
Polystyrene nanoplastics target lysosomes and affect lipid metabolism in RTgutGC and head kidney macrophages from *Oncorhynchus mykiss*

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Abstract

The presence of nanoplastics (NPs) in aquatic environments is widely recognized as a major threat as they can accumulate and affect living organisms. The interaction between NPs and the cellular machinery is not well characterized and scarce information is available. Aquatic organisms are highly exposed to NPs and fish can be particularly affected because these animals share an intimate relationship between gills and intestine and their water surroundings. In the current work, we focused on the interaction between NPs and intestinal cells and head kidney macrophages from rainbow trout to understand which are the cell organelles targeted by PS (polystyrene)-NPs and how this interaction impact on cell function. NPs possibly enter cells via endocytosis, phagocytosis, or can pass through the phospholipid membranes and other biological structures. In order to assess if the exposure of cells to PS-NPs was generating an oxidative response, we used two different fluorescent probes (H2DCFDA and DHE) to assess the production of reactive oxygen species (ROS). The results showed that under the evaluated conditions, the exposure of cells to PS-NPs do not trigger ROS production, which was further corroborated by the fact that the oxidative consumption ratio and extracellular acidification rate was also at control levels. Besides, confocal images did not show co-localisation of PS-NPs within mitochondria; nevertheless, co-localisation was found within lysosomes. RNASeq was also carried out in HKM exposed to PS-NPs, with data suggesting alterations in lipid metabolism and PPAR signalling pathways. Moreover, to assess if PS-NPs exposure were impacting the immune system, the expression of different target genes related with the immune function (*il1 β* , *tnf α* , *il6*, *il10*, *il12*, *cox2*, *mmp9* or *ppars*) were studied to determine which macrophage's phenotype was predominant.

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Results showed that even though neither HKM are M1 or M2 complete phenotype, they are more similar to M2 (M2-like macrophages).

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