Body fat distribution and obesity

8.2 Valorisation addendum

Obesity is an ever-increasing global health problem, that needs to be tackled to reduce the risk for other chronic diseases related to excess body adiposity and associated healthcare costs. The present thesis describes a series of studies that were performed to investigate (functional) differences between abdominal and femoral subcutaneous AT and adipocytes, as well as the impact of oxygen tension on the inflammatory phenotype of abdominal and femoral adipocytes. The valorisation potential of the work described in this thesis will be discussed in terms of socioeconomic relevance, the scientific implications for specific target groups, and potential applicability for commercial exploitation.

Societal relevance

Obesity is a complex chronic disease linked to increased risk of developing insulin resistance, T2DM, CVD, and various types of cancer (1-7). Furthermore, it appears to be linked to risk of nearly every chronic condition, ranging from osteoarthritis to poor mental health (8). Quality of life and life expectancy are significantly impaired in people living with obesity. Therefore, the need to better understand and treat obesity are of paramount importance. This has become even more apparent during the COVID-19 pandemic, as obesity is associated with an increased risk of infection and worse clinical outcomes in people with obesity that encounter COVID-19 (9, 10). The economic burden of obesity is associated with increased hospitalisation and healthcare-related costs (8, 11, 12). Obesity has also been linked to decreased productivity per person (8, 13). Taking these factors into account, obesity clearly is an important socio-economic problem that needs to be prevented and treated to increase population health and reduce future health care costs.

In this thesis, we have examined the properties of AT (dys)function in people with normal weight or obesity. The results may not be immediately applicable to tackle obesity. However, any attempt to expand our understanding of the pathophysiology associated with this complex condition, from a molecular and physiological approach as done in this thesis, may contribute to the development of novel and/or more personalized prevention and treatment avenues.

Scientific impact, innovation, and exploitation

Differences between distinct AT depots, like abdominal and femoral AT, seem to explain differences in chronic cardiometabolic disease risk in people with a different body fat distribution pattern. The present work underlines the presence and importance of these AT depot differences, indicating that abdominal and femoral AT differ in blood flow, the oxidative machinery, and inflammatory signatures. However, further characterisation of these (and other) AT depots is necessary, in combination with cardiometabolic risk assessment in humans.

Since data on AT depot differences in humans is scarce, better knowledge of the properties of abdominal and femoral subcutaneous AT using a translational approach is of great scientific value. In this thesis, we showed slight differences in the inflammatory

signatures of AT of the abdominal and femoral depot. However, for the first time we have presented important differences of the oxidative machinery, both *in vivo* and in primary human adipocytes.

The results described in this thesis have been presented at national (Society for Endocrinology BES 2019) and international conferences (European Congress of Endocrinology 2022, and 58th Annual Meeting of the EASD 2022) to scientists, health care professionals, physicians, and dietitians working in the field of endocrinology, obesity, and diabetes. Moreover, the results have been and will become available to the scientific community through publications in international peer-reviewed journals, with the aim to increase knowledge in the research area of obesity and AT function, inflammation, tissue oxygenation, oxidative metabolism, insulin resistance and T2DM.

I was privileged to be enrolled in a joint PhD program between the University of Birmingham (UK) and Maastricht University (the Netherlands). The nature of this joint PhD program also had a direct scientific impact. Collaborations between two countries and institutions were initiated and stimulated, which is a great example of innovation within the international scientific community. Interdisciplinary teams of clinical and basic scientists, research nurses, laboratory technicians and support staff have been involved in the studies described in this thesis.

The findings presented in this thesis are mainly focusing on the better understanding by detailed phenotyping and investigation of AT biology and *in vivo* physiology. The use of the Doppler ultrasound as a proxy method for ATBF measurement could be used by other research groups. The physiological and biological findings highlight the importance of examining (changes in) body fat distribution pattern and AT function in future clinical trials, and may give leads for the development of novel treatments (i.e. targeting AT oxygenation). In order to understand the implications of the depot-specific signatures, a deeper understanding of each adipose tissue depot's phenotype is needed. In the future, depot-specific signatures could serve as biomarkers for monitoring and/or predicting clinically relevant outcomes e.g., related to successful weight management and obesity-related risk reduction. Whether treatments can be developed based on these findings will need to be examined in future research as well, given the obstacle posed by having to address depot-specific targets rather than a systemic pathophysiological mechanism. Altogether, the scientific findings described in this thesis may be of value for academia, industry, and health care professionals.

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