

# CPM抑制了由1, 4NQ诱导的对骨肌肌质网 SR钙通道RyR1的激活效应

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利用7-diethylamino-3-(4'-maleimidylphenyl)-4-methylcoumarin(CPM)甲基化钙通道RyR1上的特异敏感性硫醇的方法,对由1,4-naphthoquinone(1,4NQ)诱导的双相性作用进行了研究,发现CPM能明显阻碍由1,4NQ诱导的对RyR1的激活,但对由1,4NQ产生的抑制没有明显作用。用经CPM预处理过和没有处理过的样品与1,4NQ温育后离心清洗,发现未经CPM处理的样品经激活和抑制浓度的1,4NQ温育后,离心清洗不能消除1,4NQ对RyR1的激活和抑制。而经CPM处理后的样品,在1,4NQ的激活浓度和抑制浓度下,离心清洗后未能观测到1,4NQ诱导的激活态,但抑制态仍然明显存在。以上结果说明,CPM所识别的特异活性硫醇参与了1,4NQ激活作用:CPM与此硫醇发生甲基化作用,因此阻断了1,4NQ对RyR1上的激活部位硫醇发生作用,使钙通道不能被激活。

## CPM INHIBITS THE ACTIVATION OF THE CALCIUM RELEASE CHANNEL OF SKELETAL MUSCLE SARCOPLASMIC RETICULUM INDUCED BY 1,4NQ

By using an alkalating agent 7-diethylamino-3-(4'-maleimidylphenyl)-4-methylcoumarin (CPM) which specifically reacts with hyperreactive thiols in calcium release channel protein RyR1, the biphasic effect of 1,4-naphthoquinone (1,4NQ) on RyR1 was investigated. It shows that CPM could partially block the activation phase of either concentration or time dependence ryanodine binding induced by 1,4NQ, but had no effect on the inhibition phase. The samples were treated with or without CPM in the presence of various concentrations of 1,4NQ. Results show that neither activation nor inhibition effects of 1,4NQ could be removed by re-spin wash in the absence of CPM; while in the presence of CPM, only the activation effect of 1,4NQ can be washed out, but not the inhibition effect. All the data suggest that the hyperreactive thiols identified by CPM are involved in the activation effect of 1,4NQ on the channel protein. By blocking the thiols on the activation site of RyR1, CPM inactivates the channel gating.

### 关键词

CPM; 1,4NQ; 钙通道(Calcium release channel); 硫醇(Thiol); 激活部位(Activation site); SR