WNT11 PRETREATMENT PROTECTS AGAINST OXIDATIVE STRESS-INDUCED APOPTOSIS BY STAT3 ACTIVATION

Poster Contributions
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Authors: Anweshan Samanta, Lei Chen, Lin Zhao, Arash Davani, Kashyap Choksi, Guangming Cheng, Amy Cantilena, Robert Vincent, Magdy Girgis, Buddhadeb Dawn, Cardiovascular Research Institute, University of Kansas Medical Center, Kansas City, KS, USA

Background: Noncanonical Wnt11 signaling plays a key role in heart development. Very little is known about Wnt11 signaling in cardiomyocyte survival. We hypothesized that exposure to Wnt11 will induce a cytoprotective program and promote cardiomyocyte survival against oxidative stress.

Methods: The effects of Wnt11 on H2O2-induced oxidative stress were tested in H9c2 cardiomyocytes. H9c2 cells were pretreated for 24 h with either 50 ng/ml BSA (control) or with 50 ng/ml Wnt11 before exposure to 200 μM H2O2 for 6 h.

Results: The H2O2-induced decrease in cell viability was significantly attenuated in Wnt11-pretreated cells. TUNEL staining confirmed that cellular apoptosis was significantly reduced in Wnt11-treated group compared with controls. Consistently, the levels of cleaved PARP, an indicator of apoptosis was significantly lower in Wnt11-treated cells (Figure). Wnt11 treatment also increased the levels of phosphorylated STAT3, and upregulated the expression of antiapoptotic molecules Bcl-2 and Bcl-xL. The specific role of STAT3 as a transcription factor for Bcl-2 and Bcl-xL was confirmed by the use of specific STAT3 inhibitor WP1066, which also reversed the Wnt11-induced protection.

Conclusion: We conclude that pretreatment with Wnt11 protects against oxidative stress-induced apoptosis through the activation of STAT3 and induction of cytoprotective molecules. These novel findings may have important implications for the development of therapeutic cardioprotective strategies.