Response to Promotion of Apoptosis Does Not Necessarily Mean Inhibition of Remodeling

We thank Shi et al.1 for their interest in our study. It is well known that vascular remodeling is characterized by changes in pulmonary vascular structure associated with medial hypertrophy because of an imbalance between proliferation and apoptosis of pulmonary artery smooth muscle cells (PASMCs).2–5 Exactly how apoptosis contributes to remodeling still remains unclear, but we disagree with the opinion expressed by Shi et al.1 that increased PASMC apoptosis translates to inhibition of remodeling. On the contrary, increased PASMC proliferation and decreased PASMC apoptosis can occur concurrently to promote thickening of the pulmonary vasculature.4,5 Our findings show that downregulating miR-328 by hypoxia decreases PASMC apoptosis, leading to pulmonary arterial remodeling. We believe that these processes are related phenomena and that miR-328–associated PASMC apoptosis plays an important role in pulmonary arterial remodeling. On the other hand, we are in agreement with Shi et al.1 that the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide assay is not an ideal approach to evaluate apoptosis. We used it to quickly screen the influence of miR-328 on PASMC function but agree that the results may not necessarily reflect apoptosis. A better conclusion based on the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide data would have been that miR-328 causes a decrease in the viability of PASMCs. However, we used multiple approaches to evaluate apoptosis, including TUNEL, acridine orange staining, and caspase 3 activity, all of which supported the findings that miR-328 downregulation induced by hypoxia leads to PASMC resistance to apoptosis, an effect that may involve insulin-like growth factor 1 receptor. It is a good suggestion made by Shi et al.1 that we should observe the effect of overexpression of insulin-like growth factor 1 receptor on miR-328–induced PASMC apoptosis, which will further strengthen our conclusion. However, it is not necessary to add these experiments, because our current results are enough to draw our conclusion. The molecular mechanisms underlying pulmonary vessel remodeling in hypoxic conditions are obviously complex, and apoptosis of PASMCs seems to be critically involved.

Disclosures

None.

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