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Olfactory receptors in pulmonary arterial hypertension: A novel pathway of vascular remodeling?

Audrey Courboulain, Guenhaël Sanz, Sandra Breuils-Bonnet, Marceau Quatremaire, Matthieu Vocelle, Mathilde Lafond, Frédéric Perros, Sébastien Bonnet, Edith Pajot-Augy, Marc Humbert, Sylvia Cohen-Kaminsky

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Abstract

Pulmonary arterial hypertension (PAH) is due to progressive obstruction of pulmonary arteries, thus leading to right heart failure and death. Breath volatile organic compounds (VOCs) can discriminate PAH and controls. Thus, a unique breath-print of PAH is detected using an artificial nose. VOCs target olfactory receptors (ORs) in olfaction. Interestingly, ORs are detected in peripheral tissues not related to olfaction and their deregulation is associated to cancer development. PSGR, encoded by the OR51E2 gene, is one of the ORs. Because vascular cells in PAH exhibit properties of cancer cells, we propose the ground-breaking hypothesis that ORs participate to vascular remodeling leading to PAH.

Thus we aim to determine whether a deregulated expression and function of the pulmonary vascular PSGR could participate to the pathological phenotype of vascular cells, and its potential use as a novel therapeutic target in PAH.

PSGR gene and protein expression were assessed in total lung, distal pulmonary arteries and PASMCs from PAH patients compared to controls using qRT-PCR and western blot. We evaluated proliferation (Ki67) and apoptosis (TMRM) after siRNA-directed silencing of PSGR expression in PASMCs.

We demonstrate that PSGR expression is significantly increased (50%) in PASMC, in total lung and isolated pulmonary arteries from PAH patients compared to controls. PSGR silencing in PAH-PASMCs decreased both cell proliferation (20%) and resistance to apoptosis (25%).

This deregulated OR expression in PAH PASMCs opens a new avenue in PAH pathophysiology. The whole spectrum of ORs is currently investigated using microarrays and deregulated ORs will be evaluated both *in vitro* and *in vivo*.