AB052. SOH21AS116. Visceral fat as a tumour promotor: the role of adipose-derived factors in the immune-mediated chemoresistance of oesophageal adenocarcinoma

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Background: Visceral obesity is a key risk factor for development of oesophageal adenocarcioma (OAC). Greater than 70% of OAC patients are resistant to chemoradiotherapy and the visceral fat has been implicated in therapy-resistance, via secretion of tumour-promoting mediators into the periphery enhancing OAC cell survival/growth. This study investigates the effect of the secretome from visceral fat of OAC patients on chemo-sensitivity and anti-tumour T-cell immunity, with potential implications for therapy resistance.

Methods: The effect of visceral adipose conditioned media (ACM) on OAC cell viability and FLOT-chemotherapy induced-toxicity was assessed by crystal violet assay (n=16). The effect of ACM on immune checkpoint (IC) expression was also assessed on OAC cells and T-cells by flow cytometry (n=20). Anti-tumour cytokine profiles (IFN-γ, TNF-α and IL-2), cytotoxicity (CD107a), activation markers (CD27, CD69) and T-cell subsets (naïve, effector and central memory) were also investigated following treatment with ACM by flow cytometry (n=12).

Results: ACM increased OAC cell growth and decreased the toxicity of FLOT ($P<0.05$). Anti-tumour cytokine production was enhanced following treatment with ACM, however, ACM generated from patients with early-stage tumours enhanced T-cell cytotoxicity more substantially than ACM generated from patients with advanced tumours. Markers of T cell activation were decreased and ICs were increased by ACM generated from patients with more advanced stage tumours.

Conclusions: The visceral fat from OAC patients protected OAC cells from FLOT chemotherapy via secretion of soluble mediators. ACM from patients with more advanced stage tumours exhibited a more immunosuppressive profile highlighting the role of the tumour in subverting distal organs toward a tumour-promoting milieu.

Keywords: Visceral fat; adipose tissue; oesophageal adenocarcinoma immunosuppression; chemoresistance

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Footnote

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