95% CI 0.84-1.42) variants failed to reach statistical significance. In contrast, the distribution of the 4a4b genotype differed significantly between MI patients and controls (χ^2= 9.82, p=0.007). Allele 4a was significantly more frequent in MI patients than in controls (p=0.0007, OR=1.76, 95% CI 1.25-2.49).

Conclusion: The present study demonstrates that 4a4b polymorphism but not 894G>T and –786T>C is associated with MI in the Tunisian population.

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CC chemokine receptors (CCR5 and CCR2) polymorphisms in Tunisian patients with myocardial infarction

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Aims: Myocardial infarction (MI) is a disease with multifactorial background. Inflammation is involved in the pathophysiology of atherosclerosis and its clinical complications, such as MI. Several proinflammatory molecules have been identified in atherosclerotic lesions. Chemokines and their receptors seem to play a pivotal role in the genesis and progression of atherosclerosis. Two of these are CCR2 and CCR5 that bind MCP-1, macrophage inflammatory proteins-1α (MIP-1) α or MIP-1β respectively. Several polymorphisms in the CCR2 and CCR5 genes appear to play a role in MI. Conflicting results have been reported regarding the effect of these polymorphisms on MI. The aim of our study was to examine both the association between CCR2 (CCR2-64I), CCR5 (CCR5Δ32) variants and the estimation of haplotypes with Myocardial Infarction in Tunisian population.

Methods: This study included 572 unrelated Tunisians divided into 290 MI patients and 282 healthy controls. CCR5Δ32 and CCR2-64I polymorphisms were carried out by PCR-RFLP.

Results: The frequency of CCR5Δ32 allele was 0.10 in MI patients and 0.18 in controls. Genotypes were distributed as follows: 236 (w/w) (81.4%) and 54 (w/t) (18.6%) in MI; 178 (w/w) (63.1%) and 104 (w/t) (36.9%). No Δ32/Δ32 genotype was detected among tested population. The frequency of the CCR2-64I was 0.16 and 0.14 in MI patients and controls respectively. The frequencies were in accordance with Hardy-Weinberg equilibrium. The CCR5Δ32 allele was underrepresented in MI patients and over-represented in controls (p<0.001). CCR2-CCR5 haplotypes were not associated with risk of MI.

Conclusion: Our work suggests that the genetic variation at the CCR2 and CCR5 genes did not contribute to the risk of MI, but CCR5 polymorphism could modulate the risk of MI in Tunisian population.

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The myocardium is influenced by sarcoplasmic reticulum calcium transport and apoptotic factors from early ischemia/reperfusion to late remodelling

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We aimed to determine the short and long-term effects of Serca2, Pln, Hax1, cleaved caspase-3, Bax, and Bcl2 protein levels in early post-ischemia/reperfusion cardiac injury and late remodeling after acute myocardial infarction (MI). Male Wistar rats underwent left coronary artery ligation and left to recover for 48 hours, 2 weeks and 8 months post-surgery. Sham-operated animals served as controls. Congestive heart failure (CHF) at 8 months was defined by increase in lung and right ventricular weight and a drop in ejection fraction. At 48-hours after MI, an acute increase of Serca2 (29%) expression was observed with unchanged Pln levels. An increase of Hax1 (68%) levels was seen, which could promote the formation of Pln monomers, the active inhibitory units of Serca2. Hax1 overexpression was found to affect apoptosis as measured by activated cleaved caspase-3 and Bax/Bcl2 ratio levels. Two weeks post MI, although Serca2, Hax1 and Pln levels were at Sham levels but the apoptosis markers were reduced by 35%. By 8-months post surgery, some of the animals developed CHF. The expression levels of the proteins tested were examined in the border (BR) and remote (RM) areas from the infarct region. Serca2 protein levels were reduced by 50% in both BR and RM CHF tissues, while in non CHF Serca2 did not change. Hax1 was 30% lower in all MI cardiac RM segments but not in BR. Pln was not significantly altered. Cleaved caspase-3 protein levels were higher in CHF and non-CHF RM segments, while the Bax/Bcl2 ratio was increased in all samples, indicating stronger intrinsic apoptotic pathway triggering. In conclusion, an early increase of Serca2 may reflect the need for improve SR Ca-transport after MI but Hax1 overexpression may be compensatory to rescue cells from apoptosis. In long-term, apoptosis is increased controlling by intrinsic signaling in BR, while Serca2 downregulation is the hallmark of CHF progression.

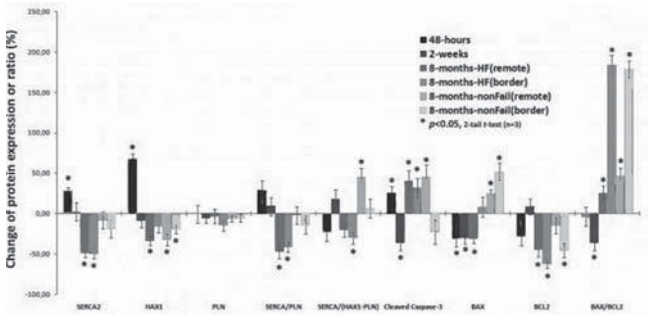

Figure 1. Changes in SR calcium transport and cell survival in post-ischemic cardiac remodeling

Changes in SR calcium transport and cell survival in post-ischemic cardiac remodeling

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Clenbuterol favourably remodels neonatal cardiac cells via activation of p38 MAPK signalling pathway: potential therapeutic implications

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Pharmacologic treatments which aim to induce physiological hypertrophy are now thought as novel treatments for heart failure. Thus, clenbuterol, a beta-2 adrenergic agonist has recently been shown to partially reverse cardiac remodeling by inducing physiological hypertrophy. The present study further investigated potential underlying mechanisms of this effect in a neonatal cardiomyocytes cell based model.

Neonatal cardiomyocytes obtained from newborn rats were exposed to clenbuterol (CLEN, 1μM) for 5 days, while untreated cells served as controls. CLEN administration resulted in well organized and orientation of cytoskeletal fibers manifesting as a longitudinal cell shape, while had no effect on myosin heavy chain (MHC) isoform expression. CLEN increased cell growth as indicated by protein content: total protein per cell (pg/cell) was 116 (6.0) for CLEN and 77 (5.0) for the untreated cells, p<0.05. This response was accompanied by a 2.2 fold increase in phospho-p38 MAPK levels as compared to untreated cells, p<0.05 while no changes were observed in ERK, JNK and Akt. Administration of SB203580 (a specific p38 MAPK inhibitor) abrogated the CLEN induced changes in cardiomyocyte morphology, while it had no effect on protein content. In conclusion, clenbuterol induces favorable changes in neonatal cardiomyocyte shape, geometry and growth without affecting MHC isoform expression. Activation of p38 MAPK signaling seems, at least in part, to be implicated in this response.