Modulation of innate immune response by exosome in colorectal cancer

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Introduction

A key survival mechanism for cancer cells is the ability to escape recognition by the immune system. It is suggested that secretion of exosomes secreted by cancer cells may modify gene expression of immune cells, thus their behavior of immune around tumors. In this study, human leukemia cells (THP1) were differentiated into macrophage-like cells which is one of the most abundant innate immune cells in the tumour microenvironment. The aim of this project is to identify how exosomes might affect the response of immune cells to colorectal tumors.

Methodology

Extraction of exosome

- Human colorectal cancer cells (HCT116) were put into serum-free media (SF) for 72 hr. Harvested SF were centrifuge at 500g for 10 min. Supernatant filtered with 0.22µm syringe filter and the filtrate was centrifuged at 4000g for 30 min. Residue volume were collected.

Cell culture

- THP1 and HCT116 were cultured to 90% confluency. For control setup, THP1 was treated with PMA and incubated for 48 hr prior to LPS treatment. In experimental setup, fresh residue volume of SF were transferred to THP1 24 hr prior to LPS treatment.

Quantitative real time-PCR (qRT-PCR)

- 4 hr post-LPS treatment, RNA was harvested using RNeasy kit and cDNA was synthesised using iScript cDNA synthesis kit. Quantitative real time-PCR (qRT-PCR) for GAPDH, TNF-α IL-6 and IL-8 were done.

Results

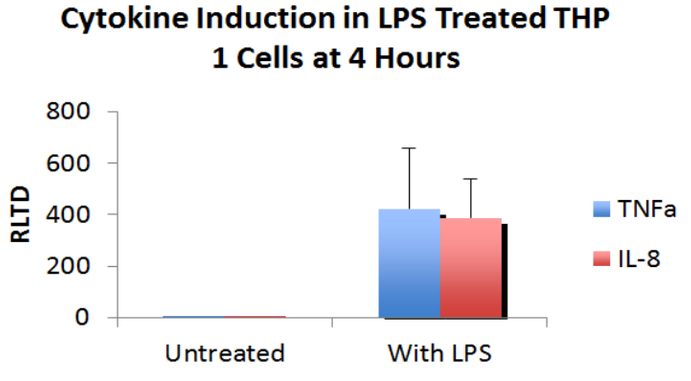

Fig.1 Cytokine induction in LPS treated THP1 cells at 4 hours

This showed that LPS treatment can increase cytokines production in PMA differentiated THP1.

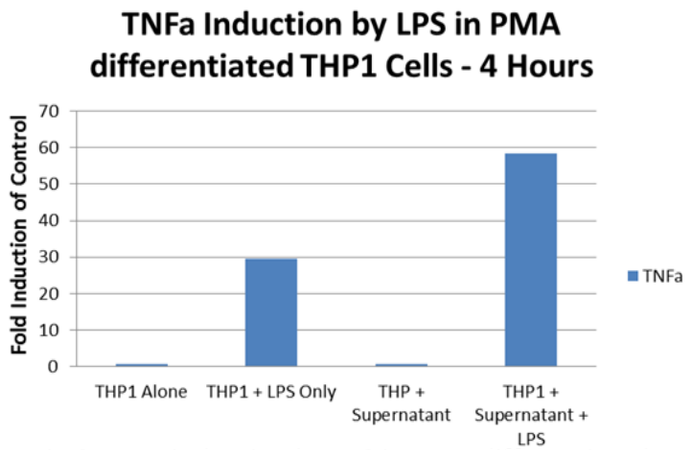

Fig.2 TNFα induction by LPS in PMA differentiated THP1 cells – 4 hours

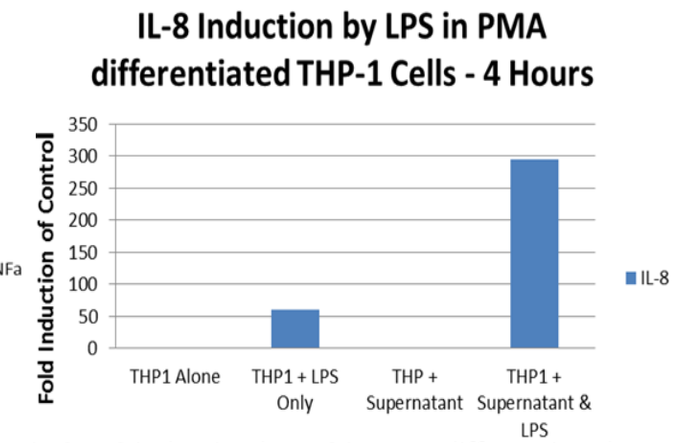

Fig.3 IL-8 induction by LPS in PMA differentiated THP1 cells – 4 hours

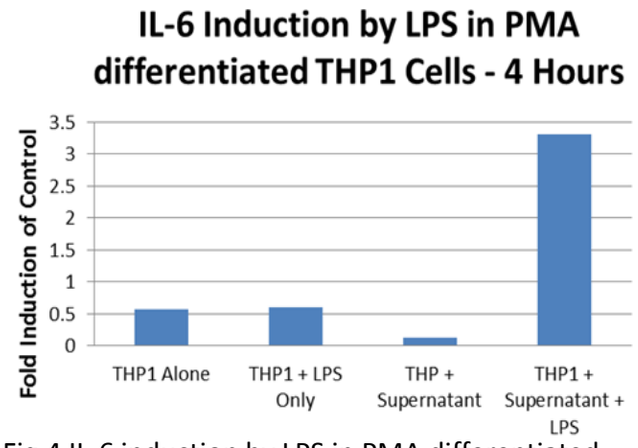

Fig.4 IL-6 induction by LPS in PMA differentiated THP1 cells – 4 hours

TNF-α, IL-6 and IL-8 productions were greatly enhanced by HCT116 exosomes.

Discussion

It is evidenced that HCT116 exosomes can enhance inflammatory response of THP1 to LPS treatment. TNF-α can enhance the migration and invasiveness of tumour cells via epithelial mesenchymal transition (EMT) which promote tumour metastasis (Wu and Zhou, 2009). Il-6 up-can regulate acute-phase proteins such as fibrinogen and α1-antitrypsin which can act as growth factors for tumour cells (Naka et al., 2002). Thus, these pro-inflammatory cytokines can promote tumour progression and metastasis in colorectal cancer.

reference

1. Wu, Y. and Zhou, B. P. (2009) 'Inflammation: a driving force speeds cancer metastasis', Cell Cycle, 8(20), pp. 3267-73.
2. Naka, T., Nishimoto, N. and Kishimoto, T. (2002) 'The paradigm of IL-6: from basic science to medicine', Arthritis Res, 4 Suppl 3, pp. S233-42.