Terameprocol, a new therapeutic strategy for the management of pulmonary arterial hypertension

Rita Nogueira-Ferreira[1,2],Manuel J. Ferreira-Pinto[2], Ana Filipa Silva[2], Rui Vitorino[2,3], Joana Justino[1], Raquel Costa[4], Daniel Moreira-Gonçalves[2,5], Jean-François Quignard[6], Thomas Ducret[6], Jean-Pierre Savineau[6], Adelino F. Leite-Moreira[2], Rita Ferreira[1], Tiago Henriques-Coelho[2]

Pulmonary arterial hypertension (PAH) is a severe cardiopulmonary disease with a high mortality rate and limited therapeutic options. Pulmonary artery smooth muscle cells (PASMCs) play a central role in PAH pathophysiology, presenting a hyperproliferative and apoptotic-resistant phenotype. In order to evaluate the potential therapeutic role of terameprocol (TMP), an inhibitor of cellular proliferation and promoter of apoptosis, in PAH, we used an iTRAQ-based proteomic approach to study the biological pathways modulated by TMP in PASMCs collected from rats with PAH induced by monocrotaline (MCT) administration. Data showed that TMP significantly reduced pulmonary and cardiac remodeling and improved cardiac function in MCT rats. Additionally, it decreased proliferation and induced apoptosis of PASMCs, which seem to be related with the modulation of proteins involved in the regulation of DNA transcription, RNA metabolic process, transforming growth factor beta pathway and response to endoplasmic reticulum stress. Our results suggest that TMP may be an effective therapeutic option to be considered in the management of PAH.

1 — Department of Chemistry & QOPNA, University of Aveiro
2 — Department of Surgery and Physiology, Faculty of Medicine, University of Porto
3 — Department of Medical Sciences & iBiMED, University of Aveiro
4 — Department of Biochemistry, Faculty of Medicine, University of Porto
5 — CIAFEL, Faculty of Sports, University of Porto
6 — Université Bordeaux Segalen, France; Inserm, U1045, Centre de Recherche Cardio-Thoracique, France

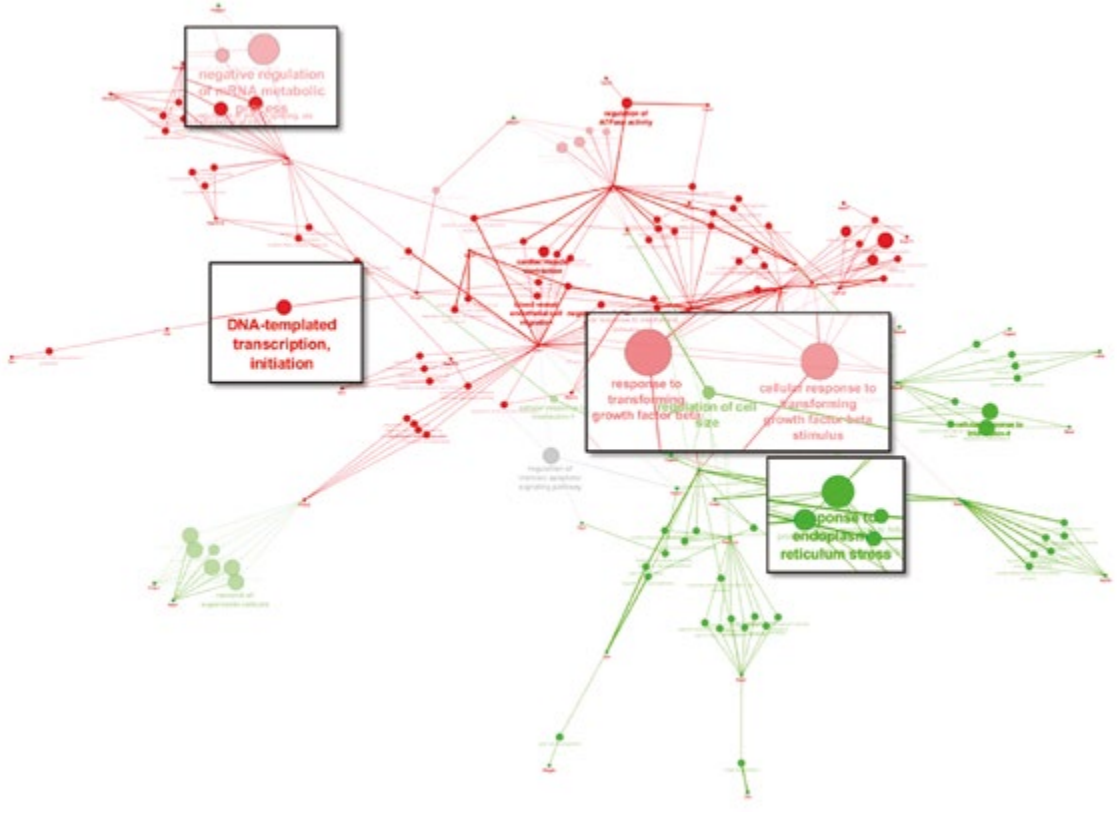

FIGURE 1
Biological processes modulated by terameprocol in pulmonary artery smooth muscle cells from rats with pulmonary arterial hypertension induced by monocrotaline. Green nodes represent the over-represented biological processes and red nodes refer to the ones under-represented (network constructed using Cytoscape v3.1.1).