Therapeutic intervention in obese humans using approaches which lower tissue AGE burden may be cost effective strategies to treat obesity related renal dysfunction.

doi:10.1016/j.orcp.2010.09.126

O61

Lack of Y6 receptor signaling in mice results in a lean phenotype on a chow diet but exacerbated high fat diet-induced obesity

E. Yulyaningsih*, L. Macia, F. Driesler, H. Herzog, A. Sainsbury

Neuroscience Research Program, Garvan Institute of Medical Research, Australia

Introduction: Neuropeptide Y (NPY) is the most abundant neuropeptide in the mammalian brain and is known to regulate several physiological functions through a family of G protein-coupled receptors: Y1, Y2, Y4, Y5 and Y6. Y6 receptor expression in the hypothalamus, a region of the brain that controls energy homeostasis and circadian rhythms, suggests a role for this receptor in the regulation of appetite and energy balance.

Methods: The metabolic phenotype of male mice lacking Y6 receptors (Y6−/−) was investigated. Mice of 7−8 weeks of age were either fed a normal chow or a high fat diet for 15 weeks.

Results: On a normal chow diet, lack of Y6 receptor signaling leads to striking reductions in body weight, lean body mass and adiposity in association with a significantly elevated metabolic rate and a marked increase in physical activity, while food intake is not different from that of wild type controls. Additionally, we report an elevated respiratory exchange ratio in chow-fed Y6−/− mice during the dark phase, indicating reduced fat utilization for energy production.

In contrast to the lean phenotype of chow-fed knockouts, 15 weeks of high fat feeding led to significantly exacerbated obesity in Y6−/− mice compared to wild type control mice on the high fat diet, as demonstrated by markedly increased body weight gain with disproportionately higher white adipose tissue accumulation, while the lean body mass remained significantly decreased relative to fat-fed wild types. In parallel to this, Y6−/− mice on the high fat diet showed increased fasting serum glucose and insulin, significantly worsened glucose tolerance and insulin resistance compared to fat-fed wild type controls.

Conclusion: These results indicate that the Y6 receptor plays a key role in homeostatic control of energy balance, likely through regulation of energy expenditure and substrate utilization.

doi:10.1016/j.orcp.2010.09.127

O62

Intra-abdominal transplantation of subcutaneous adipose tissue reduces obesity and improves glucose tolerance in fat-fed mice

M.M. Swarbrick*, D. Wilks, E. Preston, S.L. Hocking, G.J. Cooney

Diabetes and Obesity Program, Garvan Institute of Medical Research, Sydney, Australia

Background: Accumulation of excess intra-abdominal (visceral) adipose tissue is more closely related to insulin resistance (IR) and dyslipidaemia than accumulation of subcutaneous fat. This is likely due to one or more specific properties of visceral adipose tissue. We investigated the properties of different fat depots by transplanting additional visceral (epididymal) or subcutaneous (inguinal) adipose tissue into mice. Re-innervation of fat grafts by sympathetic nerve fibres was also studied.

Methods: In 7-week-old male C57BL6/J mice, inguinal (subQ) and epididymal (vis) fat pads were dissected out, washed and sutured onto the visceral side of the anterior abdominal wall of recipient littermates (subQ → vis and vis → vis mice, respectively). After recovery, recipient and sham-operated mice were provided with a high-fat diet (45% fat by energy) ad lib. for 6 weeks, when glucose tolerance tests were performed. Sympathetic innervation of fat grafts and intact pads was measured by tyrosine hydroxylase (TH) immunoreactivity.

Results: Equivalent amounts of fat were transplanted into subQ → vis, and vis → vis mice ($p = 0.21$ for difference). At 6 weeks after transplantation, there were no differences in body weight between groups; however, subQ → vis mice had better glucose tolerance than sham and vis → vis mice (mean glucose AUCs were 930 ± 117, 718 ± 106, 1125 ± 85 mmol min for sham, subQ → vis and vis → vis mice, respectively; $n = 4$−7 per group, overall $p = 0.037$, K−W test). At sacrifice, fat grafts from subQ → vis and vis → vis mice did not differ in mass ($p = 0.47$), but the masses of endogenous fat pads were reduced in subQ → vis mice (53−69% of sham controls) compared to vis → vis mice (76−101% of sham controls; overall effect of type of transplanted fat, $p = 0.004$, ANOVA). Notably, TH expression, indicating re-innervation by sympathetic nerve fibres, was detectable in protein extracts and tissue sections at 6 weeks, but