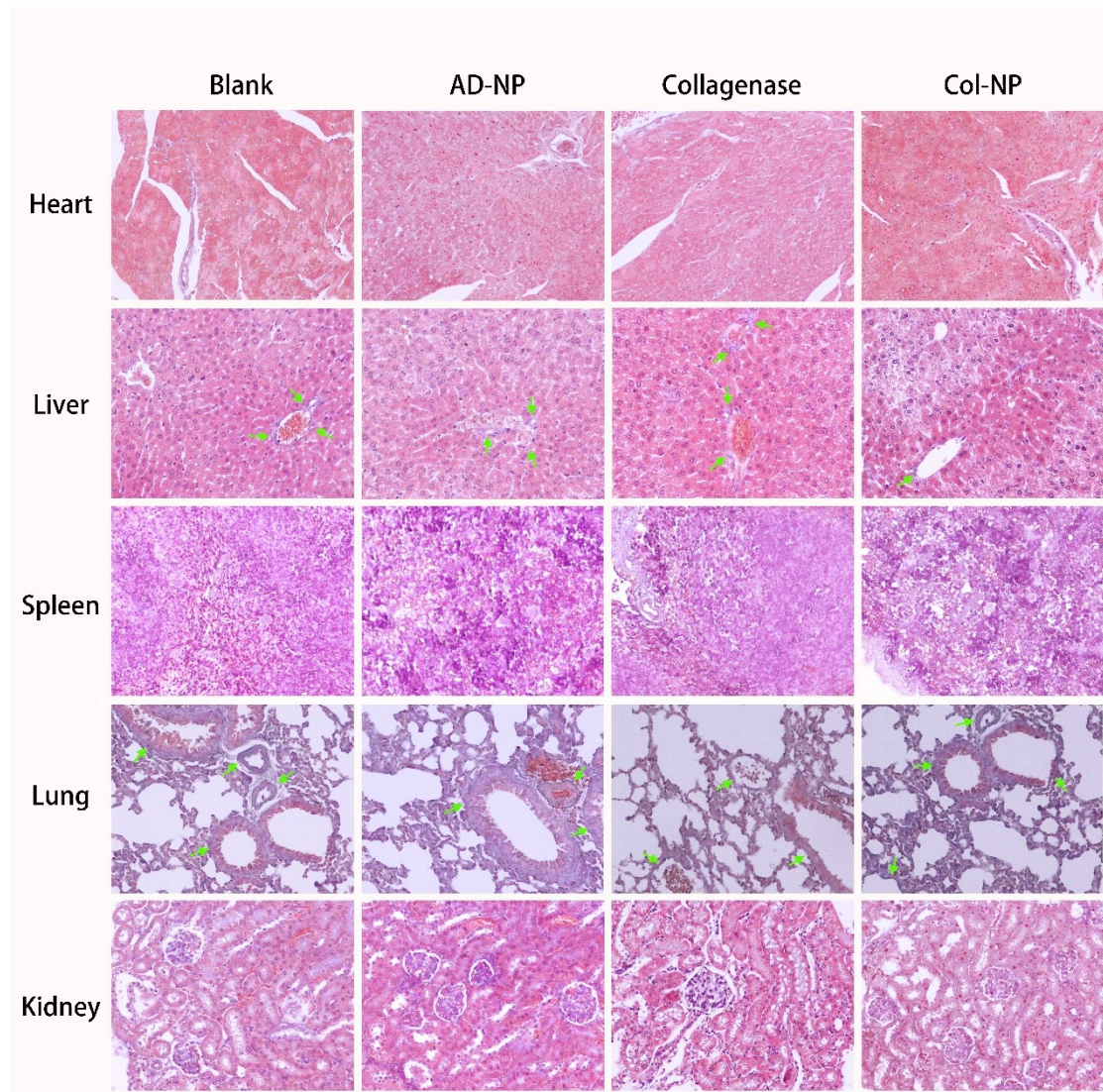


Figure S6 Masson trichrome staining images of tissue sections under 200x magnification. Masson trichrome staining results of heart, liver, spleen, lung and kidney in Blank, AD-NP, Collagenase and Col-NP group.