Supplementary Information

Solvent-driven sod-ZIF-8 ↔ ZIF-C phase transformation preserves nucleic acid functionality for gene delivery

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Table S1. Comparison of liposomal and ZIF-based (MOF) non-viral delivery systems.

Feature	**Liposomal systems**	**ZIF based (MOF) systems**	**Ref.**
Clinical status	Clinically validated; used in mRNA and siRNA therapeutics	Emerging platform; preclinical development	[1, 2]
Biocompatibility	Well-characterized and generally high	Good, but dependent on metal-ligand chemistry and cargo interactions	[1-3]
Colloidal stability	Can be limited in serum-rich environments	Typically robust; stability varies with phase/solvent	[4, 5]
Cargo protection	Moderate; potential for leakage or enzymatic degradation	Strong encapsulation protects nucleic acids	[5]
Release mechanism	Membrane fusion; tunable with formulations	Intrinsic pH-responsive degradation enables controlled release	[4, 5]
Storage needs	Often require cold-chain stability	Generally stable at room temperature	[6, 7]
Loading capacity	Moderate	High due to porous crystalline structure	[5]
Tunability	Through lipid composition and surface modification	Through metal-ligand chemistry, surface chemistry, porosity, and crystal phase	[4, 5]
Strengths	Clinically proven, versatile, biocompatible	Robust structure, strong cargo protection, pH-responsive release, high degree of flexibility and customizability	[4, 5]
Current limitations	Stability and leakage challenges; storage constraints	Phase behaviour under physiological conditions is still being fully characterized	[4, 5]

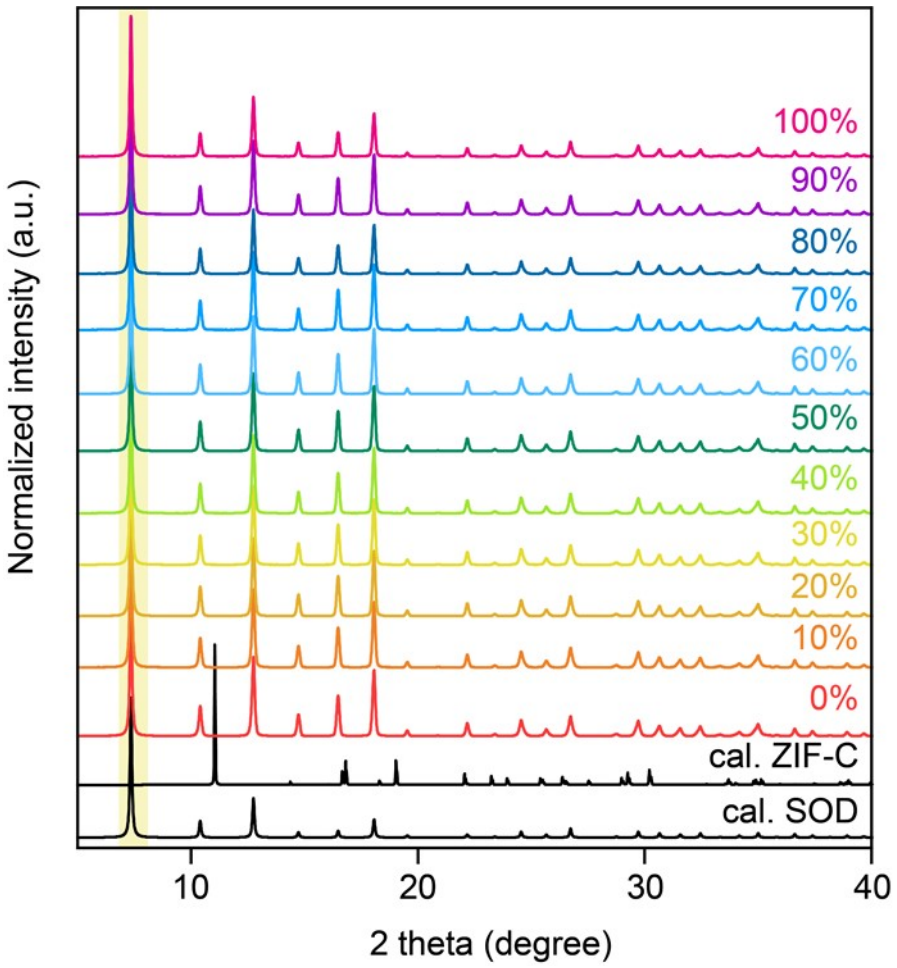


Fig S1. X-ray diffraction of DNA@ZIF synthesized using precursors made in ethanol.

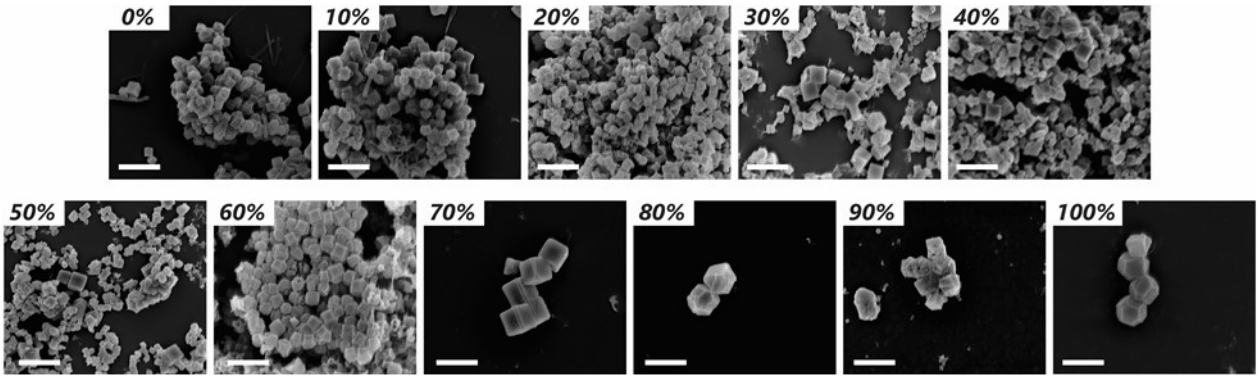


Fig S2. SEM images of DNA@ZIF were prepared with ethanolic 2HmIm and $Zn(OAc)_2$ and washed with different % of water in ethanol. Scale bar 500 nm.

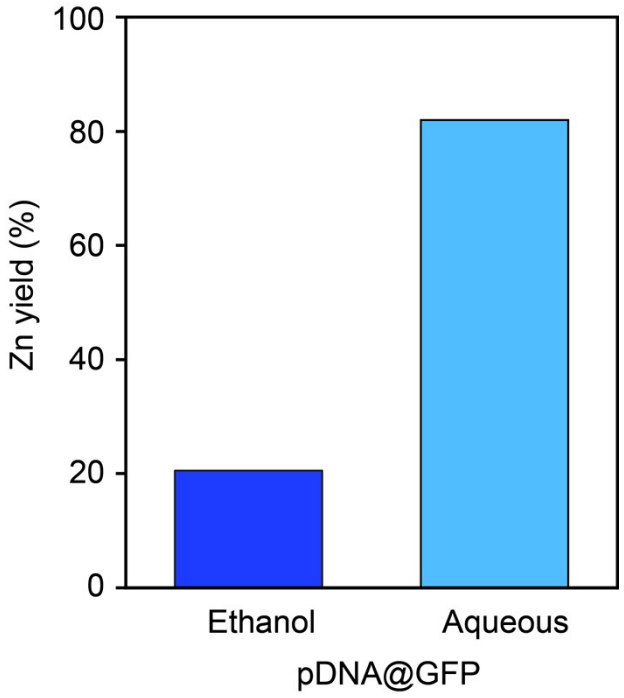


Fig S3. Zn yield (%) in DNA@ZIF prepared using organic (i.e., ethanol) and inorganic (i.e., water) conditions.

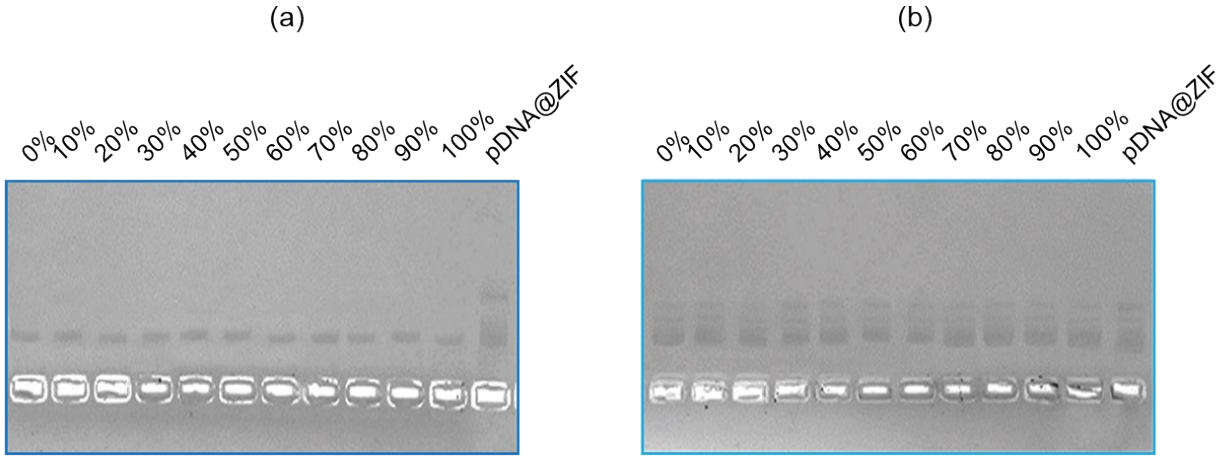


Fig S4. Agarose gel electrophoresis of DNA@ZIF prepared with (a) alcoholic and (b) aqueous precursors. The precipitates were washed with 0-100% of water in ethanol.

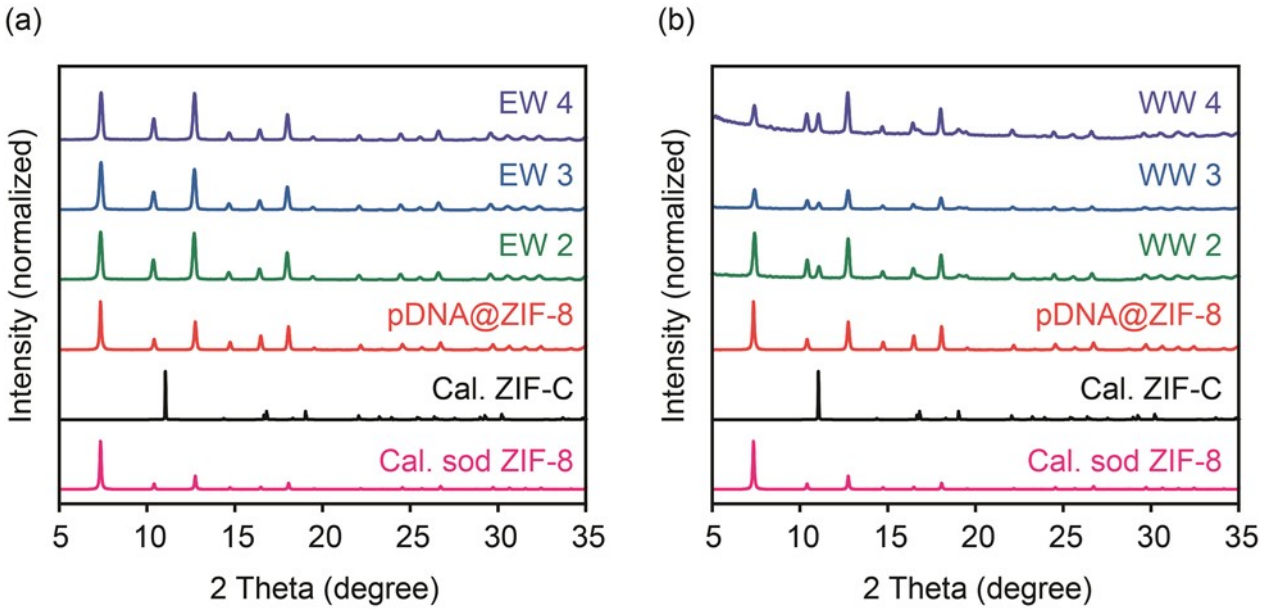


Fig S5. XRD of DNA@ZIF-8 after (a) ethanol wash (EW) and (b) water wash (WW). The numbers represent the washing steps.

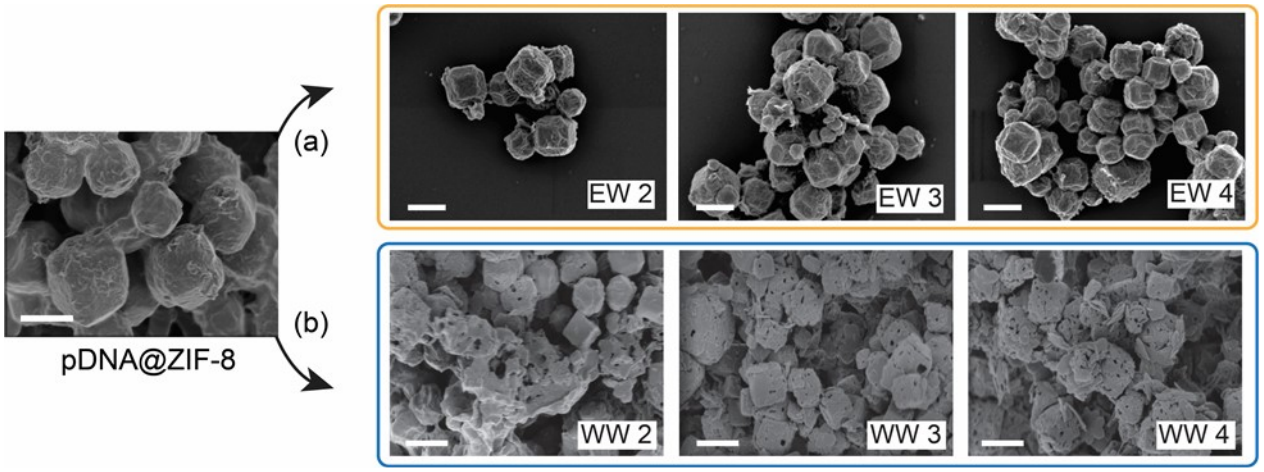


Fig S6. SEM of DNA@ZIF-8 after (a) ethanol wash (EW) and (b) water wash (WW). The numbers represent the washing steps. Scale bar refers 500 nm.

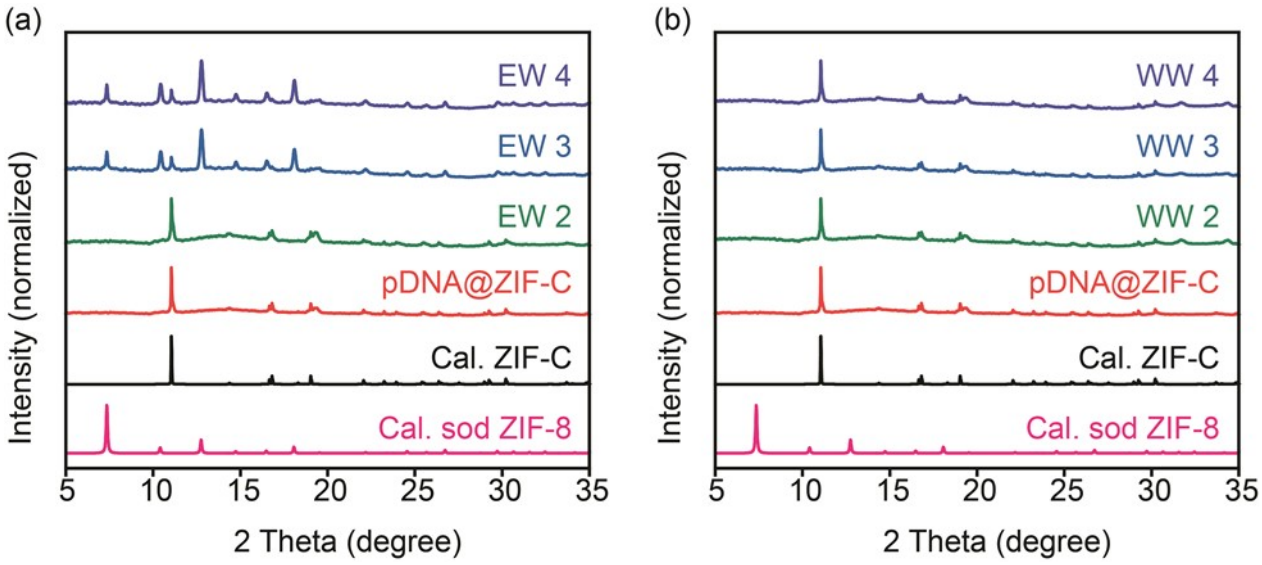


Fig S7. XRD of DNA@ZIF-C after (a) ethanol wash (EW) and (b) water wash (WW). The numbers represent the washing steps.

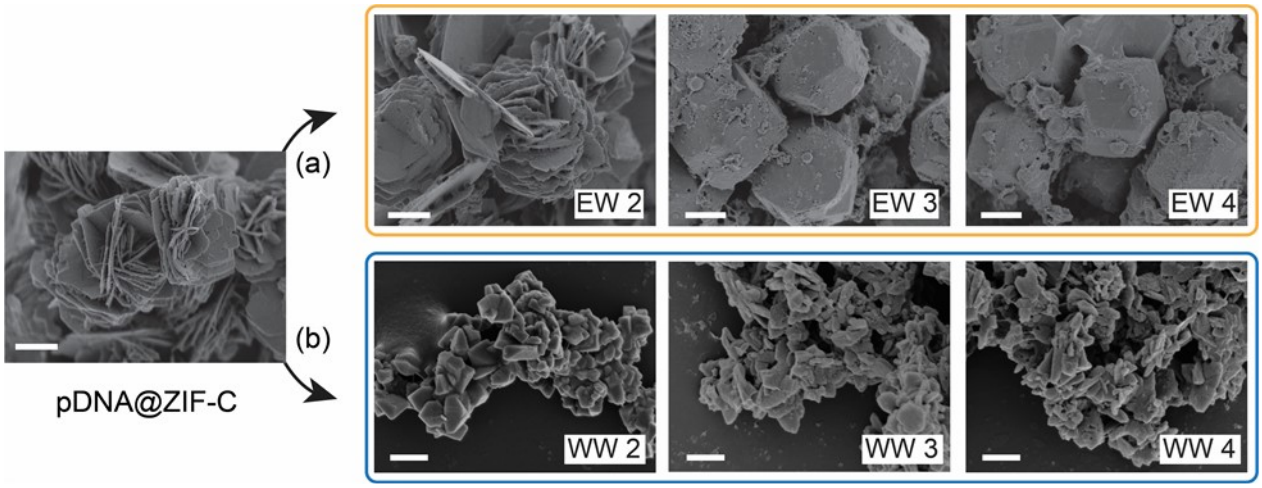


Fig S8. SEM of DNA@ZIF-C after (a) ethanol wash (EW) and (b) water wash (WW). The numbers represent the washing steps. Scale bar refers 500 nm.

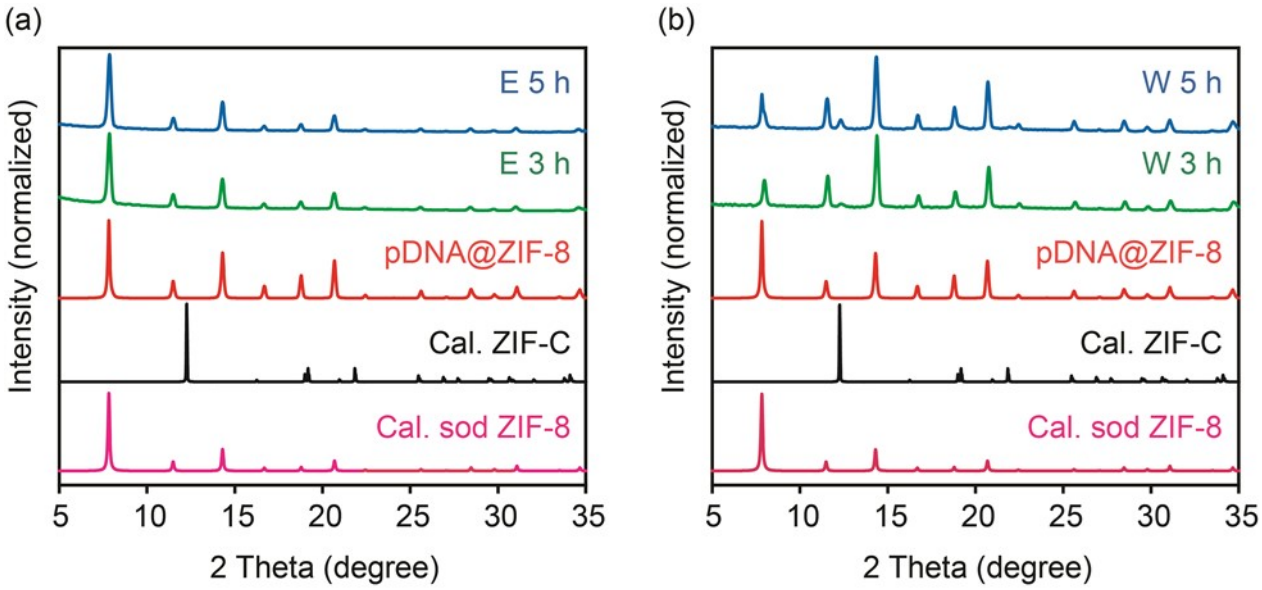


Fig S9. XRD of DNA@ZIF-8 after (a) ethanol (E) and (b) water (W) incubation.

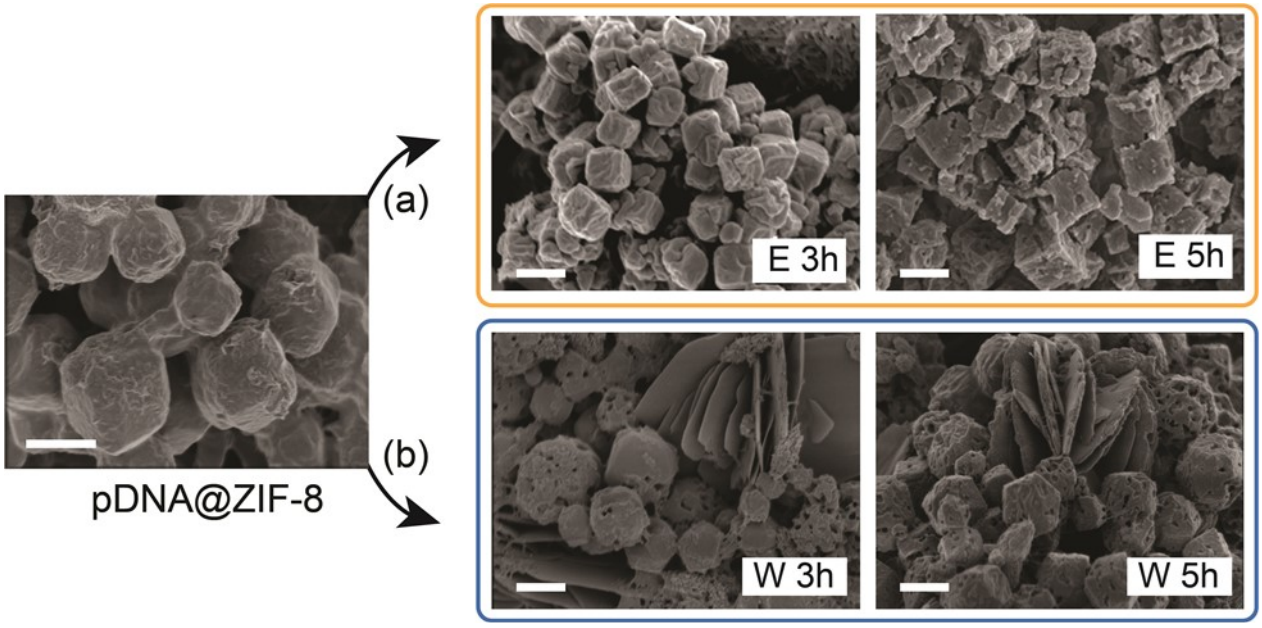


Fig S10. SEM of DNA@ZIF-8 after (a) ethanol (E) and (b) water (W) incubation. Scale bar refers 500 nm.

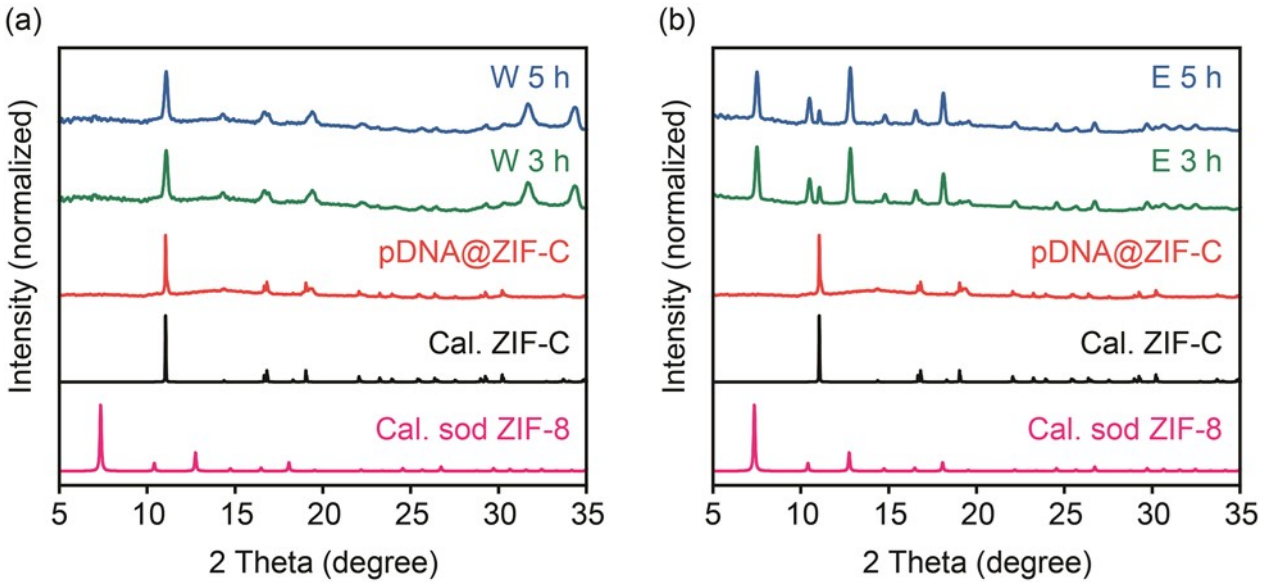


Fig S11. XRD of DNA@ZIF-C after (a) ethanol (E) and (b) water (W) incubation.

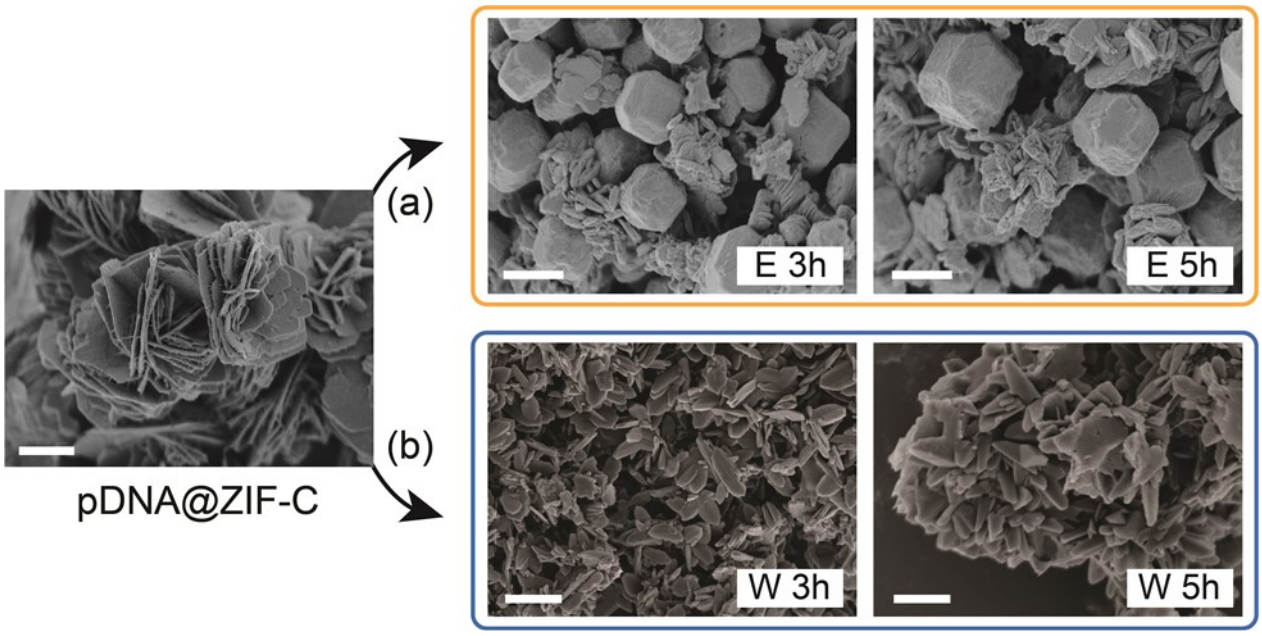


Fig S12. SEM of DNA@ZIF-C after (a) ethanol (E) and (b) water (W) incubation. Scale bar refers 500 nm.

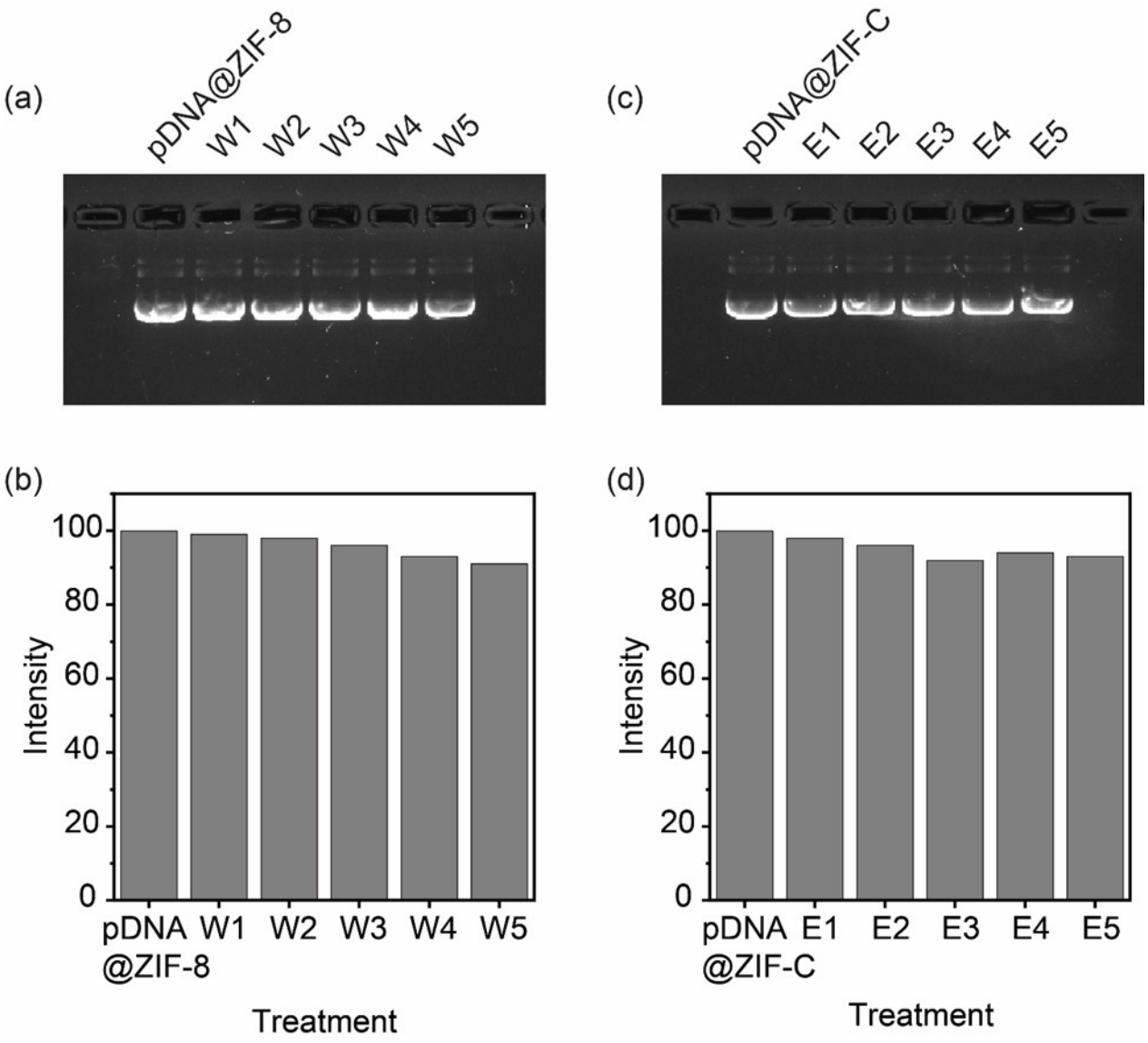


Fig. S13 Determination of DNA@ZIF content in (a-b) DNA@ZIF-8 and (c-d) DNA@ZIF-C after subsequent 5-times water (W) and ethanol (E) wash. Agarose gel electrophoresis of (a) DNA@ZIF-8 and (c) DNA@ZIF-C after 5 times washing with water and absolute ethanol, respectively. The DNA@ZIF band intensity of DNA@ZIF-8 and DNA@ZIF-C after corresponding treatment was plotted in (b) and (d).

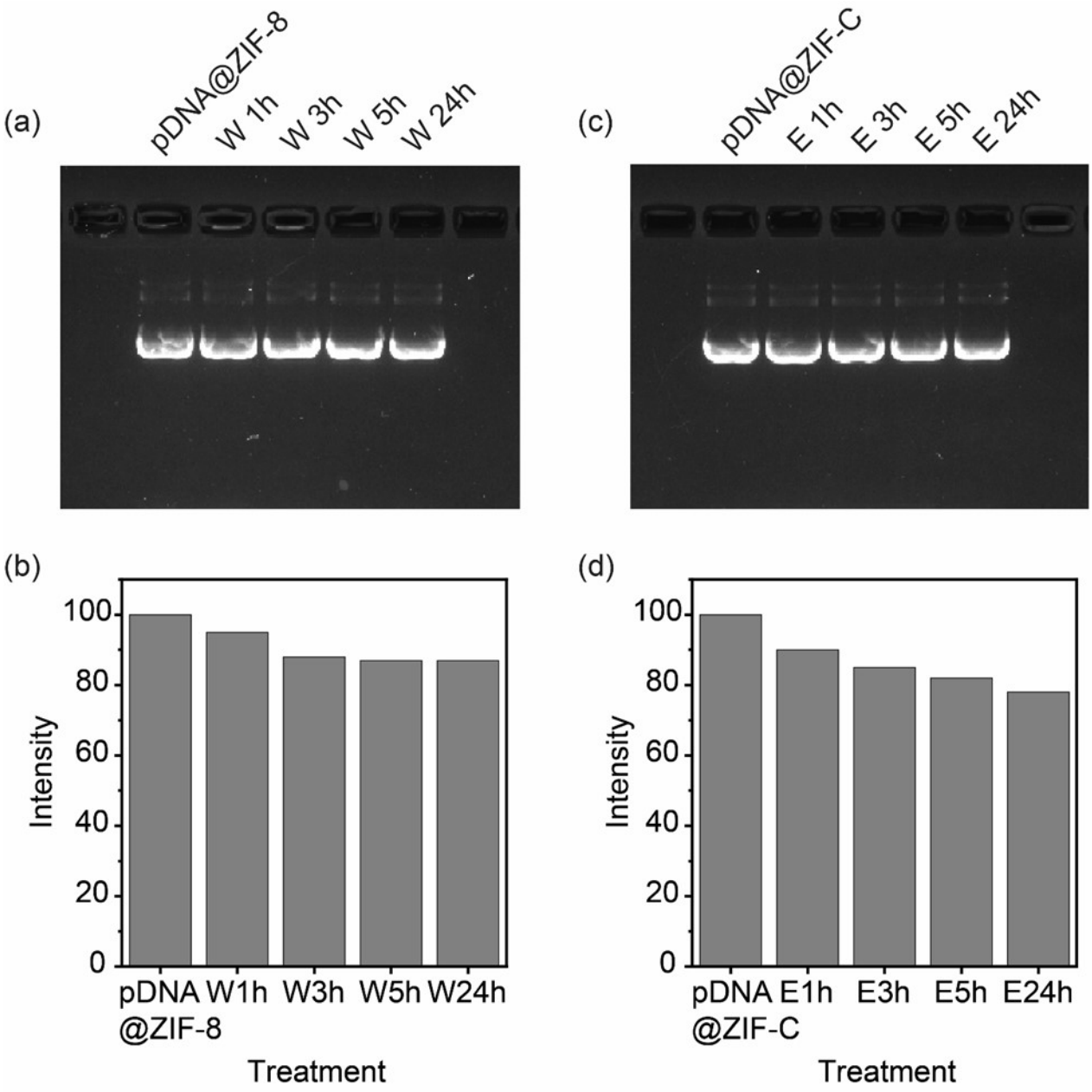


Fig S14. Determination of DNA@ZIF content in (a-b) DNA@ZIF-8 and (c-d) DNA@ZIF-C after incubation in (a) water (W) and (b) ethanol (E) for different points. Agarose gel electrophoresis of (a) DNA@ZIF-8 and (c) DNA@ZIF-C after incubating in water and absolute ethanol, respectively. The DNA band intensity in DNA@ZIF-8 and DNA@ZIF-C after the corresponding treatment was plotted in (b) and (d).

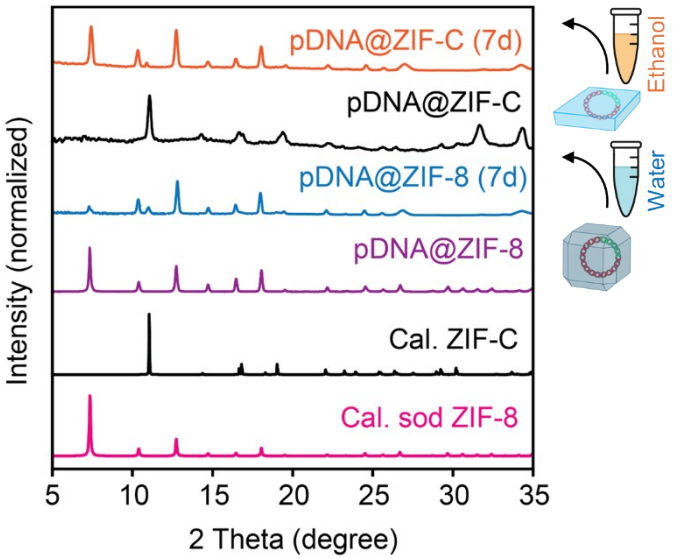
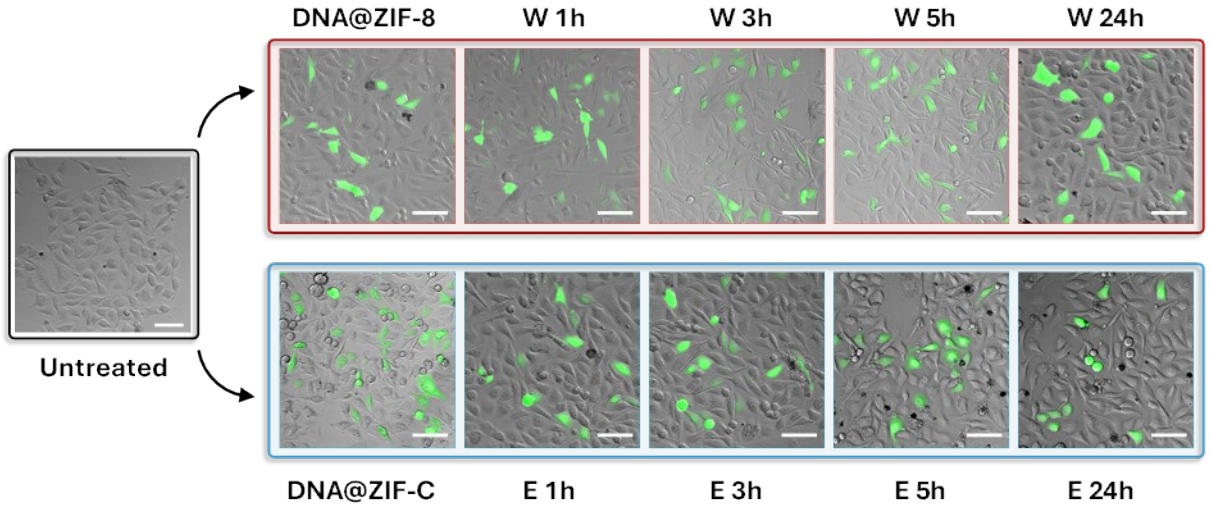


Fig S15. XRD of 7-days aged ZIF biocomposites.



a

Fig S16. PC-3 cells transfected with GFP plasmid. Scale bar refers 100 µm.

References:

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