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Autophagic response to cellular exposure to titanium dioxide nanoparticles

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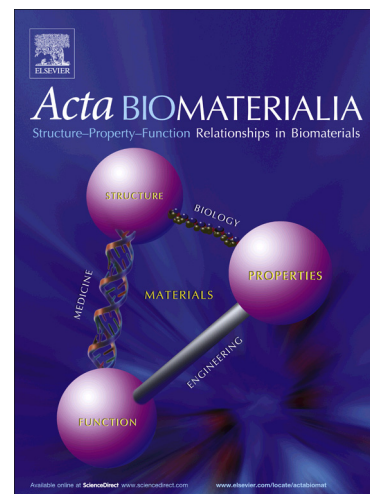
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Manuscript**Autophagic response to cellular exposure to titanium dioxide nanoparticles**

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Titanium dioxide is “generally regarded as safe” and titanium dioxide nanoparticles (TiO₂ NPs) are used in a wide variety of consumer products. Cellular exposure to TiO₂ NPs results in complex effects on cell physiology including induction of oxidative stress and impairment of lysosomal function, raising concerns about the impact of TiO₂ NPs on biological systems. We investigated the effects of TiO₂ NPs (15, 50, and 100 nm in diameter) on the lysosome-autophagy system, the main cellular catabolic pathway that mediates degradation of nanomaterials. Specifically, we monitored a comprehensive set of markers of the lysosome-autophagy system upon cell exposure to TiO₂ NPs, ranging from transcriptional activation of genes required for the formation of autophagic vesicles to clearance of autophagic substrates. This study reveals that uptake of TiO₂ NPs induces a response of the lysosome-autophagy system mediated by the transcription factor EB and consequent upregulation of the autophagic flux. Prolonged exposure to TiO₂ NPs, however, was found to induce lysosomal dysfunction and

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