**DOI:** https://doi.org/10.54393/pbmj.v9i1.1327

PAKISTAN BIOMEDICAL JOURNAL
https://www.pakistanbmj.com/journal/index.php/pbmj/index
ISSN (E): 2709-2798, (P): 2709-278X
Volume 9, Issue 01 (January 2026)

# Agonists and Antagonists of Peptide Receptors: Therapeutic Approaches to Combat Cancer

OPEN ACCESS

**Rafael Coveñas**[1,2]

[1]Laboratory of Neuroanatomy of the Peptidergic Systems, Institute of Neurosciences of Castilla and León, University of Salamanca, Salamanca, Spain
[2]Bases Moleculares del Desarrollo, University of Salamanca, Salamanca, Spain
***covenas@usal.es***

## ARTICLE INFO

***How to Cite:***

Covenas, R. (2026). Agonists and Antagonists of Peptide Receptors: Therapeutic Approaches to Combat Cancer: Agonists and Antagonists of Peptide Receptors. Pakistan BioMedical Journal, 9(1), 01-02. https://doi.org/10.54393/pbmj.v9i1.1327

Despite the significant advances made in cancer diagnosis and treatment, much remains to be learned and explored. New strategies and lines of research must be pursued, in combination with those currently used (surgery, radiotherapy, chemotherapy, immunotherapy). Peptidergic systems are involved in many physiological functions and are also implicated in many human pathologies, including cancer. There is increasing research on these systems in relation to cancer development and progression, peptide receptor overexpression, biomarkers, prognosis, aggressiveness, relapse risk, and tumor size. Endogenous bioactive peptides exert oncogenic actions (e.g., cell proliferation and migration, anti-apoptotic action, angiogenesis) and antitumor effects (counteracting previous mechanisms). These bioactive peptides bind to peptide receptors that are overexpressed in cancer cells compared to normal cells. This is crucial for establishing more specific therapeutic strategies using antitumor peptides and oncogenic peptide antagonists, since these antagonists produce antitumor effects, including the apoptosis of tumor cells which is greater in tumor cells than in normal cells. Therefore, the co- administration of antitumor agonists and oncogenic peptide antagonists is a very promising anticancer line of research that needs to be developed. This treatment would not depend on either the clinical state or the biology of the tumor, since by overexpressing peptide receptors different tumors (e.g., glioma, lung cancer, hepatoblastoma, breast cancer), they could be treated with the same antitumor therapeutic procedure. What data currently exists to support what was written above and what peptide receptor agonists and antagonists act as antitumor agents? Fortunately, there is very promising data, some examples: 1) Neurokinin receptor antagonists: Aprepitant (Emend, neurokinin-1 receptor antagonist) exerts a broad antitumor action against numerous types of cancer (breast, pancreas, liver, lung, larynx, prostate, glioma, neuroblastoma, retinoblastoma, osteosarcoma, melanoma, thyroid, gastric, colon, leukemia) and the repurposing of this antiemetic used in clinical practice as an anticancer agent has been suggested [1]; 2) Angiotensin II receptor antagonists: Telmisartan and losartan (DuP-753, angiotensin II type 1 receptor antagonists) and PD-123,177, PD-123,319 ditrifluoroacetate, olodanrigan (EMA401) and A3E (angiotensin II type 2 receptor antagonists) exert an anticancer action against glioma and neuroblastoma [2]; 3) Neurotensin receptor antagonists: SR- 48692 and meclinertant (SR-48692) (neurotensin type 1 receptor antagonists) against glioma and ovarian cancer [2]; 4) Bradykinin receptor antagonists: SSR-240,612 (bradykinin type 1 receptor antagonist), Firazyr (HOE-140, bradykinin type 2 receptor antagonist), and BKM-570 (mainly a bradykinin type 2 receptor antagonist) against glioma [2]; 5) Vasopressin receptor antagonists: Tolvaptan (vasopressin type 2 receptor antagonist) against neuroblastoma [3]; 6) Neuropeptide Y receptor antagonists: BIBP- 3226 (neuropeptide type 1 receptor antagonist),

**DOI:** https://doi.org/10.54393/pbmj.v9i1.1327

BIIE-0246 (neuropeptide type 2 receptor antagonist) and L-152,804 (neuropeptide type 5 receptor antagonist) exert anticancer actions against neuroblastoma and breast, colon and prostate cancer [4]; 7) Galanin receptor antagonists: SNAP-37889 (HT-2157, galanin type 3 receptor antagonist) acts against leukemia [5], and 8) Glucagon-like peptide-1 receptor agonists, galanin type 2 receptor agonists (M89b) and angiotensin II type 2 receptor agonists also exert antitumor effects against pancreatic and colorectal cancer [6]. And there is something else, and it is very important: Somatostatin peptide analogs and gonadotropin-releasing hormone receptor agonists (triptorelin, lupron, zoladex (goserelin)) are currently used in clinical practice to fight lung, prostate, breast and neuroendocrine tumors [7]. These are some examples of the great antitumor potential of peptide receptor agonists and antagonists, alone or in combination with current therapies. In sum, peptide receptors are promising anticancer therapeutic targets and its exhaustive study will improve the diagnosis, management and treatment of tumors.

## REFERENCES

[1] Coveñas R, Rodríguez FD, Robinson P, Muñoz M. The Repurposing of Non-Peptide Neurokinin-1 Receptor Antagonists as Antitumor Drugs: An Urgent Challenge for Aprepitant. International Journal of Molecular Sciences. 2023; 24: 15936. doi: 10.3390/Ijms242115936.

[2] Sánchez ML, Mangas A, Coveñas R. Glioma and Peptidergic Systems: Oncogenic and Anticancer Peptides. International Journal of Molecular Sciences. 2024; 25: 7990. doi: 10.3390/Ijms25147990.

[3] Marroncini G, Ancesci C, Naldi L, Fibbi B, Baldanzi F, Maggi M et al. The V2 Receptor Antagonist Tolvaptan Counteracts Proliferation and Invasivity in Human Cancer Cells. Journal of Endocrinological Investigation. 2022; 45: 1693-1708. doi: 10.1007/S40618-022-01807-5.

[4] Pascetta SA, Kirsh SM, Cameron M, Uniacke J. Pharmacological Inhibition of Neuropeptide Y Receptors Y1 And Y5 Reduces Hypoxic Breast Cancer Migration, Proliferation, And Signaling. BioMed Central Cancer. 2023; 23: 494. doi: 10.1186/S12885-023-10993-1.

[5] Koller A, Rid R, Beyreis M, Bianchini R, Holub BS, Lang A. In Vitro Toxicity of the Galanin Receptor 3 Antagonist SNAP 37889. Neuropeptides. 2016; 56: 83-88. doi: 10.1016/J.Npep.2015.12.003.

[6] Moll GN. Agonists of Galanin Subtype 2 Receptor May Prevent Pancreatic Cancer and Agonists of Angiotensin II Type 2 Receptor May Prevent Colorectal Cancer. European Journal of Pharmacology. 2024; 978: 176772. doi: 10.1016/J.Ejphar.2024.176772.

[7] Al Musaimi O. Peptide Therapeutics: Unveiling the Potential Against Cancer – A Journey Through 1989. Cancers. 2024; 16: 1032. doi: 10.3390/Cancers16051032.