Development of a pH-Responsive DNA: Functional Nanostructures, Nanodevices and Effective Nanoscale Drug Delivery

Lei Song[1], Dongsheng Liu[2], Rongjun Chen[1] and Dejian Zhou*[1]

[1] *School of Chemistry and Astbury Centre for Structural Molecular Biology, University of Leeds, Leeds LS2 9JT, United Kingdom, email: d.zhou@leeds.ac.uk*

[2] *Department of Chemistry, Tsinghua University, Beijing 100084, P. R. China.*

Abstract

Over the past two decades, DNA has been demonstrated as an extremely powerful and versatile building material for nanotechnology, where a wide range of novel structures, isolated individual nanostructures, two dimensional grid and three-dimensional assemblies (DNA hydrogels) as well as a range of DNA based molecular nanomachines and nanowalkers have also been reported.[1,2] These novel structures and nanomachines offer a wide range of potential biosensing and biomedical applications. However, most of the DNA nanomachines/nanowalkers are powered by DNA fuels which often lead to slow operation speed and significant performance degradation as the number of cycle increases, which can limit their potential application. Herein, we report our recent developments of robust functional DNA nanostructures and devices uisng a robust, highly reversible proton-fuelled DNA nanomachine.[3] We show that the force generated from the closing and opening of this DNA nanomachine can be harnessed to construct a reconfigurable DNA nanotriangle.[4] We also show that this DNA nanomachine is functional when being immobilized on surface, and can be used to construct a novel DNA based optical nanoswitch array.[5] We have also extended the DNA assembly to un-restricted three dimensions and constructed a novel pH-responsive hydrogel that is made of entirely DNA.[6] Finally, we show this DNA nanomachine can be used to controllably bind and release a model anti-cancer drug, doxorubicin, in response to environmental pH changes. It can also be combined with nanoparticles to develop a novel pH-responsive nanoscale drug delivery system that can be exploited for effective cancer chemotherapy at the cellular level.

Key Words: DNA, Nanostructure, Drug Nanocarrier, Cancer Chemotherapy, Nanoparticle

Acknowledgements

We thank the Royal Society (RG 2009R1), the University of Leeds for funding this research. LS is supported by a fully-funded international research scholarship (FIRS) at the University of Leeds.[1]

---

[1] See Seeman, N. C. *Nature* **2003**, *421*, 427. Bath, J.; Turberfield, A. J. *Nature Nanotech*. **2007**, *2*, 275.
[2] Li, Y.; Tseng, Y. D.; Kwon, S. Y.; Espaux, L.; Bunch, J. S.; McEuen, P. L.; Luo, D. *Nature Mater.* **2004**, *3*, 38.
[3] Liu, D.; Balasubramanian, S. *Angew. Chem. Int. Ed*. **2003**, *42*, 5734.
[4] Wang, W.; Yang, Y.; Cheng, E.; Zhao, M.; Meng, H.; Liu, D.; Zhou, D. *Chem. Commun.* **2009**, 824.
[5] Liu, D.; Bruckbauer, A.; Abell, C.; Kang, D.; Balasubramanian, S.; Klenerman, D.; Zhou, D. *J. Am. Chem. Soc.* **2006**, *118*, 2067.
[6] Cheng, E.; Xing, Y.; Chen, P.; Yang, Y.; Sun, Y.; Zhou, D.; Xu, L.; Fan, Q.; Liu, D. *Angew. Chem. Int. Ed.* **2009**, *48*, 7660.