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Repositioning the mineralocorticoid receptor antagonists: pathophysiological basis and therapeutic innovations

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Aldosterone (aldo) is a major regulator of renal Na balance and therefore participates to arterial blood pressure control. Aldo binds the mineralocorticoid receptor (MR) a transcription factor of the nuclear receptor family. The MR is expressed in the kidney but also in non-epithelial cells more recently recognized as novel non-classical aldo/MR targets such as cardiomyocytes, endothelial and vascular smooth muscle cells, adipocytes, macrophages, etc). Novel pathophysiological effects have been characterized, extending the deleterious effects of aldo and MR activation towards the cardiovascular system and diseases with important vascular implication such as myocardial infarct, ischemic renal diseases or retinopathies for example. The activation of signalizing pathways by aldo/MR affects endothelial and vascular smooth muscle functions and modulates vascular tone, decreasing acetylcholine-induced vasodilation or increasing the responses to vasoconstrictors. Identifying novel pathophysiological roles of MR in non-classical targets open the way to novel therapeutic indications of pharmacological MR antagonists by repositioning antagonists already used in clinics or by using novel non-steroidal antagonists currently under development.

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Curriculum vitae

Frederic JAISSER, MD, PhD got a permanent position as Director of Research at the National Institute of Health and Medical Research (INSERM) in 1996. Dr. JAISSER received his medical training and degrees from the Reims Medical School and was qualified as Nephrologist in 1990. In 2003, he joined the Collège de France in Paris as an independent INSERM team and is currently the director of a team of the INSERM Unit U1138, at the Cordeliers Research Centre, Paris. He is the head of the "Integrative Physiology and Pathophysiology " Department of the Cordeliers Research Centre http://www.crc.jussieu.fr/crc/index.php . Since 2010, he is Scientific Delegate of the Pathophysiology Committee of the French National Research Agency.

The aim of his current studies is to improve the understanding of the pathophysiological roles and signaling pathways whereby the hormone aldosterone promotes pathologies in various organs including the kidney and the cardiovascular system. His work combines cellular and molecular approaches, animal physiology, pharmacological studies and has implications in human diseases. His interest includes translational research aimed to identify and validate biomarkers of Mineralocorticoid Receptor activation in cardiovascular and kidney diseases and novel therapeutic use of MR antagonists. Dr JAISSER belongs to several research networks, including EU-granted programs. More recently he was appointed as Coordinator of a European Network on Aldosterone with more than 45 laboratories from 15 EU countries dedicated to the Aldosterone field, covering the continuum from experimental to clinical studies

(http://www.cost.eu/domains_actions/bmbs/Actions/BM1301).