EFFICACY OF STAPHYLOCOCCAL ENTEROTOXIN C IN THE TREATMENT OF MALIGNANT MESOTHELIOMA

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Background

Malignant mesothelioma (MM) is a highly aggressive tumour with a very poor survival rate of 6 to 18 months post-diagnosis. MM is highly resistant to conventional forms of treatment such as chemotherapy and radiotherapy and therefore alternative therapeutic strategies are required. Cancer immunotherapy represents a viable alternative as it aims to generate a tumour-specific immune response resulting in eradication of tumour. Bacterial products have been trialled in an effort to enhance local immunity and have demonstrated tumouricidal activity. Staphylococcal enterotoxins (SE) are classic models of superantigens that have potent mitogenic activity on T cells and demonstrated anti-tumour effects in several cancer models. Intrapleural delivery of staphylococcal enterotoxin C (SEC) has been used in China for many years as a pleurodesing agent. However, it is unknown whether SEC actually kills cancer cells.

Rationale and Methods

In this study, we examined the efficacy of staphylococcal enterotoxin C (SEC) in the treatment of MM in vitro. SEC was added at various concentrations (0-10ng/ml) to several human and murine MM cell lines and a human benign mesothelial cell line in vitro.

Results

Dose dependant cytotoxicity was observed in all cell lines resulting in a significant reduction in viability at higher doses (10ng/ml) when using trypan blue exclusion and WST-1 assays ($p<0.05$). In an effort to elucidate the mechanism of action of SEC, annexin V staining and flow cytometry were used to measure apoptosis. Results demonstrated a significant increase in apoptosis in MM cells when treated with SEC compared to untreated controls ($p<0.05$). On the contrary, benign mesothelial cells appeared to be resistant to the apoptotic effects of SEC at equivalent concentrations ($p>0.05$). ELISA based assays were used to examine cytokine profiles in culture supernatants of SEC treated MM cells and benign mesothelial cells. The chemotactic cytokine MCP-1 was expressed at similar levels in all cells with significant decreases only observed at the highest concentration (10ng/ml). In contrast, levels of the pro-inflammatory cytokine IL-8 decreased in SEC treated MM cells ($p<0.05$) compared to a significant increase in levels observed in benign mesothelial cells ($p<0.05$).

Conclusion

These results suggest that SEC kills MM cells in vitro with some specificity and its activity against MM in vivo warrants investigation.

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