Engineering DNA nanostructures for therapeutic delivery and biomimetic applications

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DNA is a unique polymer that enables the creation of biodegradable and versatile nanomaterials. Through nucleic acid nanotechnology, oligonucleotides self-assemble into programmable nanostructures via Watson-Crick-Franklin base-pairing. [1] These DNA-based nanostructures (DNS) can be finely tuned in size and function at the nanoscale, a feature that is highly valuable for biomedical and nanotechnological applications. In this work, we leverage these properties to engineer tailored DNS, both as therapeutic delivery nanocarriers and as dynamic architectures for biomimetics.

We first show that subtle structural modifications in simple DNS directly influence properties relevant to therapeutic delivery. [2,3] Specifically, variations in the flexibility of Y-shaped DNS or in the length of rod-like DNS affect their biological stability, cellular uptake, and the release and cytotoxicity of the anticancer drug doxorubicin (Figure 1a). [2] Likewise, the layout design in nanohydrogel-type DNS has been demonstrated to directly affect their functional performance in microRNA cardiac therapy using luciferase reporter cells. [3]

We finally present stimuli-responsive DNS integrating strand-displacement or dynamic chemistries to interact with liposomes, generating hybrid systems relevant in biomimetics and for controlled release purposes. [4,5] In particular, these DNS were equipped with dynamic architectures that enable sequence-specific triggered release of encapsulated cargo [4] or with innovative bioconjugation strategies [5] to dynamically control their coupling to lipid assemblies (Figure 1b).

Altogether, our results demonstrate how DNS can be customized to optimize therapeutic delivery and equipped with precise dynamic moieties to expand their scope as advanced hybrid nanocarriers in nanobiotechnology.

References

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Figures

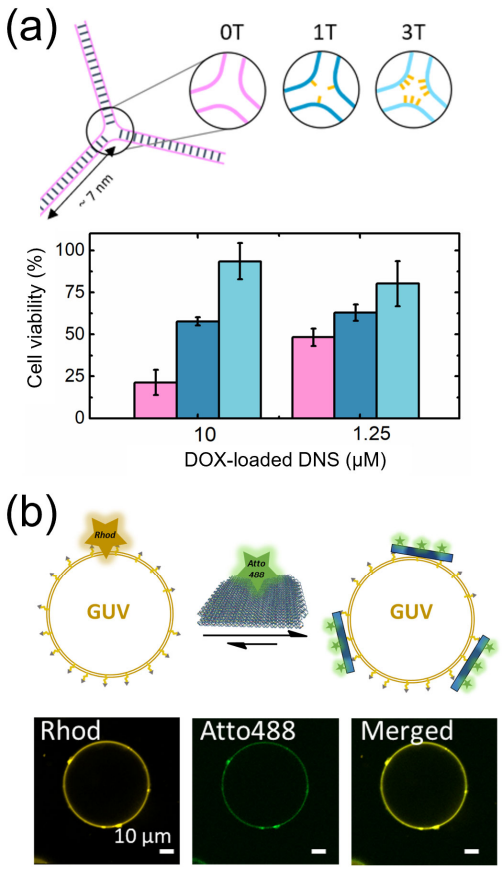

Figure 1. a) Y-shaped DNS with tunable flexibility controlled by the number of unpaired thymines (T) at the junction and their cytotoxicity upon doxorubicin (DOX) loading in MiaPaCa-2 cancer cells. b) Schematic of the dynamic anchoring of Atto-488–labelled origami DNS to lipid giant unilamellar vesicles (GUVs), together with confocal microscopy images showing their coupling to rhodamine-labelled GUVs.