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BITS AND BYTES

Getting to the heart of the matter: CCN2 plays a role in cardiomyocyte hypertrophy

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Abstract Connective tissue growth factor (CTGF/CCN2) is overexpressed in diabetes. Diabetic rats possess myocardial and cardiomyocyte hypertrophy. In a recent report, Wang and colleagues (Am J Physiol Cell Physiol. 2009 Jul 22. [Epub ahead of print]) show that CCN2 directly mediates cardiomyocyte hypertrophy as well as that induced by high glucose and fatty acid. CCN2 acted via the TrkA receptor. These data are the subject of this commentary, and emphasize that CCN2 may be an excellent target for therapy in diabetes.

Keywords Connective tissue growth factor · CCN2 · Diabetes · Cardiac hypertrophy · TrkA

Diabetes not only characterized by kidney failure but also can cause acute and chronic heart failure (diabetic cardiomyopathy) characterized by cardiac hypertrophy, apoptosis and excess accumulation of extracellular matrix (Karnik et al. 2007; Feuvray and Darmellah 2008). The proadhesive matricellular protein CCN2 is overexpressed in diabetes and can promote hypertrophy, apoptosis and fibrosis (Leask and Abraham 2006). Although CCN2 has been proposed as a target for drug therapy in diabetes (Mason 2009), whether CCN2 contributes to diabetic cardiomyopathy is unknown.

A recent report by Wang et al. (2009) showed that recombinant CCN2 could directly promote both apoptosis and hypertrophy in a cardiac myocyte cell line. Glucose and the fatty acid palmitate induced both apoptosis and hypertrophy in the same cell line. Glucose and the fatty acid palmitate induced CCN2 mRNA and protein, and siRNA against CCN2 significantly reduced the apoptosis and hypertrophy caused by these agents. Previously, it had been shown that CCN2 can bind and activate the TrkA receptor in human kidney mesangial cells (Wahab et al. 2005). Wang and colleagues (2009) found that pharmacological inhibition of TrkA blocked aspects of CCN2 activity.

That fatty acids can induce CCN2 lengthens the list of agents, which were initially believed to include only TGFβ, to promote CCN2 mRNA and protein expression (Blom et al. 2002). These data are significant as these strongly suggest that anti-CCN2 strategies may be useful in targeting several aspects of diabetes in addition to diabetic nephropathy and retinopathy (Mason 2009), and also suggest that CCN2 may contribute to additional pathologies induced by fatty acids including fatty liver disease (Paradis et al. 2001). Future efforts, no doubt, will be focused on expanding the scope of these studies to animal models and, ultimately, humans.

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