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**Hsp90 protected chicken primary myocardial cells from heat-stress injury by inhibiting oxidative stress and calcium overload in mitochondria**

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**Abstract:**

**Background:** Severe heat stress can cause human and animal heart failure and sudden death, which is an important issue of public health worldwide. Our previous studies in animals showed that myocardial cells injury was critical in the above process, and Hsp90 induction has a definite anti-myocardial injury effect, especially through aspirin (ASA). But the mechanism has not been fully clarified.

**Methods:** In this study, an in vitro heat stress model of chicken primary myocardial cells (CPMCs) most sensitive to heat stress was used to explore the cell injuries and corre- sponding molecular resistance mechanism.

**Results:** We found that heat stress resulted in serious oxidation stress and calcium overload in mitochondria, which destroyed the mitochondrial structure and function and then triggered the cell death mechanism of CPMCs. Hsp90 was proven to be a central regulator for resisting heat-stress injury in CPMCs mitochondria using its inhibitor and inducer (geldanamycin and ASA), respectively. The mechanism involved that Hsp90 could activate Akt and PKM2 signals to promote Bcl-2 translocation into mitochondria and its phosphorylation, thereby preventing ROS production and subsequent cell apoptosis. In addition, Hsp90 inhibited mitochondrial calcium overload to overcome MPTP opening and MMP suppression through the inhibitory effect of Raf-1-ERK activation on the CREB-IP3R pathway.

**Conclusion:** This study is the first to reveal a pivotal reason for heat-stressed damage in chicken myocardial cells at subcellular level and identify an effective regu- lator, Hsp90, and its protective mechanisms responsible for maintaining mitochondrial homeostasis.

**Keywords:** Heat stress ;Mitochondrial damage; Hsp90; Signaling pathway; Chicken primary myocardial cells