

# Polarization of TAMs to a pro-inflammatory phenotype by SPIONs as an adjuvant lung cancer therapy

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Tumour Associated Macrophages (TAMs) shape the tumour microenvironment (TME) and can promote tumour metastasis. Superparamagnetic Iron Oxide Nanoparticles (SPIONs) have been developed as a biocompatible and safe iron source for diagnostic and therapeutic purposes. When applied to the TME, SPIONs specifically activate TAMs and induce a pro-inflammatory phenotype. SPION-loaded TAMs exhibit anti-tumour activity indicating a potential window for therapeutic development and application (Costa da Silva et al. 2017 *Frontiers Immunology*). We have developed a novel form of nanoparticles with or without an iron core. These nanoparticles are taken up quickly and efficiently by bone marrow-derived macrophages (BMDMs). Importantly, our nanoparticles containing an iron core induce polarization to a pro-inflammatory phenotype significantly more than nanoparticles lacking the iron oxide core. The nanoparticle-induced pro-inflammatory phenotype is characterized by increased expression of cytokines and chemokines such as TNF $\alpha$ , IL1 $\beta$ , IL6 and CXCL10, as well as cell surface proteins such as CD86 and MHC II. Interestingly, in co-cultures of macrophages and Lewis lung carcinoma (LLC) cells, our SPIONs trigger an increased rate of tumour cell death at an earlier time point compared to the control nanoparticles and compared to cultures of macrophages or LLC cells alone. Future testing will include administration of these SPIONs to target macrophages in the TME of tumour bearing mice that have been intratracheally instilled with LLC cells, as well as a genetically engineered mouse model of Non-small Cell Lung Cancer expressing the EML4-ALK chromosomal rearrangement. Targeting TAMs in the TME with SPIONs may render lung tumours more susceptible to treatment leading to a novel avenue for adjuvant drug development.  
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Keywords : Tumour Associated Macrophages (TAMs), lung tumour microenvironment, nanoparticles, pro-inflammatory polarization, iron

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