Dynamic monitoring of drug release from nanoparticles using the combination of two powerful tools: FLIM and RICS

Hien T.T. Duong, 1 Elizabeth Hinde,1,2* Alexander Macmillan,3 Johan S. Basuki,1 Katharina Gaus,1,2 Renee Whan,1,3 Thomas P. Davis4,5* and Cyrille Boyer1*

1Australian Centre for Nanomedicine and Centre for Advanced Macromolecular Design School of Chemical Engineering, University of New South Wales, Sydney, Australia 2052
2Centre for Vascular Research, University of New South Wales, Sydney, Australia 2052
3Biomedical Imaging Facility, University of New South Wales, Australia 2052
4Monash Institute of Pharmaceutical Sciences, Monash University, Parkville, Melbourne 3052
5Department of Chemistry, University of Warwick, UK
E-mails: hien.duong@unsw.edu.au

The advance in polymerization techniques have led to the design of a wide range of promising stimuli-responsive polymeric nanocarrier systems with improved pharmacokinetics and biodistribution for drug delivery. However, the understanding of the dynamic release of drugs from the nanocarriers in response to specific stimuli in the biological environment is still very limited. Here, we report the dynamic intracellular release and accumulation of doxorubicin (DOX), an intrinsically fluorescent anticancer drug, conjugated to hybrid organic/inorganic nanoparticles via a pH-responsive bond with two advanced microscopy techniques: fluorescence lifetime imaging microscopy (FLIM) and raster image correlation spectroscopy (RICS). Our recent publications have illustrated the advantages of fluorescence lifetime imaging (FLIM) and phasor analysis to monitoring drug delivery by using polymeric nanoparticle.1-2 The FLIM measurement allowed us to monitor the dynamic release of DOX from the nanoparticles, whilst RICS analysis determined drug diffusion in the different cell compartments and the number of DOX molecules in the compartments. RICS was developed by Digman and Gratton to monitor the dynamics of fluorophores in living cells using commercial laser scanning confocal microscopy.3 RICS data revealed different diffusion rates in the nucleus of the active moiety in the MCF-7 breast cancer cells, compared to MRC-5 normal fibroblast cells. Using both techniques, we were able determine the active drugs release, whether it reached its target and accumulated more effectively.