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Title: Genistein rescues pulmonary hypertension and attenuates abnormal vasoconstriction in rats lungs

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Body: Background) Recent studies suggest that the deregulation of endothelial nitric oxide synthase (eNOS) is accountable for in the development of pulmonary hypertension (PH). Genistein, a phytoestrogen derived from soybean, has been reported to improve endothelial function. Objective) We hypothesized that chronic treatment with genistein would prevent and reverse of hypoxic PH (HX) by improvement of eNOS function. Method) Daily treatment with either genistein (0.2mg/kg) or vehicle was started. After 3-wk hypoxic exposure, rats underwent cardiac catheterization, examination of right ventricular hypertrophy, morphological features, Western blot analysis, and immunoprecipitation were performed. For evaluation of the reversal effect, genistein treatment started after rats had been exposed to 3-wk hypoxia exposure, and were examined in the similar way as described above. Furthermore, we examined if genistein would attenuate abnormal vasoconstriction in HX by isolated perfused lung examination. Result) Genistein treatment prevented the progression of PH to right ventricular failure and restored vascular remodeling in HX. And also, genistein rescued preexisting PH. These effects were mediated by improvement of eNOS function and restoring the interaction of eNOS and eNOS-related proteins. Furthermore, exogenously administration of genistein rapidly attenuated abnormal vasoconstriction in HX by improvement of eNOS function. Conclusion) These results indicated that genistein not only had protective and reversal effects against the development of hypoxic PH, but also attenuated abnormal vasoconstriction of PH. The underlying mechanism might be related to the improvement of eNOS function.