Photodegradable Acetal block copolymer for drug delivery

T. Manouras[1*], G. Pasparakis[2], P. Argitis[3] and M. Vamvakaki[1,4]

[1]*Institute of Electronic Structure and Laser, FORTH, 71110 Heraklion, Greece*
[2]*University College London, School of Pharmacy, WC1N 1AX London, UK*
[3]*Institute of Nanoscience and Nanotechnology, NCSR 'Demokritos', 15310 Aghia Paraskevi, Greece*
[4]*Department of Materials Science and Technology, University of Crete, 71003 Heraklion, Greece*

The development of polymers or other type of materials that degrade upon application of a light-stimulus would be highly desirable in a number of applications in nanomedicine and biofabrication such as exogenous activated drug delivery, and handling/manipulation of precious biological samples at the microscale (i.e. cell sorting, on-chip patterning, light directed cell migration, etc.).

In the present study, we demonstrate for the first time, the application of photochemical internalization in combinatorial photo-chemotherapy against cancer cells using a new class of dual degradable nanoparticles loaded with a potent chemotherapeutic anticancer compound (CPT) and a phototoxic drug (hematoporphyrin, HP). We recently reported on a new class of polymers based on the ketal family [1] that exhibits remarkably low ablation thresholds owing to their very low photolysis threshold. Furthermore, polyacetals have got a well-established hydrolysis profile under mildly acidic conditions (pH 5.5) found in the late endosome. In an effort to introduce red shifted photolability on the backbone of the polymer in the visible 2-nitroresorcinol monomers were used. Our system can be activated using visible and potentially infrared wavelengths at very low doses and exhibits simultaneous photo- and chemo- degradation, ideal for concerted light and pH controlled intracellular trafficking of drug cocktails, allowing for aggressive photoinduced cancer cell death.

In conclusion, we have developed new materials that exhibit mild and tunable photolytic cleavage under clinically relevant conditions. We demonstrated the use of dual photo- and chemo degradable NPs in photochemical internalization-mediated delivery of cytotoxic agents and proved the concept of enhanced cytotoxicity against cancer cell lines in vitro [2].

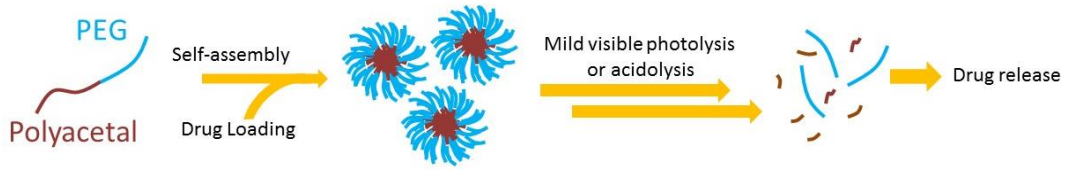

Figure 1: Our proposed generalized strategy

References

[1] G. Pasparakis, T. Manouras, A. Selimis, M. Vamvakaki and P. Argitis, Angewandte Chemie International Edition 50, 4142-4145 (2011).
[2] G. Pasparakis, T. Manouras, A. Selimis, M. Vamvakaki and P. Argitis, Nature Comm., 5, 3623 (2014).

* tman@iesl.forth.gr