Department of Chemical and Biomolecular Nanotechnology Seminars

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DNA nanostructures as chemotherapeutic delivery system for cancer therapy

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Location
"Sala d'Actes" room
Institute of Advanced Chemistry of Catalonia (IQAC-CSIC)
C/Jordi Girona 18-26, 08034 Barcelona

Abstract
Since 5-Fluorouracil (5-FU) discovery, it has become the mainstay chemotherapeutic agent in the treatment of diverse types of cancers, especially colorectal cancer.1 The extensive use of 5-FU and the urgent need to overcome its recognized drawbacks such as, low bioavailability, lack of specificity to cancer cells and cell resistance, motivated us to develop novel multifunctional DNA-based nanocarriers incorporating the active metabolite of 5-FU, 5-fluoro-2'-deoxyuridine (FdUn) in polymeric form. The insertion of these chemotherapeutic oligonucleotides of 5-fluoro-2'-deoxyuridine in staples belonging to the classic DNA nanoscaffolds, DNA tetrahedron (Td) and rectangle DNA origami was carried out. In addition, to enhance cellular uptake of DNA nanostructures, staples synthesized with cholesterol moieties were also included. Results showed that newly developed FdUn-modified nanostructures are more cytotoxic than conventional drugs, 5-FU and 5-fluoro-2'-deoxyuridine (FdU) and are able to overcome 5-FU cell sensitivity of colorectal cells. Cholesterol acts as an active delivery agent in the improvement of FdUn nanostructures uptake and significantly boosts their cytotoxic activity. Using Td, FdUn was administrated at 33-fold higher concentration than in rectangle DNA origami, yet they present comparable values of cytotoxicity. Thus, the cytotoxic effect produced by the higher concentration of Td seems to be counterbalanced by the higher capacity of rectangle DNA origami to induce cell apoptosis. In turn, Td shows to be highly efficient as antiproliferative agent suggesting that this response is directly correlated to the concentration of nanoscaffolds. This work provides valuable insights to the development of biocompatible and easily programmable DNA-based nanostructures as privileged carriers of fluoropyrimidines, and it may envisage the promising capacity of DNA nanoscaffolds to attain smart targeted nanoparticles for cancer treatment.

Refererences
1. Longley, D. B.; Harkin, D. P.; Johnston, P. G., 5-fluorouracil: mechanisms of action and clinical strategies. Nat Rev Cancer 2003, 3 (5), 330-8.

Acknowledgements
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