

Syndecan-4 Provides Protection Against Myofibroblast Differentiation

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Cardiac remodelling which includes fibrosis, are major pathophysiological processes in heart failure progression. Cardiac fibrosis results from excessive production of extracellular matrix (ECM), mainly structural collagens, by cardiac myofibroblasts. Fibroblast-to-myofibroblast differentiation is characterized by expression of α smooth muscle actin (SMA).

The transmembrane proteoglycan syndecan-4 (SDC4) is expressed by cardiac fibroblasts and has been proposed to regulate myofibroblast differentiation. It is unregulated in the hearts of patients and mice with heart failure. Here we investigated the role of SDC4 in myofibroblast differentiation in cardiac fibroblasts.

We used cultured human foetal cardiac fibroblasts (hfCFB) to observe the effect of SDC4 knockdown (SDC4-KD), by siRNA, on ACTA2/ α SMA mRNA and protein levels, which showed through SDS-PAGE protein analysis, a significant increase compared to control siRNA and an mRNA 3 fold increase compared to control siRNA.

SDC4 has also been identified as a regulator of subunits of the integrin family, which are important for myofibroblast activation and ECM deposition, therefore we investigated the effect of SDC4-KD on mRNA levels of subunits α v, α 5, β 1. For SDC4-KD siRNA there was a significant protein level decrease of α v, α 5, β 1 and β 3 and a significant mRNA fold decrease of 0.48 (α v), 0.19 (α 5), 0.38 (β 1) and 0.73 (β 3) compared to CTL siRNA.

In conclusion, a reduction of SDC4 levels increases α SMA, suggesting that SDC4 inhibits myofibroblast differentiation. This indicates a protective role of SDC4 in the failing heart, limiting progression of cardiac fibrosis. We aim to further investigate the mechanisms behind this.

Biography

Francesca completed her research masters from the University of Portsmouth and is currently completing a PhD at the University of Oslo, specialising in mechanisms of activation of the myofibroblast, leading to cardiac fibrosis. She has completed an Erasmus placement at the University of Rouen during her Pharmacology bachelors, which she completed with honors.