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1 .Topic in Research Achievements in the Year 2006

Weight gain is associated with infiltration of fat by macrophages, suggesting that they are an important source of inflammation in obese adipose tissue. Using an in vitro co-culture system composed of 3T3-L1 adipocytes and RAW264 macrophages, we demonstrated that saturated fatty acids and TNF□ derived from adipocytes and macrophages, respectively, play a critical role in the co-culture-induced inflammatory changes. These observations suggest that a paracrine loop involving saturated fatty acids and TNF□ between adipocytes and macrophages establishes a vicious cycle that aggravates inflammatory changes in obese adipose tissue (**Arterioscler. Thromb. Vasc. Biol.** 25: 2062-2068, 2005).

Co-culture of adipocytes and macrophages resulted in NF-□B activation in both cell types. Moreover, pharmacological inhibition of NF-□B markedly suppressed the co-culture-induced production of pro-inflammatory cytokines and adipocyte lipolysis. Peritoneal macrophages obtained from C3H/HeJ mice carrying a functional mutation in the TLR4 gene exhibited marked attenuation of TNF□ production in response to saturated fatty acids. Notably, co-culture of hypertrophied adipocytes and C3H/HeJ peritoneal macrophages resulted in marked inhibition of pro-inflammatory cytokine production and adipocyte lipolysis. Furthermore, adiponectin production was reduced by co-culture of hypertrophied adipocytes and C3H/HeN peritoneal macrophages. We, therefore, postulate that saturated fatty acids, which are released in large quantities from hypertrophied adipocytes via the macrophage-induced adipocyte lipolysis, serve as a naturally occurring ligand for TLR4, thereby inducing the inflammatory changes in obese adipose tissue (**Arterioscler. Thromb. Vasc. Biol.** 27: 84-91, 2007). Very recently, we have demonstrated the attenuation of adipose tissue inflammation in C3H/HeJ mice relative to control C3H/HeN mice during a high-fat diet (**Biochem. Biophys. Res. Commun.** in press, 2007).

Our data provide *in vivo* and *in vitro* evidence that the saturated fatty acids/TLR4/NF-□B pathway plays a critical role in obesity-related adipose tissue inflammation and thus help identify the therapeutic targets that may reduce obesity-induced inflammation and the metabolic syndrome.

2 .Publications in the year 2006

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3 . Abstracts in the year 2006
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