

Adrenomedullin

Adrenomedullin (ADM or AM) is a [vasodilator peptide](#) hormone of uncertain significance in human health and disease. It was initially isolated in 1993 from a pheochromocytoma.

Adrenomedullin (ADM) has been reported to induce glioblastoma cell growth.

[miR-1297](#) sensitizes glioma cells to TMZ treatment by targeting ADM. The Bax/Bcl-2, Akt, and Erk1/2 signaling pathways, as well as mitochondrial functions might be involved ¹⁾

Adrenomedullin (ADM) has been identified as a promising [biomarker](#) of [mortality](#) and [outcome](#) in [sepsis](#), [heart failure](#) and after [major surgery](#). A recently developed assay specific for bioactive adrenomedullin (bio-ADM) has not yet been assessed in [aneurysmal subarachnoid hemorrhage](#) (aSAH). The objective of a [prospective trial](#) was to assess the time course of bio-ADM after aSAH in relation to the development of [delayed cerebral ischemia](#) (DCI) and its association with [clinical outcome](#).

Bio-ADM levels in [plasma](#) and [cerebrospinal fluid](#) (CSF) were measured during five predefined epochs, for up to 21 days in 30 aSAH patients: early, (day 0 to day 3); acute, (day 4 to day 8); early critical, (day 9 to day 12); late critical, (day 13 to day 15), and late (day 16 to day 21). DCI was diagnosed clinically or based on multimodal monitoring and imaging, and the occurrence of DCI-related cerebral infarction, and outcome after 12 months (extended Glasgow outcome scale), was noted.

Higher median bio-ADM levels in plasma during the acute phase were predictive of long-term unfavorable outcome (AUC = 0.97; 95% CI 0.91 to 1.00; $p < 0.001$). Early critical bio-ADM levels during DCI were lower in CSF and confirmed DCI occurrence (AUC = 0.80; 95% CI 0.59 to 1.00; $p = 0.044$).

The dynamics of bio-ADM levels in CSF present a fairly different course compared to plasma with observed higher bio-ADM concentrations in patients spared from DCI and/or developing favorable outcome ²⁾.

Unclassified

2: Huang L, Wang D, Feng Z, Zhao H, Xiao F, Wei Y, Zhang H, Li H, Kong L, Li M, Liu F, Zhang H, Zhang W. Inhibition of Intermedin (Adrenomedullin 2) Suppresses the Growth of Glioblastoma and Increases the Antitumor Activity of Temozolomide. *Mol Cancer Ther*. 2021 Feb;20(2):284-295. doi: 10.1158/1535-7163.MCT-20-0619. Epub 2020 Dec 9. PMID: 33298587.

3: Gracia Arnillas MP, Alvarez-Lerma F, Masclans JR, Roquer J, Soriano C, Manzano D, Zapatero A, Diaz Y, Duran X, Castellví A, Cuadrado E, Ois A. Impact of adrenomedullin levels on clinical risk stratification and outcome in subarachnoid haemorrhage. *Eur J Clin Invest*. 2020 Nov;50(11):e13318.

doi: 10.1111/eci.13318. Epub 2020 Jul 13. PMID: 32535893.

4: Rodríguez-Lorenzo S, Ferreira Francisco DM, Vos R, van Het Hof B, Rijnsburger M, Schroten H, Ishikawa H, Beaino W, Bruggmann R, Kooij G, de Vries HE. Altered secretory and neuroprotective function of the choroid plexus in progressive multiple sclerosis. *Acta Neuropathol Commun*. 2020 Mar 19;8(1):35. doi: 10.1186/s40478-020-00903-y. PMID: 32192527; PMCID: PMC7083003.

5: Liu L, Xu H, Zhang J, Yin L, Zhao Q. Intermedin attenuates cardiomyocytes hypoxia-injury through upregulating Long non-coding RNA MALAT1. *J Cell Biochem*. 2020 Jan 6. doi: 10.1002/jcb.29642. Epub ahead of print. PMID: 31904148.

6: Wang M, Wang J, Liu Z, Guo X, Wang N, Jia N, Zhang Y, Yuan J. Effects of intermedin on autophagy in cerebral ischemia/reperfusion injury. *Neuropeptides*. 2018 Apr;68:15-21. doi: 10.1016/j.npep.2017.10.004. Epub 2017 Nov 8. PMID: 29128104.

7: Kawano T, Miyashita K, Takeuchi M, Nagakane Y, Yamamoto Y, Kamiyama K, Manabe Y, Todo K, Metoki N, Akaiwa Y, Toyoda K, Nagatsuka K. Blood biomarkers associated with neurological deterioration in patients with acute penetrating artery territory infarction: A multicenter prospective observational study. *Int J Stroke*. 2018 Feb;13(2):207-216. doi: 10.1177/1747493016677982. Epub 2016 Nov 2. PMID: 27807280.

8: Neumann JT, Schwerg M, Dörr O, Mortensen K, Franzen K, Zeller T, Ojeda F, Blankenberg S, Hamm C, Nef H, Stangl V, Möckel M, Sydow K. Biomarker response and therapy prediction in renal denervation therapy - the role of MR- proadrenomedullin in a multicenter approach. *Biomarkers*. 2017 May-Jun;22(3-4):225-231. doi: 10.3109/1354750X.2016.1172112. Epub 2016 May 6. PMID: 27153479.

9: Wang Z, Martorell BC, Wälchli T, Vogel O, Fischer J, Born W, Vogel J. Calcitonin gene-related peptide (CGRP) receptors are important to maintain cerebrovascular reactivity in chronic hypertension. *PLoS One*. 2015 Apr 10;10(4):e0123697. doi: 10.1371/journal.pone.0123697. PMID: 25860809; PMCID: PMC4393086.

10: Mitome-Mishima Y, Miyamoto N, Tanaka R, Shimosawa T, Oishi H, Arai H, Hattori N, Urabe T. Adrenomedullin deficiency and aging exacerbate ischemic white matter injury after prolonged cerebral hypoperfusion in mice. *Biomed Res Int*. 2014;2014:861632. doi: 10.1155/2014/861632. Epub 2014 Jun 16. PMID: 25028667; PMCID: PMC4084515.

11: Cai JY, Chen XD, Ba HJ, Lin JH, Lu C, Chen MH, Sun J. Identification of plasma adrenomedullin as a possible prognostic biomarker for aneurysmal subarachnoid hemorrhage. *Peptides*. 2014 Sep;59:9-13. doi: 10.1016/j.peptides.2014.06.014. Epub 2014 Jul 5. PMID: 25009125.

12: Zhu Y, Zhang L, Gidday JM. Deferoxamine preconditioning promotes long- lasting retinal ischemic tolerance. *J Ocul Pharmacol Ther*. 2008 Dec;24(6):527-35. doi: 10.1089/jop.2008.0082. PMID: 19046123; PMCID: PMC2720806.

13: Kubo Y, Ogasawara K, Kakino S, Kashimura H, Yoshida K, Ogawa A. Cerebrospinal fluid adrenomedullin concentration correlates with hyponatremia and delayed ischemic neurological deficits after subarachnoid hemorrhage. *Cerebrovasc Dis*. 2008;25(1-2):164-9. doi: 10.1159/000113734. Epub 2008 Jan 23. PMID: 18212522.

14: Betchen SA, Musatov S, Roberts J, Pena J, Kaplitt MG. PTEN inhibits adrenomedullin expression and function in brain tumor cells. *J Neurooncol*. 2006 Sep;79(2):117-23. doi: 10.1007/s11060-005-9035-7. Epub 2006 Jul 5. PMID: 16821090.

- 15: Honda M, Nakagawa S, Hayashi K, Kitagawa N, Tsutsumi K, Nagata I, Niwa M. Adrenomedullin improves the blood-brain barrier function through the expression of claudin-5. *Cell Mol Neurobiol*. 2006 Mar;26(2):109-18. doi: 10.1007/s10571-006-9028-x. Epub 2006 Apr 20. PMID: 16763778.
- 16: Kaur B, Khwaja FW, Severson EA, Matheny SL, Brat DJ, Van Meir EG. Hypoxia and the hypoxia-inducible-factor pathway in glioma growth and angiogenesis. *Neuro Oncol*. 2005 Apr;7(2):134-53. doi: 10.1215/S1152851704001115. PMID: 15831232; PMCID: PMC1871894.
- 17: Benes L, Kappus C, McGregor GP, Bertalanffy H, Mennel HD, Hagner S. The immunohistochemical expression of calcitonin receptor-like receptor (CRLR) in human gliomas. *J Clin Pathol*. 2004 Feb;57(2):172-6. doi: 10.1136/jcp.2003.12997. PMID: 14747444; PMCID: PMC1770218.
- 18: Ji SM, Yue H, He RR. Effect of intracarotid administration of adrenomedullin on the spontaneous electrical activity of area postrema neurons in sino-aortic denervated rats. *Sheng Li Xue Bao*. 2003 Aug 25;55(4):395-400. PMID: 12937817.
- 19: Watanabe K, Takayasu M, Noda A, Hara M, Takagi T, Suzuki Y, Yoshia J. Adrenomedullin reduces ischemic brain injury after transient middle cerebral artery occlusion in rats. *Acta Neurochir (Wien)*. 2001 Nov;143(11):1157-61. doi: 10.1007/s007010100007. PMID: 11731867.
- 20: Knerr I, Schuster S, Nomikos P, Buchfelder M, Dötsch J, Schoof E, Fahlbusch R, Rascher W. Gene expression of adrenomedullin, leptin, their receptors and neuropeptide Y in hormone-secreting and Non-Functioning Pituitary Neuroendocrine Tumors, meningiomas and malignant intracranial tumours in humans. *Neuropathol Appl Neurobiol*. 2001 Jun;27(3):215-22. doi: 10.1046/j.0305-1846.2001.00324.x. PMID: 11489141.
- 21: Moreno MJ, Cohen Z, Stanimirovic DB, Hamel E. Functional calcitonin gene-related peptide type 1 and adrenomedullin receptors in human trigeminal ganglia, brain vessels, and cerebrovascular or astroglial cells in culture. *J Cereb Blood Flow Metab*. 1999 Nov;19(11):1270-8. doi: 10.1097/00004647-199911000-00012. PMID: 10566974.
- 22: Ueta Y, Hara Y, Setiadji VS, Isse T, Shibuya I, Kitamura K, Kangawa K, Matsuo H, Eto T, Hattori Y, Yamashita H. Adrenomedullin-like immunoreactivity in the rat hypothalamo-neurohypophyseal tract. *Peptides*. 1999;20(2):199-204. doi: 10.1016/s0196-9781(98)00156-9. PMID: 10422875.
- 23: Kikumoto K, Kubo A, Hayashi Y, Minamino N, Inoue S, Dohi K, Kitamura K, Kangawa K, Matsuo H, Furuya H. Increased plasma concentration of adrenomedullin in patients with subarachnoid hemorrhage. *Anesth Analg*. 1998 Oct;87(4):859-63. doi: 10.1097/00005339-199810000-00021. PMID: 9768783.
- 24: Kaneko H, Mitsuma T, Nagai H, Mori S, Iyo T, Kusugami K, Tache Y. Central action of adrenomedullin to prevent ethanol-induced gastric injury through vagal pathways in rats. *Am J Physiol*. 1998 Jun;274(6):R1783-8. doi: 10.1152/ajpregu.1998.274.6.R1783. PMID: 9841551.
- 25: Saita M, Shimokawa A, Kunitake T, Kato K, Hanamori T, Kitamura K, Eto T, Kannan H. Central actions of adrenomedullin on cardiovascular parameters and sympathetic outflow in conscious rats. *Am J Physiol*. 1998 Apr;274(4):R979-84. doi: 10.1152/ajpregu.1998.274.4.R979. PMID: 9575959.
- 26: Martínez V, Cuttitta F, Taché Y. Central action of adrenomedullin to inhibit gastric emptying in rats. *Endocrinology*. 1997 Sep;138(9):3749-55. doi: 10.1210/endo.138.9.5397. PMID: 9275061.
- 27: Mori Y, Takayasu M, Suzuki Y, Shibuya M, Yoshida J, Hidaka H. Effects of adrenomedullin on rat cerebral arterioles. *Eur J Pharmacol*. 1997 Jul 9;330(2-3):195-8. doi: 10.1016/s0014-2999(97)01028-5.

PMID: 9253953.

28: Jougasaki M, Aarhus LL, Heublein DM, Sandberg SM, Burnett JC Jr. Role of prostaglandins and renal nerves in the renal actions of adrenomedullin. *Am J Physiol.* 1997 Feb;272(2 Pt 2):F260-6. doi: 10.1152/ajprenal.1997.272.2.F260. PMID: 9124405.

29: Dogan A, Suzuki Y, Koketsu N, Osuka K, Saito K, Takayasu M, Shibuya M, Yoshida J. Intravenous infusion of adrenomedullin and increase in regional cerebral blood flow and prevention of ischemic brain injury after middle cerebral artery occlusion in rats. *J Cereb Blood Flow Metab.* 1997 Jan;17(1):19-25. doi: 10.1097/00004647-199701000-00004. PMID: 8978383.

30: Champion HC, Erickson CC 3rd, Simoneaux ML, Bivalacqua TJ, Murphy WA, Coy DH, Kadowitz PJ. Proadrenomedullin NH2-terminal 20 peptide has cAMP-mediated vasodilator activity in the mesenteric vascular bed of the cat. *Peptides.* 1996;17(8):1379-87. doi: 10.1016/s0196-9781(96)00240-9. PMID: 8971935.

31: Majid DS, Kadowitz PJ, Coy DH, Navar LG. Renal responses to intra-arterial administration of adrenomedullin in dogs. *Am J Physiol.* 1996 Jan;270(1 Pt 2):F200-5. doi: 10.1152/ajprenal.1996.270.1.F200. PMID: 8769840.

32: Baskaya MK, Suzuki Y, Anzai M, Seki Y, Saito K, Takayasu M, Shibuya M, Sugita K. Effects of adrenomedullin, calcitonin gene-related peptide, and amylin on cerebral circulation in dogs. *J Cereb Blood Flow Metab.* 1995 Sep;15(5):827-34. doi: 10.1038/jcbfm.1995.103. PMID: 7673375.

1)

He Z, Cheng M, Hu J, Liu L, Liu P, Chen L, Cao D, Tang J. miR-1297 sensitizes glioma cells to temozolomide (TMZ) treatment through targeting adrenomedullin (ADM). *J Transl Med.* 2022 Oct 1;20(1):443. doi: 10.1186/s12967-022-03647-6. PMID: 36183123.

2)

Veldeman M, Dogan R, Weiss M, Stoppe C, Simon TP, Marx G, Clusmann H, Schubert GA, Albanna W. Levels of bioactive [adrenomedullin](#) in [plasma](#) and [cerebrospinal fluid](#) in relation to [delayed cerebral ischemia](#) in patients after [aneurysmal subarachnoid hemorrhage](#): A prospective observational study. *J Neurol Sci.* 2021 Jun 5;427:117533. doi: 10.1016/j.jns.2021.117533. Epub ahead of print. PMID: 34111763.

From:

<https://neurosurgerywiki.com/wiki/> - **Neurosurgery Wiki**

Permanent link:

<https://neurosurgerywiki.com/wiki/doku.php?id=adrenomedullin>

Last update: **2024/06/07 02:51**

