低氧/厌氧产品案例——心肌细胞

文章题目：Melatonin-Induced Protective Effects on Cardiomyocytes Against Reperfusion Injury Partly Through Modulation of IP3R and SERCA2a Via Activation of ERK1

褪黑素可通过激活 ERK1 调节 IP3R 和 SERCA2a 对心肌细胞再灌注损伤发挥保护作用

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工作站使用情况：BAKER RUSKINN InvivO$_2$ 400

使用气体 浓度：低氧（0 % O_2 , 5 % CO_2 ,95% N_2）

主要内容：心肌缺血-再灌注损伤通常发生在出现急性 ST 段抬高型心肌梗死(STEMI)的患者中。在这些患者中，减少急性心肌缺血损伤和限制心肌梗死的最有效的治疗干预是及时和有效的心肌再灌注治疗。再灌注诱导的心肌细胞死亡是一个关键的治疗靶点，对患者的预后有显著影响。本研究采用缺氧/复氧构建大鼠心肌细胞缺血/再灌注（H/R）损伤模型，研究结果表明，褪黑素抑制 H/R 诱导的心肌细胞凋亡，改善心肌细胞肌动蛋白丝的组织结构，减少钙超载，进一步抑制 IP3R 的表达，并通过 ERK1 途径促进心肌细胞对 H/R 的 SERCA2a 的表达。本研究为使用褪黑素保护接受心肌再灌注治疗的 STEMI 患者的心功能提供了更多的证据。

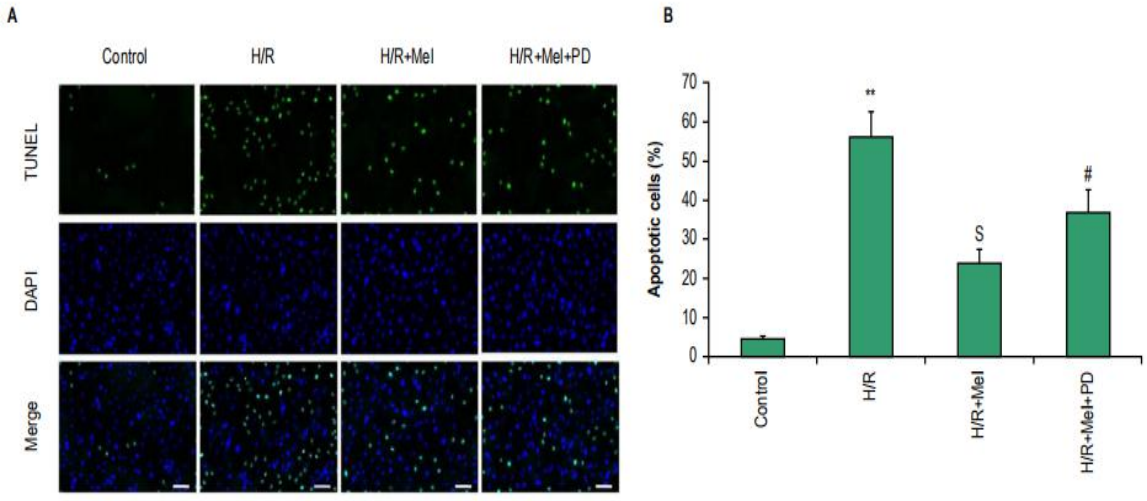

Fig2 Figure 2 – Melatonin prevents H9C2 cells apoptosis against H/R via ERK1 in vitro. Apoptosis was assessed by fluorescence TUNEL. Representative TUNEL staining images (A) and quantitative analysis in H9C2 cells(B). bar = 50 μm. All values are presented as the mean±SD. n = 3.**p < 0.01 vs. control group; Sp < 0.05 vs. H/R group; #p < 0.05 vs. H/R+Mel group. (Control: control group; H/R:H/R group; H/R+mel: H/R+ melatonin group; H/R+mel+PD: H/R+ melatonin+PD98059 group)

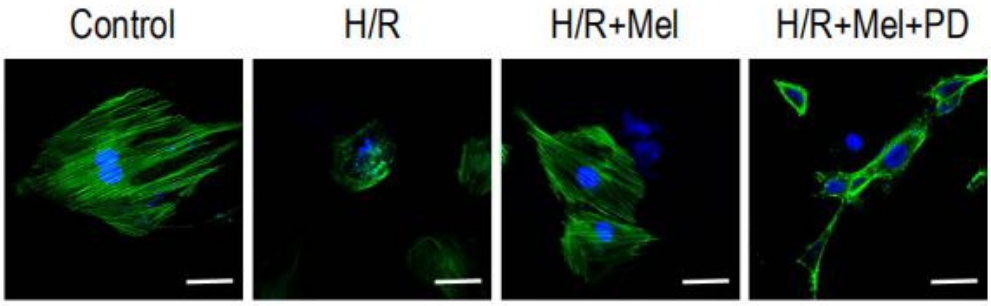

Fig3 . Melatonin protects F-actin organization in H9C2 cells against H/R via ERK1 in vitro. Representative confocal microscopy images show H9C2 cells stained with FITC-phalloidin. The results showed that simulated H/R induced more diffuse and irregular actin disposition compared with control group. Melatonin preserved more regular and well-defined actin organization and PD98059 (ERK1 inhibitor) reduced the protection of melatonin. bar = 20μm. (Control: control group; H/R:H/R group; H/R+mel: H/R+ melatonin group; H/R+mel+PD: H/R+ melatonin+PD98059 group)

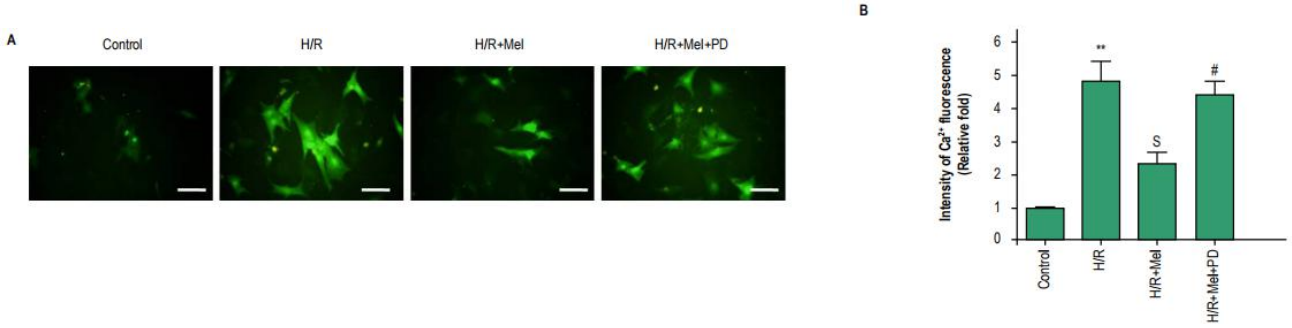

Fig4. Melatonin reduces Ca2+ overload in H9C2 cells against H/R via ERK1 in vitro. Ca2+ content was assessed using Fura-2/AM in H9C2 cells incubated in normal condition or in simulated H/R condition, in simulated H/R condition plus pretreatment with melatonin, or in simulated H/R condition plus pretreatment with melatonin and PD98059 (ERK1 inhibitor). The green fluorescence intensity by Fura-2 was obviously stronger in H/R group, and melatonin pretreatment reversed the change which was inhibited by ERK1 inhibitor.bar = 30 μm. All values are presented as the mean ± SD. n = 3.**p < 0.01 vs. control group; Sp <0.05 vs. H/R group; #p < 0.05 vs. H/R+Mel

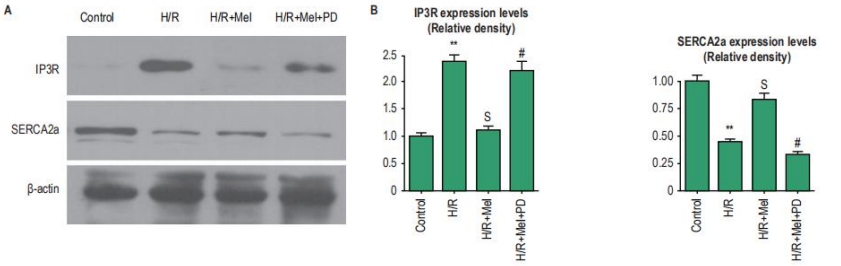

Fig5.Melatonin modulated expression of SERCA2a and IP3R in H9C2 cells against H/R via ERK1 pathway in vitro. The results indicated melatonin inhibited expression of IP3R and promoted expression of SERCA2a which was reduced by PD98059. Representative Western blot images (A) and quantitative analysis (B-C) showed melatonin’ s effect on expression of IP3R and SERCA2a via ERK1 pathway in H9C2 cells against H/R.

缺氧（0% O_2）/复氧（H/R）可诱导 H9C2 大鼠心肌细胞发生凋亡，褪黑素通过体外 ERK1 途径抑制缺氧/复氧诱导的心肌细胞凋亡（图 2）；H/R 可诱导大鼠心肌细肌动蛋白束发生损伤，褪黑素通过 ERK1 途径保护 H9C2 细胞中的肌动蛋白免受 H/R 损伤（图 3）；H/R 可诱导大鼠心肌细胞钙超载，褪黑素通过 ERK1 途径抑制 H/R 诱导的钙超载（图 4）；H/R 可诱导大鼠心肌细胞 IP3R and SERCA2a 蛋白表达，褪黑素通过 ERK1 途径抑制心肌细胞 IP3R 和 SERCA2a 的表达（图 5）。