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Adrenomedullin (AM) is a novel vasodilator peptide first purified from human pheochromocytoma by tracing its capacity to stimulate cAMP production in platelets. AM immunoreactivity is widely distributed in the central nervous system (CNS) and in the rat has been demonstrated by immunohistochemical techniques to be present in many neurons throughout the brain and spinal cord, as well as in some vascular endothelial cells and perivascular glial cells. Electron microscopy shows that the immunoreactivity is located mainly in the neuronal cytoplasm, but also occurs in the cell nucleus in some cells of the caudate putamen and olfactory tubercle. Biochemical analyses suggest that higher molecular forms, presumably precursor forms, may predominate over fully processed AM in some brain areas. The expression of AM immunoreactivity is increased in cortical neurons, endothelial cells, and perivascular processes after a simulation of ischemia by oxygen and glucose deprivation. Immunohistochemical, electrophysiological, and pharmacological studies suggest that AM in the CNS can act as a neurotransmitter, neuromodulator, or neurohormone, or as a cytoprotective factor in ischemic/hypoxic conditions, in addition to its vasodilator role. Copyright 2002 Wiley-Liss, Inc.

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