

## Inducers of pulmonary arterial hypertension upregulate the expression of plasma membrane calcium atpase 1 in pulmonary artery smooth muscle cells

Item Type	Conference contribution
Authors	Ihugba, Jude C;Kurusamy, Sathishkumar;Arnold, Nadine;Polla, Priscille PC;Cotton, James;Gomez-del Arco, Pablo;Miguel Redondo, Juan;Lawrie, Allan;Armesilla, Angel
Citation	Ihugba, J. C., Kurusamy, S., Arnold, N., Polla, P. P., Cotton, J., Gomez-del-Arco, P., Redondo, J. M., Lawrie, A. and Armesilla, A. L. (2017) Inducers of pulmonary arterial hypertension upregulate the expression of plasma membrane calcium atpase 1 in pulmonary artery smooth muscle cells, Heart, 103(Suppl 5): A113.
DOI	<a href="https://doi.org/10.1136/heartjnl-2017-311726.155">10.1136/heartjnl-2017-311726.155</a>
Publisher	BMJ
Journal	Heart
Download date	2025-05-13 14:24:53
License	<a href="https://creativecommons.org/licenses/by-nc/4.0/">https://creativecommons.org/licenses/by-nc/4.0/</a>
Link to Item	<a href="http://hdl.handle.net/2436/623118">http://hdl.handle.net/2436/623118</a>

# Inducers of pulmonary arterial hypertension upregulate the expression of Plasma Membrane Calcium ATPase 1 in pulmonary artery smooth muscle cells

Jude C Ihugba<sup>1</sup>, Sathishkumar Kurusamy<sup>1</sup>, Nadine Arnold<sup>2</sup>, Priscille P C Polla<sup>1</sup>, James Cotton<sup>3</sup>, Pablo Gomez-del Arco<sup>4,5,6</sup>, Juan Miguel Redondo<sup>4,5</sup>, Allan Lawrie<sup>2</sup>, Angel Luis Armesilla<sup>1</sup>

<sup>1</sup>Cardiovascular Molecular Pharmacology Laboratory, School of Pharmacy, Research Institute in Healthcare Science, Faculty of Science and Engineering, University of Wolverhampton, Wolverhampton, UK; <sup>2</sup>Pulmonary Vascular Research Group, Infection, Immunity and Cardiovascular Disease, University of Sheffield, Sheffield, UK; <sup>3</sup>Department of Cardiology, Heart and Lung Centre, New Cross Hospital, Wolverhampton, UK; <sup>4</sup>Gene Regulation in Cardiovascular Remodelling and Inflammation Group, Centro Nacional de Investigaciones Cardiovasculares, Madrid, Spain; <sup>5</sup>CIBERCV; <sup>6</sup>Department of Molecular Biology, Universidad Autonoma de Madrid, CBM-SO, Madrid, Spain.

Pulmonary arterial hypertension (PAH) is a chronic and life-threatening disease with high morbidity and mortality in adult and paediatric patients. PAH is characterized by a progressive narrowing and occlusion of small pulmonary arteries leading to increased pulmonary resistance, right ventricular hypertrophy, and, finally, right ventricular failure.

A large body of data has shown that proliferation and migration of pulmonary arterial smooth muscle cells (PASMCs) represent key events in the vascular remodelling of pulmonary arteries that occurs during PAH. Levels of cytoplasmic calcium are an important determinant of PASMC proliferation and migration, and failure in maintaining appropriate levels of intracellular calcium are associated with PAH. The plasma membrane calcium ATPase (PMCA) proteins extrude calcium from the cytosol to the extracellular medium, and in doing so, play a critical role in the modulation of intracellular calcium levels. In this work, we have investigated whether inducers of PAH trigger any changes in the expression of PMCA proteins in PASMCs.

Analysis of RNA expression levels for *PMCA* genes has revealed that treatment of PASMCs with PDGF results in a significant increase in the level of the RNA encoding for the protein PMCA1. Interestingly, *PMCA1* RNA levels were also elevated in lungs of rats with monocrotaline-induced PAH. No changes were observed in the RNA levels for PMCA4, the other major PMCA isoform expressed in PASMCs. Although previous studies on the regulation of *PMCA1* gene expression have identified functional binding sites for the transcription factors NFAT in the *PMCA1* promoter region, we show here that PDGF-mediated upregulation of *PMCA1* transcriptional expression is independent of activation of the calcineurin/NFAT signalling pathway.

Our results suggest the involvement of PMCA1 in PASMC deregulation during PAH, although determination of the link between increased expression of *PMCA1* and PAH requires further investigation.