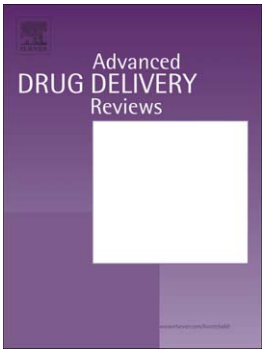

Molecular links among non-biodegradable nanoparticles, reactive oxygen species, and autophagy

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Title: Molecular links among non-biodegradable nanoparticles, reactive oxygen species, and autophagy

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Abstract
For nanoparticles to be successful in combating diseases in the clinic in the 21st century and beyond, they must localize to target areas of the body and avoid damaging non-target, healthy tissues. Both soft and stiff, bio-degradable and non-biodegradable nanoparticles are anticipated to be used to this end. It has been shown that stiff, non-biodegradable nanoparticles cause reactive oxygen species (ROS) generation and autophagy in a variety of cell lines in vitro. Both responses can lead to significant remodeling of the cytosol and even apoptosis. Thus these are crucial cellular functions to understand. Improved assays have uncovered crucial roles of the Akt/mTOR signaling pathway in both ROS generation and autophagy initiation after cells have internalized stiff, non-biodegradable nanoparticles over varying geometries in culture. Of particular – yet unresolved – interest is how these nanoparticles cause the activation of these pathways. This article reviews the most recent advances in nanoparticle generation of ROS and autophagy initiation with a focus on stiff, non-biodegradable technologies. We provide experimental guidelines to the reader for fleshing out the effects of their nanoparticles on the above pathways with the goal of tuning nanoparticle design.

Keywords
Autophagy; apoptosis; autophagosome; cell stress; endosome; xenophagy; LC3; lysosome; mTOR; myopathy

Chemical Compounds Studied in this Article
Aluminium oxide (PubChem CID: 9989226); LY294002 (PubChem CID: 3973); carbon (PubChem CID: 5462310); doxorubicin (PubChem CID: 31703); polystyrene (PubChem CID: 7501); silica (PubChem CID: 24261); ferrous oxide (PubChem CID: 14945); nitrous oxide (PubChem CID: 948); ethylene glycol (PubChem CID: 174); titanium dioxide (PubChem CID: 26042);

Abbreviations
AANTs, anodic alumina nanotubes; Akt, protein kinase B; AMPK, AMP-activated protein kinase; AONs, aluminum oxide nanorods; CNFs, cellulose nanofibers; CTNs, carboxylated titanium nanobelts; H295R, human adrenocarcinoma cells; HepG2, hepatocellular carcinoma cells; HUVECs, human umbilical vein endothelial cells; IFNA2,