Hyaluronic Acid Immobilized Polyacrylamide Nanoparticle Sensors for CD44 Receptor Targeting and pH Measurement in Cells

Our ability to design receptor-targeted nanocarriers aimed at drug release after endocytosis is limited by the current knowledge of intracellular nanoparticle (NP) trafficking. It is not clear if NP size, surface chemistry, and/or targeting of cell surface receptors changes the intracellular fate of NPs; i.e., will all NPs enter acidic compartments and eventually end up in lysosomes or are there escape mechanisms or receptor-specific signaling that can be induced to change the cellular processing of an internalized NP? To give new insight into the intracellular trafficking of NPs that target the CD44 receptor, which is overexpressed on the surface of a broad variety of cancer cells, we have synthesized an NP pH sensor system that targets CD44. We used a polyacrylamide nanoparticle matrix bearing hyaluronic acid (HA) on the surface as a CD44 targeting ligand. The HA-coated NPs were prepared by radical polymerization followed by post functionalization with sensor fluorophores and physically absorbed or chemically conjugated HA. Cell uptake studies showed significant uptake of HA-coated nanosensors in HeLa cells and no uptake under the same conditions without the HA targeting ligand. The pH distribution profile in cells was measured for nanosensors with HA, cationic, and noncharged NP surface coatings giving a clear indication of the intracellular pH environment that the different NPs experience after internalization. The pH profile of cationic nanosensors in comparison to HA conjugated nanosensors indicates that the intracellular trafficking is aimed at lysosomes regardless of whether CD44 receptor-specific or unspecific uptake is induced.

General information
Publication status: Published
Organisations: Department of Micro- and Nanotechnology, Colloids and Biological Interfaces, Center for Nanomedicine and Theranostics, Amphiphilic Polymers in Biological Sensing
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Pages: 2247-2255
Publication date: 2012
Peer-reviewed: Yes

Publication information
Journal: Bioconjugate Chemistry
Volume: 23
Issue number: 11
ISSN (Print): 1043-1802
Ratings:
BFI (2012): BFI-level 1
Scopus rating (2012): CiteScore 4.8 SJR 2.064 SNIP 1.259
Web of Science (2012): Impact factor 4.58
ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes
Original language: English
DOIs: 10.1021/bc300349n
Source: dtu
Source-ID: n:oai:DTIC-ART:acs/373263770::25100
Research output: Contribution to journal → Journal article – Annual report year: 2012 → Research → peer-review