

The Skinny on CCN2

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ABSTRACT

The CCN family of matricellular proteins directly or indirectly affects development and differentiation. A recent report written by Tan and colleagues (*Am J Physiol Cell Physiol* 295: C740–C751, 2008) shows that CCN2 inhibits adipocyte differentiation. This commentary summarizes these observations.

Formation of new adipose tissue occurs in adult mammals in response to excess energy supply. Adipocytes differentiate from mesenchymal stem cells to adipocytes through a series of well-characterized morphological and biological changes, eventually accumulating lipid droplets (Fasshauer et al., 2000). These changes result from alterations of expression and organization of the extracellular matrix and cytoskeleton (Croissant et al., 2002).

Transforming growth factor β (TGF- β) inhibits adipocyte differentiation (Ignatz and Massague, 1985), and is found in increased levels in adipose tissue of both animal and human models of obesity (Alessi et al., 2000). CCN2 (connective tissue growth factor, CTGF) is a downstream mediator and/or co-regulator of the actions of TGF- β in fibrosis (Leask and Abraham, 2004). Although TGF- β 1 inhibits adipocyte differentiation, whether CCN2 has a similar role has not been reported.

In a recent study, the effect of CCN2 on adipogenesis was assessed. NIH/3T3-L1 fibroblast cells were differentiated into fat by standard methods, in the presence or absence of CCN2 (Tan et al., 2008). The degree of differentiation was measured by the expression of differentiation markers as well as the accumulation of lipids, as visualized by Oil Red O staining. CCN2 inhibited adiponectin expression and lipid accumulation, and suppressed the expression of the decreased lipogenic enzyme glycerol-3-phosphate dehydrogenase. The CCAAT/enhancer binding proteins (C/EBPs) are a family of transcription factors. Of these, C/EBP- α and C/EBP- β being transiently increased at the early phase of adipocyte differentiation; C/EBP- α is required for the differentiation of preadipocytes to mature adipocytes in most white adipose tissue depots (Lane et al., 1999). Tan and colleagues (2008) found that CCN2 suppressed C/EBP- α mRNA expression and nuclear localization. Similar results were observed in CCN2-treated primary adipocytes. Finally, CCN2 expression was observed in central fat depots in vivo.

Collectively, these data suggest that CCN2 may influence the degree of adipocyte differentiation in vivo. However, further experiments are required to clarify this issue. Moreover, although the results presented suggest that CCN2 may act by suppressing C/EBP- α , this hypothesis has yet to be tested. In fact, the mechanism by which CCN2 acts to reduce adipogenesis needs to be thoroughly investigated. In the future, it will be

interesting to see whether CCN2 suppresses obesity in vivo. Nonetheless, the data presented in this novel work are an important first step, and suggest the intriguing notion that CCN2 may ultimately be used as a therapy for obesity.

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