Growth factors and cardiac remodelling

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In many patients cardiac hypertrophy precedes cardiac failure. In most cases cardiac hypertrophy is a maladaptive response to hypertension or post myocardial infarction.
In contrast in athletes the cardiac adaptation to exercise is reversible and beneficial. Therefore the quest is ongoing to identify molecular pathways that represent beneficial cardiac adaptation and the unfavourable signalling events that can occur in the cardiomyocyte. Currently the general concept is that growth hormones more in particular the growth hormone-insuline like growth factor axis is involved in beneficial cardiac growth and hypertrophy. In contrast activation of the MAP kinases in general is indicative for irreversible cardiac remodelling. Several gene targeted mouse models will be discussed including MAPK deficient and overexpressing mice. In these animals studies have been performed to induce hypertrophy through pressure overload in an aorticng model (1, 2). In addition, more recently we analyzed the effect of ischemia reperfusion in these models. In addition, mice were studied overexpressing human FGF or deficient in IGF-1(3, 4). In all these models show a remarkable overlap in the response to ischemia and pressure overload. This can be partly explained by the central role of cardiomyocyte apoptosis. Furthermore these studies will show the importance of circulating and tissue hormone levels in cardiac physiology and adaptation. The mouse model appears to be a suitable model to study various aspects of cardiac endocrinology.

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