SHAREABLE PDF

Angiotensin converting enzyme 2 and angiotensin (1–7) axis in pulmonary arterial hypertension

Julio Sandoval[1], Leonardo Del Valle-Mondragón[2], Felipe Masso[3], Nayeli Zayas[1], Tomás Pulido[1], Ricardo Teijeiro[1], Hector Gonzalez-Pacheco[1], Rossana Olmedo-Ocampo[1], Carlos Sisniega[1], Araceli Paez-Arenas[3], Gustavo Pastelin-Hernandez[2], Jose Gomez-Arroyo[1,4] and Norbert F. Voelkel[5]

Affiliations: [1]Cardiopulmonary Dept, Instituto Nacional de Cardiologia, Mexico City, Mexico. [2]Pharmacology Dept, Instituto Nacional de Cardiologia Ignacio Chavez, Mexico, Mexico. [3]Physiology and Molecular Biology Dept of the "Ignacio Chávez", National Institute of Cardiology, Mexico City, Mexico. [4]Division of Pulmonary and Critical Care Medicine, University of Cincinnati, Cincinnati, OH, USA. [5]Dept of Pulmonary Medicine, Amsterdam University Medical Centers, Amsterdam, The Netherlands.

Correspondence: Julio Sandoval, Cardiopulmonary and Immunology Depts, Ignacio Chávez National Institute of Cardiology of Mexico, Juan Badiano # 1, Colonia Sección XVI Tlalpan, 14080, México D.F., México. E-mail: sandovalzarate@prodigy.net.mx

@ERSpublications
This study demonstrates that in patients with PAH of different aetiologies there are alterations of the ACE2-angiotensin (1–7)-MAS axis. Analysis of blood samples also demonstrates the presence of antibodies directed against ACE2 https://bit.ly/3alEbnJ

Cite this article as: Sandoval J, Del Valle-Mondragón L, Masso F, *et al*. Angiotensin converting enzyme 2 and angiotensin (1–7) axis in pulmonary arterial hypertension. *Eur Respir J* 2020; 56: 1902416 [https://doi.org/10.1183/13993003.02416-2019].

ABSTRACT

Background: In animal models of pulmonary arterial hypertension (PAH), angiotensin-converting enzyme (ACE)2 and angiotensin (Ang)-(1–7) have been shown to have vasodilatory, antiproliferative, antifibrotic and antihypertrophic properties. However, the status and role of the ACE2-Ang(1–7) axis in human PAH is incompletely understood.

Methods: We studied 85 patients with a diagnosis of PAH of distinct aetiologies. 55 healthy blood donors paired for age and sex served as controls. Blood samples were obtained from the pulmonary artery in patients with PAH during right heart catheterisation. Peripheral blood was obtained for both groups. Ang (1–7) and -II were measured using zone capillary electrophoresis. Aldosterone, Ang(1–9), AngA and ACE2 were measured using ELISA, and ACE2 activity was determined enzymatically.

Results: Of the 85 patients, 47 had idiopathic PAH, 25 had PAH associated with congenital heart disease and 13 had PAH associated with collagen vascular disease. Compared to controls, patients with PAH had a higher concentration of AngII (median 1.03, interquartile range 0.72–1.88 pmol·mL^{-1} *versus* 0.19, 0.10–0.37 pmol·mL^{-1}; p<0.001) and of aldosterone (88.7, 58.7–132 ng·dL^{-1} *versus* 12.9, 9.55–19.9 ng·dL^{-1}; p<0.001). Conversely, PAH patients had a lower concentration of Ang(1–7) than controls (0.69, 0.474–0.91 pmol·mL^{-1} *versus* 4.07, 2.82–6.73 pmol·mL^{-1}; p<0.001), and a lower concentration of Ang(1–9) and AngA. Similarly, the ACE2 concentration was higher than in controls (8.7, 5.35–13.2 ng·mL^{-1} *versus* 4.53, 1.47–14.3 ng·mL^{-1}; p=0.011), whereas the ACE2 activity was significantly reduced (1.88, 1.08–2.81 nmol·mL^{-1} *versus* 5.97, 3.1–17.8 nmol·mL^{-1}; p<0.001). No significant differences were found among the three different aetiological forms of PAH.

Conclusions: The AngII–ACE2–Ang(1–7) axis appears to be altered in human PAH and we propose that

this imbalance, in favour of AngII, plays a role in the pathogenesis of the severe PAH. Further mechanistic studies are warranted.