O21 Macrophage-associated changes in peri-prostatic adipose tissue; a novel local driver of prostate tumorigenesis?

Eur Urol Suppl 2019;18(8):e3060

Narayanan P.[1], Martinez Campesino L.[2], Kim T.[2], Muthana M.[1], Wilson H.L.[2], Kiss-Toth E.[2]

[1]University of Sheffield, Oncology and Metabolism, Sheffield, United Kingdom, [2]University of Sheffield, Infection Immunity and Cardiovascular Disease, Sheffield, United Kingdom

Introduction & Objectives: There is significant evidence suggesting that adipose dysfunction during obesity is associated with increased risk of prostate cancer (PCa) mortality and cancer recurrence even after radical prostatectomy. Cross-talk between adipose tissue (AT) cells and PCa cells modulates lipolysis, macrophage recruitment and polarisation creating a pro-tumorigenic microenvironment. Given that the number of immune cells in the adipose depot increases significantly during obesity, we believe that adipose tissue macrophages (ATMs) are key regulators of tumorigenesis in this context.

Materials & Methods: Alterations in the AT morphology and inflammatory state during obesity were analysed by subjecting C57BL/6 littermate mice to a low or high-fat diet. The peri-prostatic AT was isolated and either fixed for histological analysis or the ATM were isolated for gene expression analysis. To assess the phenotype of ATM and adipose homeostasis in relation to PCa, 7-week-old BALB/c nude mice were injected with LnCAP cells into the prostate, ultimately developing PCa. Tumour tissues were collected for gene expression analysis. The peri-prostatic AT was isolated and either fixed for histological analysis or the ATMs were isolated for gene expression profiling. These results were compared to those from a low and high-fat diet. Mature adipocytes from the peri-prostatic AT were also isolated and cultured in media for secretome analysis.

Results: Obesity induced by a high-fat diet increased the peri-prostatic AT adipocyte size. Gene expression analysis of ATMs suggests they are polarised towards a pro-inflammatory phenotype, but do still express anti-inflammatory markers. In contrast, in the presence of PCa tumour, the peri-prostatic AT environment is “re-educated”. Secretion of pro-inflammatory cytokines such as TNF-α by adipocytes is reduced, the ATMs are polarised towards an anti-inflammatory phenotype, with decreased RNA expression of *Tnf* and *Nos2*.

Conclusions: The local adipose environment changes differently under obesity and PCa. Obesity promotes infiltration of macrophages leading to inflammation in the adipose, supporting a more pro-tumorigenic state of inflammation, proliferation and metastasis. However, cross-talk between PCa cells and AT cells promotes changes in the adipose environment, where ATMs switch to an anti-inflammatory phenotype resembling that of a tumour associated macrophage.