ADRENOMEDULLIN – WHAT DO WE KNOW 10 YEARS SINCE ITS DISCOVERY?

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Adrenomedullin (ADM) is a 52-amino acid peptide with structural homology to calcitonin gene-related peptide (CGRP) initially isolated from human pheochromocytoma. ADM is synthesized by many mammalian tissues including the adrenal medulla, endothelial and vascular smooth muscle cells, myocardium and central nervous system. ADM binds to plasma membrane receptors composed of calcitonin receptor-like receptor (CRLR), a member of serpentine receptor superfamily, and receptor activity modifying protein (RAMP) type 2 or 3. ADM has also some affinity for CGRP receptor composed of CRLR and RAMP1. ADM dilates blood vessels in both endothelium-dependent and independent manner and decreases systemic arterial pressure. Intrarenally administered ADM increases natriuresis by vascular and tubular mechanisms. In addition, ADM inhibits migration and proliferation of vascular smooth muscle cells and attenuates myocardial remodelling by inhibiting protein synthesis in cardiomyocytes and proliferation of cardiac fibroblasts. ADM is expressed in various tissues from early stage of embryogenesis and is also synthesized in placenta, uterus and fetal membranes. Plasma ADM level is increased in arterial hypertension, acute coronary syndromes, heart failure, renal diseases and septic shock, being involved in the pathophysiology of these disorders. Experimental ADM treatment is beneficial in arterial and pulmonary hypertension, heart failure, septic shock and ischemia/reperfusion injury. Proadrenomedullin N-terminal peptide (PAMP) is another product of ADM gene which is co-secreted by ADM-producing tissues, with some effects similar and some opposite to ADM.

Key words: adrenomedullin, proadrenomedullin N-terminal 20-peptide

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