

Endothelins and Urotensin II

Powerful Vasoconstrictors and Tumor Growth Stimulators

Ofra Gohar Ph.D.

Endothelins (ET-1,2,3) and Urotensin II are peptides that are considered to be very powerful vasoconstrictive substances. In humans, endothelins mediate their actions via two specific G-Protein coupled receptors, ET_AR and ET_BR. Both ET_AR and ET_BR are present in the heart and in human myocardium at similar levels.^{1,2}

Until recently it was thought that all cellular activities of the endothelins were mediated through their interactions with their cell surface receptors. However, a recent study demonstrated that cardiac nuclei also possess both ET_AR and ET_BR subtypes, which are functional and coupled to signaling mechanisms within the nuclear membrane.² The endothelin receptors differ in their ligand specificity. While ET_AR has varying affinities for the endothelin isoforms (ET-1 >ET-2 >ET-3), ET_BR shows no selective affinity.^{2,3} Subsequent studies have demonstrated the presence of endothelins in vascular as well as in non-vascular cells and tissues, having multiple biological activities.

The human Urotensin II receptor (UTIIIR) was originally isolated as an orphan receptor (GPR14) in neural and sensory tissues. Urotensin II is expressed in various human tissues such as CNS,

skeletal muscle, pancreas, and heart.⁴⁻⁶ The role and the importance of ET-1 and Urotensin II as cardiovascular peptides in humans are already well established.⁷⁻⁸

Recently, evidence has accumulated indicating that ET-1, Urotensin II and their receptors are expressed in various kinds of tumor cells. Urotensin II was reported to stimulate cell growth of adrenal tumors and neuroblastomas suggesting the possibility that Urotensin II may act as a growth stimulator in tumors.⁸⁻¹⁰ Overexpression of ET-1 and ET_AR was reported in different malignancies including prostate cancer, breast and ovarian carcinomas, and human Kaposi's sarcoma.¹¹⁻¹⁶ Hypermethylation of the ET_BR correlated with transcriptional down-regulation. Reduced expression of ET_BR receptor was observed in several prostate, bladder and colon cancer cell lines.³

Currently there is increasing evidence that ET-1 may modulate mitogenesis, apoptosis, angiogenesis, tumor invasion and the development of metastases.³

In breast carcinomas it has been demonstrated that overexpression of ET-1 and ET_AR receptor correlated with parameters that characterize aggressive types of breast cancer¹⁵ suggesting that analysis of ET_AR expression might be used as a diagnostic marker for evaluating the progression of the disease and effectiveness of treatment. These and other findings have made ET receptors, and especially ET_AR, promising therapeutic targets for pharmacological intervention.

Alomone Labs offers polyclonal antibodies to ET_AR (#AER-001), ET_BR (#AER-002) and UTIIIR (#AER-003) that can be used as research tools for exploring the role of endothelins and Urotensin-II in cancer and other pathologies.

Related Antibodies

Compound	Product #
Endothelin Receptors	
Anti-ET-A	AER-001
Anti-ET-B	AER-002
Urotensin II Receptor	
Anti-UTIIIR	AER-003

References:

- Davenport, A.P. (2002) *Pharmacol. Rev.* **54**, 219.
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- Grant, K. *et al.* (2003) *Br. J. Cancer.* **88**, 163.
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- Matsushita, M. *et al.* (2001) *J. Hypertens.* **19**, 2185.
- Maguire, J.J. and Davenport, A.P. (2002) *Br. J. Pharmacol.* **137**, 579.
- Yanagisawa, M. *et al.* (1988) *Nature* **332**, 411.
- Takahashi, K. *et al.* (2000) *Clin. Sci.* **103**, 35S.
- Takahashi, K. *et al.* (2001) *Peptides* **22**, 1175.
- Takahashi, K. *et al.* (2003) *Peptides* **24**, 301.
- Asham, E. *et al.* (2001) *Br. J. Cancer.* **85**, 1759.
- Kopetz, E.S. *et al.* (2002) *Invest. New Drugs.* **20**, 173.
- Rosano, L. *et al.* (2003) *Am. J. Pathol.* **163**, 753.
- Rosano, L. *et al.* (2003) *Cancer Res.* **63**, 2447.
- Wulfing, P. *et al.* (2003) *Clin. Cancer Res.* **9**, 4125.
- Nelson, J.B. (2003) *J. Urol.* **170**, S65.

Anti-Endothelin Receptor A (ET-A)

Product #: AER-001

Host: Rabbit

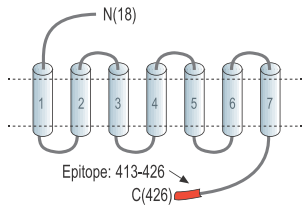
Epitope: Peptide (C)NHNTSSSHKDSMN, corresponding to amino acid residues 413-426 of rat ET-A.

Putative epitope location:

Intracellular, C-terminus.

Homology with other species:

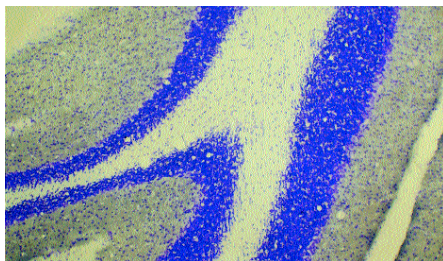
Human, swine, bovine - 13/14 residues identical; chicken - 12/14 residues identical.



Applications:

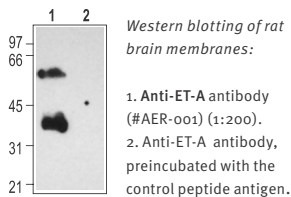
Immunohistochemistry:

Rat brain frozen sections.



Immunohistochemical staining of rat cerebellum with Anti-ET-A antibody (#AER-001). The specific staining is black. The counterstain is cresyl violet.

Western Blotting:



Anti-Endothelin Receptor B (ET-B)

Product #: AER-002

Host: Rabbit.

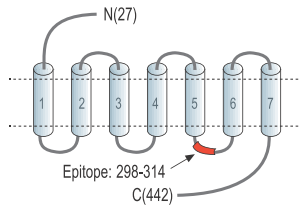
Epitope: peptide CEMLRKKSGMQIALND, corresponding to residues 298-314 of rat ET-B.

Putative epitope location:

Intracellular, i3 loop.

Homology with other species:

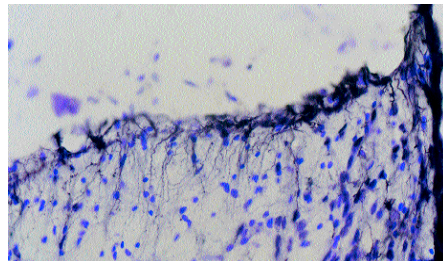
All known vertebrate sequences - identical.



Applications:

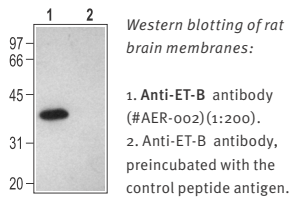
Immunohistochemistry:

Rat brain frozen sections.



Immunohistochemical staining of rat dorsal peri-ventricular thalamus with Anti-ET-B antibody (#AER-002). The specific staining is black. The counterstain is cresyl violet.

Western Blotting:



Anti-Urotensin II Receptor (UTIIR)

Product #: AER-003

NEW

Host: Rabbit

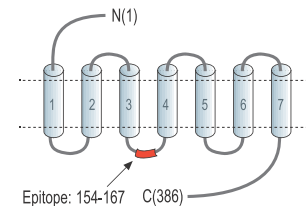
Epitope: Peptide (C)RPLDTVQRSGYRK, corresponding to residues 154-167 of rat UTIIR.

Putative epitope location:

Intracellular, 2nd Cytoplasmic loop.

Homology with other species:

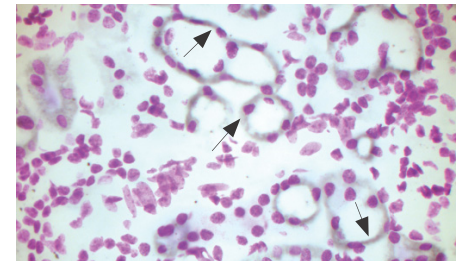
Bovine – identical; Human, canine (13/14 residues identical).



Applications:

Immunohistochemistry:

Mouse paraffin kidney section.



Immunohistochemical staining of UTIIR in mouse kidney using Anti-UTIIR antibody (#AER-003). UTIIR was visualized with immuno-peroxidase methods and final brown-black diaminobenzidine color product (arrows). The counterstain is cresyl violet.

Western Blotting:

