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ARIAL, 9Pt 18β-GLYCYRRHETINIC ACID PREVENTS SUSTAINED HYPOXIC PULMONARY VASOCONSTRICTION DEVELOPMENT

Arial, 9 pt ***Kizub I.V., Soloviev A.I.***

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Arial 9 pt It is known that hypoxia causes pulmonary artery constriction normally maintaining optimal ventilation-perfusion matching in the lung but leading to pulmonary hypertension development. Although it is known that sustained hypoxic pulmonary vasoconstriction (HPV) is critically dependent on the endothelium and glycolysis, the signaling pathways remain unclear (1). The aim of this study was using gap junctions inhibitor 18β-glycyrrhetinic acid (18β-GA) (2, 3), a saponin isolated from licorice root (Glycyrrhizia glabra L.), to determine gap junctions role in HPV, and specifically to test the hypothesis that signaling via these junctions contributes to development of the sustained phase of HPV.

The vascular tone was measured on isolated Wistar rat small intrapulmonary arteries (IPA) using a wire myography technique.

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Hypoxia (PO_2 - 2–3 mmHg) elicited a biphasic response in tension in IPA without preconstriction or preconstricted with prostaglandin $F_{2\alpha}$ (3 μM) or 25 mM K^+ consisted of the transient phase I and the sustained HPV phase II during 40 min of hypoxia. 20 min prior application of gap junctions inhibitor 18β-GA (30 μM) had no effect on HPV transient phase (P>0.05) but abolished the sustained HPV in IPA precontracted with $F_{2\alpha}$ (3 μM) or 25 mM K^+ (P<0.05). Elevation in 18β-GA concentration to 60 and 100 μM evoked a significant suppressing of both HPV phases (P<0.05). In nonpreconstricted IPA, 30 μM 18β-GA also led to reduction of the sustained HPV (P<0.05) without effect on the transient HPV phase (P<0.05). Endothelium removing in IPA resulted in reduction in the HPV transient phase amplitude (P<0.05) and abolished the sustained HPV, whereas 30 μM 18β-GA enhanced this effect (P<0.05). Taken together, this data indicates that gap junctions involved to HPV development reflecting a novel pathway for signaling during hypoxia in pulmonary artery that supports the sustained phase of HPV.

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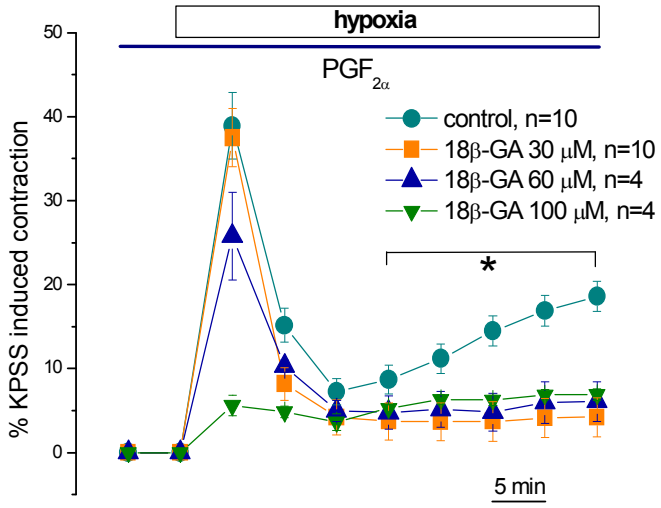

Arial 8 pt Fig. The effect of gap junctions inhibition with 18β-glycyrrhetinic acid (18β-GA) on HPV in isolated rat IPA precontracted with 3 μM PGF2α at hypoxic hypoxia. * - P<0,05

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Aial 8 pt References:

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