HUMAN FERRITIN NANOCAGES FOR THE TARGETED DELIVERY OF PHOTOSENSITIZERS TO CANCER CELLS

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Human heavy-chain (H) ferritin is a nanocage protein constituted by 24 identical subunits that self-assemble giving rise to a hollow globular structure. It is characterized by the presence of an internal cavity of 8 nm in diameter able to safely sequester thousands of iron ions preventing adverse reactions inside cells. The peculiarity of human H-ferritin is the possibility to be recognized by cells expressing the Transferrin receptor 1 (TfR1) which mediates its endocytosis. Since cancer cells commonly overexpress cellular receptors, this feature prospects kind of targeted drug delivery in the development of ferritin-based nanocarrier loaded with compounds interesting for cancer therapy. Here, human homopolymeric H-ferritin was easily produced in E. coli and successfully loaded with Ru(II)-polypyridyl photosensitizers for photodynamic therapy (PDT) application in cancer cells. The resulting Ru(II)-ferritin nanocomposites were highly luminescent, displayed great stability in physiological conditions and preserved the native shell–core structure of the protein. Moreover, the encapsulated metal complexes retained the capacity to sensitize the production of the cytotoxic singlet oxygen species upon illumination. Ru(II)-ferritin nanocomposites were exclusively internalized by cancer cells expressing the TfR1 (i.e. HeLa and A2780 cell lines with respect to non-cancerous C2C12 myoblasts lacking TfR1 expression). Immunofluorescence analysis also revealed the co-localization of Ru-compounds with the TfR1 in the internal cellular compartments of HeLa and A2780 cells, highlighting the crucial role exerted by TfR1 in the internalization of H-type ferritins. Finally, the biological effects on cancer cell of the photo-activated nanocomposites were assayed showing a marked dose-dependent cytotoxic effect uniquely against cancer cells. This study underlined the potential of human H-ferritin as a valuable tool for the tumor-targeted delivery of photosensitizers for PDT.

Keywords: Human ferritin nanocage, targeted drug delivery, photodynamic therapy

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