Cardiac remodeling and arrhythmogenesis are ameliorated by administration of Cx43 mimetic peptide Gap27 in heart failure rats

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Alterations in connexins and specifically in 43 isoform (Cx43) in the heart have been associated with a high incidence of arrhythmogenesis and sudden death in several cardiac diseases. We propose to determine salutary effect of Cx43 mimetic peptide Gap27 in the progression of heart failure. High-output heart failure was induced by volume overload using the arterio-venous fistula model (AV-Shunt) in adult male rats. Four weeks after AV-Shunt surgery, the Cx43 mimetic peptide Gap27 or scrambled peptide, were administered via osmotic minipumps (AV-ShuntGap27 or AV-ShuntScr) for 4 weeks. Cardiac volumes, arrhythmias, function and remodeling were determined at 8 weeks after AV-Shunt surgeries. At 8th week, AV-ShuntGap27 showed a marked decrease in the progression of cardiac deterioration and showed a significant improvement in cardiac functions measured by intraventricular pressure-volume loops. Furthermore, AV-ShuntGap27 showed less cardiac arrhythmogenesis and cardiac hypertrophy index compared to AV-ShuntScr. Gap27 treatment results in no change Cx43 expression in the heart of AV-Shunt rats. Our results strongly suggest that Cx43 play a pivotal role in the progression of cardiac dysfunction and

arrhythmogenesis in high-output heart failure; furthermore, support the use of Cx43 mimetic peptide Gap27 as an effective therapeutic tool to reduce the progression of cardiac dysfunction in high-output heart failure.