Perirenal Adipose Tissue and Clear Cell Renal Cell Carcinoma
“The Triad: Macrophage-Cancer Cell-Adipocyte”

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BACKGROUND
Renal Cell Carcinoma (RCC) is considered the deadliest urological cancer. Importantly, obesity is one of the well-recognized risk factors associated with RCC. Nevertheless, based on epidemiological studies reporting that obesity could also contribute to better disease outcomes, a phenomenon designated “obesity paradox” emerges. Still, these conflicting observations and the mechanisms underlying the influence of the adipose tissue in the tumour and its microenvironment, are not completely clarified. Clear Cell RCC (ccRCC) is the most common subtype of RCC, it arises from renal tubular epithelial cells in the renal parenchyma and presents aberrations, occurring by epigenetic or genetic events, such as the loss of short arm of chromosome 3 and VHL tumour suppressor gene inactivation. The morphological hallmark of ccRCC is the clear cytoplasm with lipid and glycogen accumulation. Furthermore, ccRCC is characterized by immune cell infiltration, including macrophages, which are involved in ccRCC development and progression. Therefore, this project aims at better understanding the role of the adipose tissue in the ccRCC milieu by characterizing the interplay between the triad: adipocytes, ccRCC cells and macrophages. Herein, we present the preliminary results obtained, so far, in the scope of this pilot study.

METHODS

A. In vitro study

B. Human cohort analysis

RESULTS

1. The expression of CD86 is decreased in macrophages co-cultured with 786-O cells.

2. The ccRCC 786-O cell immunogenicity profile is not altered in the presence of macrophages.

3. Macrophages and 786-O in co-culture seem to alter their cytokine secretion profile.

CONCLUSION

The 786-O cells induced an anti-inflammatory profile in macrophages. The macrophages in the presence of 786-O displayed a decreased in CD86 expression and an increased in CD206 expression. In addition, the secretion of IL-10 in the co-culture conditioned medium is significantly decreased, while IL-6 is significantly increased. Thus, our preliminary results, indicated that ccRCC cells might have mechanisms to subvert the macrophages phenotype into an M2-like phenotype.

REFERENCES

FUTURE PERSPECTIVES

In future work, we will: i) continue to analyze the cellular molecular profiles, ii) increase the number of experiments as a means to strengthen our conclusions, iii) carry out the adipocyte culture from fresh human samples and iv) perform the cultures of the triad, in order to discover potential key molecules of these interplay, v) start the immuno-localization of macrophages, tumour cells and adipocytes in the ccRCC human samples and, vi) validate the candidate key players of the triad communication.