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The aipokine zinc-α2-glycoprotein is down regulated with fat mass expansion in obesity

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Zinc-α2-glycoprotein (ZAG) is a 43 kDa glycoprotein belonging to the MHC class I family[1]. ZAG is present in a variety of tissues including white adipose tissue, and is secreted by adipocytes as an adipokine[2]. In adipose tissue it may act locally to influence adipocyte metabolism. To elucidate the potential role of ZAG in obesity the present study has examined the effect of increased adiposity on ZAG expression in adipose tissue of both obese (*ob/ob*) mice and human subjects. To explore whether ZAG has a paracrine role in the secretory function of adipocytes, the study also examined the effects of ZAG on adiponectin and leptin secretion by human adipocytes.

Adipose tissues (visceral and subcutaneous) were collected from male obese (*ob/ob*) and lean (*ob/+*) mice (ten mice per group), and from human subjects (twelve male, fourteen female) with a wide range of BMI (19–80 kg/m^2). For *in vitro* studies, human SGBS preadipocytes were used.

Studies on *ob/ob* mice revealed that ZAG mRNA was significantly reduced in subcutaneous (4-fold; $P<0.05$) and epididymal (8-fold; $P<0.05$) fat depots as compared with lean controls. Concomitantly, ZAG protein levels were decreased by 2-fold ($P<0.05$) in subcutaneous fat of *ob/ob* mice.

For human subjects ZAG mRNA and protein were detected in visceral and subcutaneous fat but there were no depot differences in expression levels. ZAG mRNA level was negatively correlated with BMI (visceral r −0.61, $P<0.001$, n 23; subcutaneous r −0.6, $P<0.05$, n 14) and fat mass (visceral r −0.62, $P<0.01$; subcutaneous r −0.6, $P<0.05$). Negative associations were also found between ZAG mRNA and insulin resistance variables, including plasma insulin (visceral r −0.65, $P<0.001$; subcutaneous r −0.55, $P<0.05$) and homeostasis model assessment of insulin resistance (visceral r −0.65, $P<0.001$; subcutaneous r −0.52, $P=0.055$). In addition, ZAG mRNA was positively correlated with adiponectin (visceral r 0.5, $P<0.05$; subcutaneous r 0.82, $P<0.001$) but negatively associated with leptin mRNA (visceral r −0.42, $P<0.05$; subcutaneous r −0.54, $P<0.05$).

Given the correlations between ZAG mRNA and adiponectin and leptin transcripts, the effect of ZAG on the secretion of these adipokines was explored in SGBS adipocytes. Recombinant ZAG stimulated adiponectin release but inhibited leptin release from differentiated human adipocytes.

It is concluded that: (1) ZAG expression in adipose tissue is down regulated with increased adiposity and circulating insulin; (2) ZAG stimulates adiponectin, but decreases leptin, secretion by adipocytes. It is suggested that ZAG may play a protective role in the susceptibility to insulin resistance and other obesity-related disorders.

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