

P019 Furin regulates hypoxic inhibition of MMP-2 activation in human cardiac fibroblasts

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Introduction Cardiac fibroblasts (CF) play a major role in myocardial remodelling e.g. after myocardial infarction. Matrix metalloproteinase-2 (MMP-2) facilitates migration of fibroblasts to repair myocardial damage, an event requiring the activity of the proprotein convertase furin. Furin activity is modulated by hypoxia, an inevitable event during myocardial infarction. In this study we therefore investigated the effects of hypoxia on furin expression and activity in human CF, and the resultant effects on MMP-2 activation. *Methods* Human CF were cultured in normoxia (21% O₂) and hypoxia (1%O₂) for up to 48 h. MMP-2 and furin mRNA was quantified using real time RT-PCR. MMP-2 secretion was analysed by zymography and furin activity was measured using a fluorimetric assay. *Results* Under hypoxic conditions MMP-2 activation was consistently attenuated by ~ 50% (P<0.01) compared with cells cultured in normoxia. Surprisingly we observed that furin expression and activity were increased to 134.7% (P<0.05) and 147.3% (P<0.05), respectively. *Conclusions* Decreased activation of MMP-2 following hypoxia potentially impairs the early response of CFs in reparative remodelling. However, a paradoxical increase in furin activity in chronic hypoxia may indicate that under hypoxic conditions the pathway of activation of MMP-2 in human cardiac fibroblasts is complex and warrants further investigation.