

# School of Pharmacy PhD Project 2017 / 2018

Understanding the metabolic profile of nanoparticulate associated toxicity

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Nanoparticles are of increasing biomedical importance, due to their use as therapeutics, drug delivery systems and diagnostics. However, increasing evidence implicates nanoparticulate matter with the aberrant stimulation of the innate immune system and acute inflammation.

We have shown that nanoparticles cause alterations in lysosomal protease activity in macrophages, consistent with lysosomal dysfunction<sup>1</sup>. Macrophages are phagocytic cells, primarily responsible for the removal of nanoparticulate matter. The initiation of lysosomal dysfunction causes impaired autophagy and reactive oxygen species (ROS) dysregulation, resulting in inflammation, toxicity and cell death. ROS are crucial regulators of numerous cellular metabolic processes, and impaired oxidative regulation has been shown to contribute to particulate matter toxicity<sup>2</sup>.

This project will examine nanoparticulate associated toxicity to dissect the molecular mechanisms by which such pharmaceutical preparations induce undesirable inflammatory side effects. We will determine their impact on lysosomal proteases, ROS activity and key cellular metabolic processes such as glycolysis and lipid metabolism, to identify a metabolomic signature that will facilitate early detection of nanoparticle toxicity and inflammation.

The aim for each year of the project is:

Year 1: Assess the impact of nanoparticles (silica, alum, polystyrene) on lysosomal function and ROS activity in macrophages.

Year 2: Undertake metabolic profiling of cells following treatment with nanoparticulate matter to identify which metabolic pathways are dysregulated.

Year 3: Develop a metabolic signature that will enable early screening of novel new materials for undesirable cellular effects.

<sup>1</sup> Hughes et al. Particle and Fibre Toxicology. 2016.

<sup>2</sup> Khanna et al. Nanomaterials. 2015.

## General Email Enquiries

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## How to Apply

Postgraduate applications should be made using Queen's University [Direct Applications Portal](#). Please note that there are two application processes: one for admission to the university and another for postgraduate awards.

## Further Information

Additional information for prospective postgraduate students can be found on the [School of Pharmacy website](#) and the [Queen's Postgraduate website](#).