Self-assembled nanoclusters of fluorinated quantum dots as delivery platform for enzymes

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Self-assembled nanoparticles are considered as one of the most promising nanosystems to deliver drugs and biological molecules such as enzymes for therapeutic applications [1]. It is well-known that non-covalent hydrophobic interactions play an important role in the organization and stabilization of many types of assembled systems [1]. In particular, fluorine-fluorine interactions have demonstrated to form more stable self-assembled nanostructures [2-4] because such interactions are stronger than other non-covalent bonds due to the unique hydrophobicity and lipophilicity of the fluorine atoms [5]. The favorable interaction between fluorine atoms and proteins has also been a subject of intensive research [6].

Herein, inspired by the role of fluorine in self-assembly and its favorable interaction with proteins, we report a novel delivery platform for enzymes based on self-assembled nanoclusters of fluorinated quantum dots. Nanoclusters of ca. 50 nm diameter were formed by self-assembly of fluorinated quantum dots in aqueous medium through fluorine-fluorine interactions. These nanoclusters were able to encapsulate different enzymes with loading efficiencies ≥ 74 % and the encapsulated enzymes maintain their catalytic activity.
Under acidic environment mimicking the conditions of endosomal/lysosomal compartments, the nanoclusters were slowly disassembled allowing the release of encapsulated enzymes (Figure 1). The effective release of α-galactosidase (*i.e.,* a therapeutic enzyme for the treatment of the Fabry disease) demonstrated the feasibility of this nanoplatform to be used in enzyme replacement therapy for lysosomal storage diseases.

Moreover, the combination of high colloidal stability of these nanoclusters, effective enzyme loading and release, and fluorescence imaging potential make them very promising nanosystems for application in theranostics.

References

[1] W. Cui, J. Li, G. Decher, Adv. Mater, 28 (2016) 1302.
[2] S. D. Xiong, L. Li, J. Jiang, L. P. Tong, S. Wu, Z. S. Xu, P. K. Chu, Biomaterials, 31 (2010) 2673.
[3] H. Wang, Y. Wang, Y. Wang, J. Hu, T. Li, H. Liu, Q. Zhang, Y. Cheng, Angew. Chem., 54 (2010) 11647.
[4] K. Niikura, N. Iyo, T. Higuchi, T. Nishio, H. Jinnai, N. Fujitani, K. Ijiro, J. Am. Chem. Soc., 134 (2012) 7632.
[5] V. Percec, M. Glodde, G. Johansson, V. S. K. Balagurusamy, P. A. Heiney, Angew. Chem., 42 (2003) 4338.
[6] J. Pollock, D. Borkin, G. Lund, T. Purohit, E. Dyguda-Kazimierowicz, J. Grembecka, T. Cierpicki, J. Med. Chem, 58 (2015) 7465.

Figures

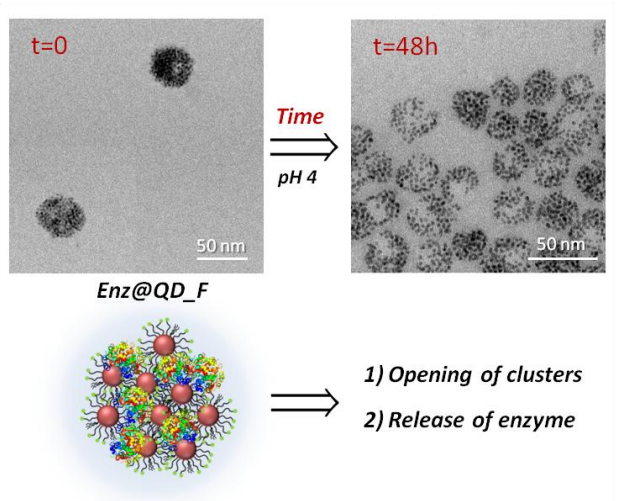

Figure 1. TEM images over time of nanoclusters with enzyme encapsulated (Enz@QD_F) under acidic conditions (acetate buffer 20 mM at pH 4), showing the opening of the nanoclusters which allows the realease of the enzyme.