living systems and are relatively unexplored as a platform for the design of bioactive amphiphiles. Moreover, carbohydrates in the form of glycosaminoglycans are able to interact directly with cellular machinery or indirectly through the activation of proteins as a part of their bioactive cascade. When compared with the PA, the carbohydrate amphiphiles (CA) present a much larger structural diversity (regio- and stereoisomers) and capacity for encoding bioinformation (Pashkuleva and Reis 2010). We, therefore, proposed a phosphorylated CA Fluorenylmethoxycarbonyl-(Fmoc)-glucosamine-6-phosphate, chemical structure depicted in Fig. 5, as a biocatalytic system able to selectively target osteosarcoma cells (SaOs2) triggering apoptotic pathways that lead to their death (Pires et al. 2015). We selected SaOs2 due to the known overexpression of alkaline phosphatase (ALP), which we hypothesized would lead to the localized biocatalytic transformation of the phosphorylated precursor into Fmoc-glucosamine. The accumulation of the latter in the pericellular space of SaOs2 caused cell death (Fig. 5). However, when ATDC5 cells (that present an ALP activity ~15–20 times lower than SaOs2) were tested under the same conditions, their metabolic activity was not affected. Moreover, the addition of a phosphatase inhibitor in the SaOs2 culture medium increased drastically the cell survival. These results demonstrated that SaOs2 cells can be targeted through their ALP overexpression.

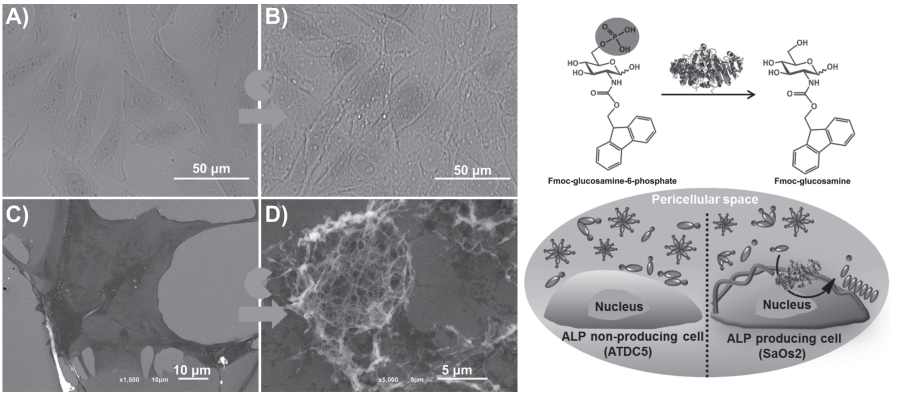

Fig. 5. (A, B) Brightfield and (C, D) SEM images of the SaOs2 cells cultured in the presence of the CA Fmoc-glucosamine-6-phosphate (0.5 mM and 7 hr of cell culture) (adapted with permission from Pires et al. 2015. Copyright 2015. American Chemical Society).

Stimuli-Responsive Systems for the Delivery of Cancer Therapeutics

Supramolecular self-assembly is considered as an important approach to design and fabricate controlled drug release materials. Drug delivery systems are typically used to enhance the efficiency of the desirable drug and overcome the toxic effects at non-target sites. Researchers have designed variant responsive materials to develop such systems including materials, which are responsive to changes in their environment (pH,