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The role of tenascin C under hyperglycaemic and hypertrophic conditions - In vitro H9c2 rat cardiomyoblasts model

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Background: The increase of Tenascin C (TN-C) expression is known to be associated with the maladaptive signalling cascade involving left ventricle remodelling following either myocardial infarction or hypertension. In addition, there is substantial evidence that diabetes induces left ventricle hypertrophy and impaired cardiac function. However, there is a lack of evidence about the impact of hyperglycaemia and cellular hypertrophy stress on the expression of TN-C expression in cardiomyocytes. Purpose: Therefore, the present study aimed to 1) clarify the effect of hyperglycaemia and hypertrophic agents on 1) TN-C expression and 2) to investigate the effect of TN-C on MMP2, MMP9, Integrin α6 and Integrin β1 in H9c2 cardiomyoblasts. Methods: H9c2 rat cardiomyoblasts were subjected to two different types of conditions 1) standard control (5.6 mM glucose) and hyperglycaemic (35 mM glucose) and 2) incubation with Angiotensin II (Ang II) and Endothelin-1 (ET-1). Furthermore, cardiomyoblasts were cultured with 1 and 10 ug/mL of human TN-C. The end of the experiments, total RNA was isolated and RT-qPCR was performed to assess the expression levels of Tnc, Mmps and integrins (normalized to Gapdh). Results: Both experimental conditions markedly increased the mRNA expression of Tnc (p<0.05, respectively). Interestingly, hyperglycaemia markedly increased the expression of Tnc (p<0.05) compared to controls, while the expression of Mmps and integrins were significantly downregulated (p<0.05, respectively). Furthermore, H9c2 cells exposed to hypertrophic stressors such as Ang II or ET-1 revealed cellular hypertrophy, associated with an increase of Tnc expression compared to controls (P<0.05). Moreover, human TN-C significantly increased expression of BNP and decreased Mmps (P<0.05 vs control, respectively) and reduced the expression of integrins. Conclusions: This is the first study providing evidence that hyperglycaemia and Ang II markedly increase the expression of TNC. In addition, TNC has a significant regulatory role on the expression of Mmps and integrins. Collectively, these results indicate the fundamental deleterious role of TNC in the progression of cardiac dysfunction in diabetes and hypertension.