OVERVIEW

Physiological determinants and impacts of the adipocyte phenotype

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The properties of adipose tissues accumulating in various compartments and ectopic sites around the body represent critical determinants of the relationship between obesity and metabolic disease. The increasingly recognized plasticity of the adipose cell phenotype led to many articles on the cellular characteristics and origins on brown, white and also of 'beige' or 'brite' adipocytes in recent years. This overview is a summary of manuscripts that were prepared by speakers at the 16th International Symposium of the Laval University Research Chair in Obesity. The data reviewed herein suggest that brown adipose tissue-inducing therapies may also modulate skeletal status through their effects on bone morphology and structure. Moreover, recently identified beige-like properties of epicardial fat in humans could eventually be considered for the management of coronary heart disease in humans. The regulation of brown adipose tissue activation through sympathetic nervous system innervation or non-sympathetic activators is also a complex phenomenon that needs further investigation. Scientific work aimed at better understanding the characteristics and regulation of metabolic homeostasis in each adipose compartment is an important aspect of our progression toward preventive or even curative approaches for obesity.

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The multiple properties of adipose tissues accumulating in various compartments and ectopic sites around the body represent critical determinants of the relationship between obesity and metabolic disease.¹ In this regard, scientific work aimed toward a better understanding of the characteristics and regulation of metabolic homeostasis in these distinct adipose organs remains a crucial aspect of, or progression toward, preventive or even curative approaches for obesity.

The great plasticity of the adipose cell phenotype has been increasingly recognized in the past decade.^{2,3} In particular, the cellular characteristics and origins on brown, white and also of 'beige' or 'brite' adipocytes have attracted much scientific attention in recent years.^{4–6} Induction of brown adipose tissue growth or browning of white adipocytes is now considered as a potentially interesting approach to mitigate obesity and related complications.^{7–9}

The present overview summarizes manuscripts that were prepared by speakers at the 16th International Symposium of the Laval University Research Chair in Obesity. The symposium was held in November 2013 in Quebec City, Canada, and was entitled '*White, Beige, Brown: What Determines the Colour of Adipose Tissue*'.

BROWN ADIPOSE TISSUE AND BONE

The first manuscript was written by Lidell and Enerbäck.¹⁰ It provides a brief overview of recent research on brown adipose tissue and also summarizes recent findings relating brown adipose tissue to bone metabolism. The manuscript reviews evidence demonstrating that human brown adipose tissue favorably affects bone structure. The mechanisms by which this connection occurs

are also reviewed. Overall, it is expected that brown adipose tissue-inducing therapies aimed at treating metabolic disease might also improve skeletal status through their effects on bone morphology and structure.

THERMOGENIC PROPERTIES OF HUMAN EPICARDIAL ADIPOSE TISSUE

The second manuscript was prepared by Chechi and Richard,¹¹ and it focuses on epicardial adipose tissue. This unique fat compartment is located within the heart pericardium and shares close anatomic proximity and vascular supply with the myocardium and coronary arteries. The manuscript first clarifies definitions of the terms used to describe adipose tissue located within and around the heart. The physiological and pathophysiological relevance of the epicardial compartment is then reviewed. The extent of this ectopic depot has been assessed in humans using various imaging modalities, and these studies have generally shown an association with the onset and progression of coronary artery disease. The mechanisms underlying this association are also reviewed. The authors then summarize evidence supporting the notion that thermogenic properties of this fat compartment could represent a potential target for the management of coronary heart disease in humans.

NEURAL CONTROL OF WHITE, BEIGE AND BROWN ADIPOCYTES

The third manuscript was prepared by Bartness and Ryu.¹² It directly addresses the important question of the sympathetic nervous system innervation of brite or beige adipocytes. The

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manuscript first provides a historical perspective on brown and brite or beige adipocytes. Evidence for sympathetic nervous system innervation of these cells is then closely reviewed. Overall, very little data are available, but it is possible to infer that sympathetic drive and norepinephrine stimulation of the β 3-adrenoceptor in white adipose tissue are important and causative factors for the browning phenomenon. The question of brain sites involved in the presence of brite or beige cells in white adipose tissue is then discussed. The dorsomedial hypothalamus appears as the only site involved in this phenomenon. The density of the sympathetic nerves innervating white adipose tissue, in conjunction with the ability of the cells to undergo the browning process, appears as a key element of the process.

NON-SYMPATHETIC CONTROL OF BROWN ADIPOSE TISSUE

The fourth manuscript was prepared by Cereijo *et al.*¹³ It provides a review of current knowledge and recent developments on browning activators belonging to the category of non-sympathetic mediators. The signals discussed include those of members of the bone morphogenetic protein family, prostaglandins, triiodothyronine, vitamin A derivatives, ligands of PPAR- γ and PPAR- α , and modulators of ion channels activity. Other activators such as irisin, natriuretic peptides, cardiotrophin, GLP-1, TGR5 and FGF21 are discussed. Overall, it is recognized that multiple peripheral tissues are capable of secreting regulatory factors that may influence brown adipose tissue activity and/or promote browning. Interestingly, the discovery of agents that could activate browning independently of the sympathetic nervous system would have the advantage of avoiding side effects of sympathomimetics.

CONCLUSION

Recent advances on the topic of brown adipocytes and its relationship with energy metabolism emphasize the importance of unraveling the pathways that may promote increased activity of these cells. Brown adipose tissue activation or browning of white adipocytes in specific fat compartments may contribute to a better handling of metabolic substrates, which may in turn promote energy expenditure and reduce the disease burden associated with obesity.

CONFLICT OF INTEREST

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DISCLAIMER

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