

# Superparamagnetic iron oxide nanoparticles with natural non-inflammatory surface coatings for diverse biological applications

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Superparamagnetic iron oxide nanoparticles (SPIONs) are used as contrast agents in magnetic resonance imaging (MRI). Their ability to be attracted by magnetic fields can enhance their interaction with specific immune cells and increase the immunogenicity of vaccines (Al Deen et al, 2017). Uncoated iron oxide nanoparticles however have toxicity and promote inflammatory reactions (Chakraborty et al., 2018). Our studies using polystyrene nanoparticles (PSNPs) have shown that vaccines do not require to be inflammatory or engage 'danger signals' to induce high levels of protective immunity (Wilson et al., In Press). In fact, lack of inflammation and toxicity is a desired feature in new generation vaccines, aiming to tackle diseases such as cancer and malaria, where inflammation is associated with unwanted clinical outcomes (Powles et al, 2015). Herein we show the synthesis and characterization of two new types of SPIONs coated with natural compounds, the carbohydrate pullulan (pSPION), or the neutral amino-acid glycine (gSPION). pSPIONs were non-toxic and non-inflammatory *in vitro* and *in vivo* and were able to be used as self adjuvanting vaccine carriers, promoting antibody responses to malaria antigens comparable to PSNP vaccine carrier formulations. gSPIONs in turn were characterized to be crystalline, colloiddally stable with a size of  $12 \pm 5$  nm and hydrodynamic diameter of  $84.19 \pm 18$  nm. Carbon, Hydrogen, Nitrogen (CHN) elemental analysis estimated approximately  $20.2 \times 10^3$  glycine molecules present per nanoparticle. It was possible to determine the biodistribution of the gSPIONs in the lung using 3D ultra-short echo time MRI. The gSPIONs were found to be taken up preferentially in deep alveoli by alveolar macrophages and neutrophils in the lung without being cleared to other organs. Importantly, the gSPIONs did not cause changes to airway resistance or induced inflammatory cytokines. Hence, the gSPIONs offer a platform to develop theranostics, with immediate utility in lung diseases where alveolar macrophages and neutrophils play a critical role, such as asthma and chronic obstructive pulmonary disease (COPD). Together these studies offer new types of SPIONs surface functionalization with neutral, natural compounds for diverse biological applications.

## References:

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