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Effects of ageing and dietary restriction in mouse adipose tissue and oleic acid in cultured human adipocytes

Abstract: Ageing is associated with redistribution of fat around the body and saturation of visceral adipose depots. Visceral adipose tissue in humans is susceptible to inflammation due to nutritional imbalance and ageing. Likewise, the presence of excess fat in obesity or during ageing places extra stress on visceral depots, resulting in chronic inflammation and increased senescence. This process can contribute to the establishment of the metabolic syndrome and accelerated ageing. Due to its importance in metabolic and inflammation regulation, fat is a prime tissue for health span determination as well as a prime target for DR and other nutritional interventions. Dietary restriction (DR) is known to alleviate physiological signs of inflammation, ageing and senescence in various tissues including adipose tissue. Dietary restriction (DR) is thought to exert its beneficial effects on health span at least partially by a senolytic and senostatic action, i.e. by reducing frequencies of cells with markers of DNA damage and senescence in multiple tissues.

We recently demonstrated that ageing and normal ad libitum (AL) nutrition in mice resulted in increased adipocyte size, DNA damage, p16INK4a expression and inflammation in visceral adipose tissue while some of these senescence markers could be alleviated by late-onset, short-term dietary restriction (DR). This highlights the health benefits of a decreased nutritional intake over a relatively short period of time at middle age. Moreover, another DR study on mice described a “metabolic memory” as protection against AL-induced senescence after shifting mice from DR back to AL nutrition.

Finally, we modelled a nutritional imbalance inducing Inflammation, hypertrophy and senescence in vitro through treatment of primary human subcutaneous and omental adipocytes with the saturated fatty acid (FA) palmitic acid (PA). This resulted in a significant increase in DNA damage as well as p16INK4a levels correlating with enhanced intracellular lipid accumulation. Hypertrophy in white adipose tissue (WAT) can result in sustained systemic inflammation, hyperlipidaemia, insulin resistance, and onset of senescence in adipocytes. In contrast, DNA damage could be prevented with the unsaturated FA oleic acid (OA). With olive oil being an important part of the Mediterranean diet another study found also other oils such as argan oil to have similar effects of preventing DNA damage in vivo and in vitro.

These studies highlight the importance of various nutritional interventions in vivo and in vitro on health parameters of adipocytes and delaying senescence and ageing.

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