低氧/厌氧应用案例——线粒体

文章题目:Targeting mitochondri-associated membranes as a potential therapy against endothelial injury induced by hypoxia

靶向线粒体相关膜（MAMs）对缺氧诱导的内皮损伤有潜在的治疗作用

文章出处：J Cell Biochem. 2019;1-12.　DOI: 10.1002/jcb.29220

气体环境：5% CO_2, 1% O_2, and 94% N_2　InvivO$_2$; Baker Ruskinn

主要内容:线粒体功能障碍在缺氧诱导的内皮细胞损伤中起主要作用，参与缺氧性肺动脉高压和缺血性心血管疾病的发生。本文通过研究发现 MAM 组成蛋白的下调减弱了缺氧诱导的线粒体 Ca^{2+}升高，抑制了线粒体损伤，导致线粒体膜电位和 ATP 生成增加，活性氧种类减少，同时减轻细胞了凋亡，表明 MAMs 的破坏可能对低氧条件下内皮细胞损伤具有治疗价值，为预防低氧性肺动脉高压和缺血性损伤提供了一种新的策略。

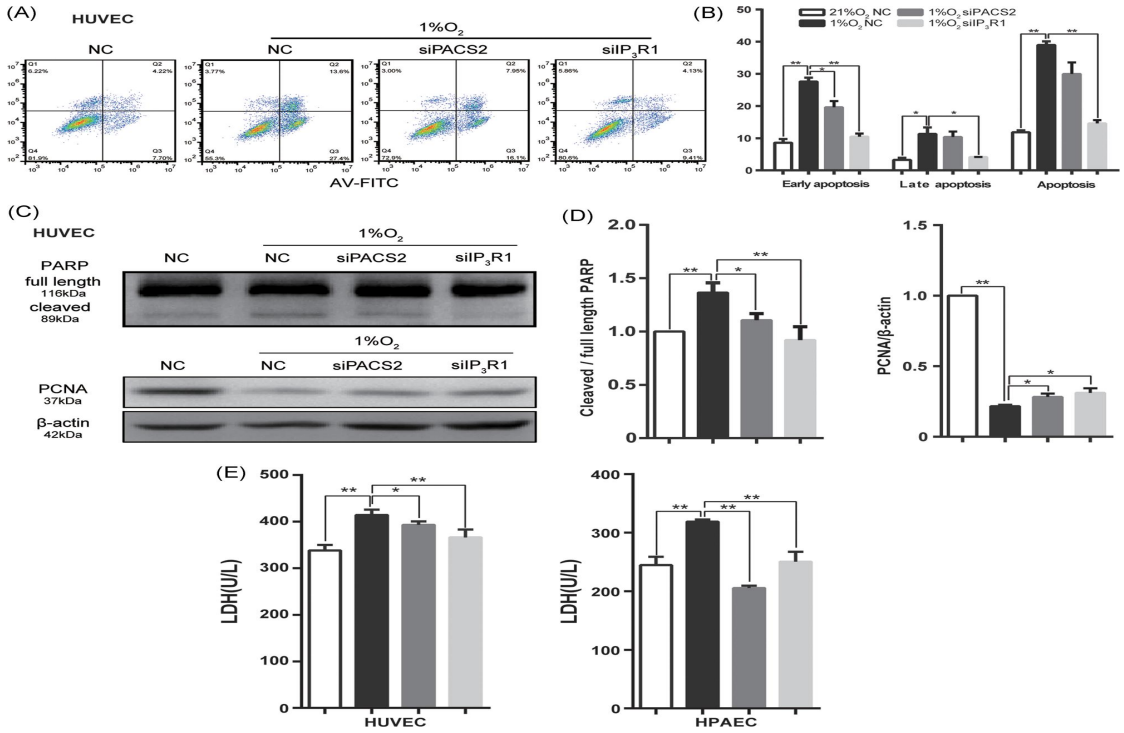

Fig3. Disruption of MAMs mitigates hypoxia-induced endothelial apoptosis. Cell apoptosis was detected by (A) AV-FITC FACS analysis in HUVECs. B, Early, late, and total apoptosis were calculated according to the values in four quadrants. n=3. C, D, The ratio of cleaved to full length PARP (n=4) and the protein level of PCNA (n=4) were calculated to reflect cell apoptosis and survival in HUVECs. E, Cell injury was reflected by the level of LDH in HUVEC (n=4) and HPAEC (n =3) culture supernatants. AV-FITC, annexin V-fluorescein isothiocyanate; FACS, fluorescence-activated cell sorting; PAEC, human pulmonary artery endothelial cell; HUVEC, human umbilical vein endothelial cell; LDH, lactate dehydrogenase; MAM, mitochondria-associated membrane; PCNA, proliferating cell nuclear antigen.s *P < .05. **P < .01

低氧（1% O_2）环境下，MAMs 的破坏不仅明显减少了细胞凋亡数（A-B），同时促进了细胞的存活（C-D）。

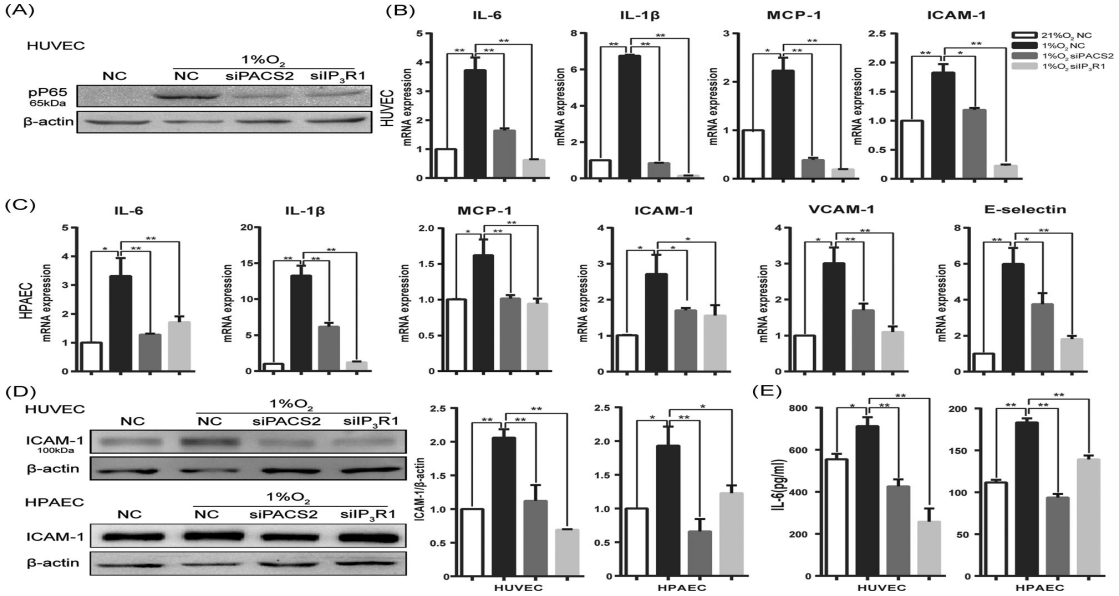

Fig.4. Disruption of MAMs attenuates the hypoxia-induced inflammatory response. A, Representative immunoblot of phosphorylation of S536 of NF-κB p65 from three separate experiments. B, mRNA expression of inflammatory molecules (IL-6, IL-1β, MCP-1 and ICAM-1) in HUVECs. n = 3. C, mRNA expression of inflammatory molecules (IL-6, IL-1β, MCP-1, ICAM-1, VCAM-1 and E-selectin) in HPAECs. n = 3. D, ICAM-1 was detected in total lysates of HUVECs and HPAECs. n = 3. E, Protein levels of inflammatory molecules (IL-6) were detected in HUVEC and HPAEC supernatants. HPAEC, human pulmonary artery endothelial cell; HUVEC, human umbilical vein endothelial cell; ICAM-1, intercellular adhesion molecule-1; IL, interleukin; MAM, mitochondria-associated membrane; MCP-1, monocyte chemotactic factor-1; mRNA, messenger RNA; NF-κB, nuclear factor-κB. n = 3. *P < .05. **P < .01

低氧（1% O_2）环境下，MAMs 的破坏不仅显著降低 p65 活性，同时明显降低了促炎分子(IL 6、IL 1β,MCP 1 和 ICAM - 1) mRNA 的表达，最终减弱了 HUVECs 细胞的炎症反应。