Acknowledgments/Funding: DEAPE, CAPES, and CNPq (307944/2022-0 and 302922/2025-3).

https://doi.org/10.1016/j.htct.2026.106276

5

ASSOCIATION BETWEEN DEPRESSIVE SYMPTOMS AND THE SYSTEMIC IMMUNE-INFLAMMATION INDEX IN PATIENTS WITH LOCALLY ADVANCED HEAD AND NECK CANCER

Angélica Christiny Ribeiro de Toledo,
Daniel Paixão Pequeno,
Carmen Silvia Passos Lima,
Gustavo Jacob Lourenço

Universidade Estadual de Campinas, Campinas, SP, Brazil

Introduction: Head and neck cancer (HNC) represents a major global health burden and is frequently associated with psychological distress, particularly depressive symptoms. Alcohol consumption is a major risk factor for HNC development due to the production of carcinogenic metabolites such as acetaldehyde, which increase oxidative stress and DNA damage. Inflammation plays a central role in tumor progression and has also been implicated in the pathophysiology of depression. Pro-inflammatory cytokines can cross the blood-brain barrier, disrupt neurotransmitter metabolism, and impair neuroplasticity, contributing to depressive symptoms. Inflammatory markers derived from routine blood counts, including the neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), lymphocyte-to-monocyte ratio (LMR), systemic immune-inflammation index (SII), and systemic inflammatory response index (SIRI), are accessible indicators of systemic inflammation. However, their relationship with depressive symptoms in HNC patients remains poorly explored. **Objective:** To investigate the association between depressive symptoms and sociodemographic characteristics, lifestyle factors, and systemic inflammatory markers in HNC patients. **Materials and methods:** A total of 110 patients with locally advanced HNC (TNM stage III or IV) were evaluated (mean age 60 years, 91 men and 19 women, 89 White and 21 Black, 21 active smokers and 10 current alcohol users). Depressive symptoms were assessed using the Beck Depression Inventory-II (BDI-II). Sociodemographic data, lifestyle factors, tumor characteristics, and inflammatory markers obtained from complete blood counts (NLR, PLR, LMR, SII, and SIRI) were collected from medical records. Data distribution was assessed using the Shapiro-Wilk test. Associations were evaluated using Spearman's correlation and the Mann-Whitney test. Variables with $p < 0.05$ were included in multivariate linear regression analysis. **Results:** Non-drinkers presented higher BDI-II scores compared with current alcohol users (19.7 vs 9.5, $p = 0.01$). NLR (? = 0.23, $p = 0.02$), PLR (? = 0.30, $p = 0.002$), and SII (? = 0.31, $p = 0.002$) showed significant positive correlations with depression symptoms scores. In multivariate analysis, non-drinking status was associated with an increase of approximately 10 points in BDI-II scores ($p = 0.02$), while SII remained independently associated with depressive symptoms (ß = 0.30, $p = 0.002$). **Conclusions:** Non-drinking status and higher SII levels were associated with increased depressive symptoms in patients with locally advanced HNC. These findings highlight the role of systemic inflammation in the emotional burden of HNC patients. Larger studies are needed to confirm these associations and clarify underlying biological mechanisms.

Keywords: Head and neck cancer, Depression symptoms, Inflammation, Systemic immune-inflammation index.

Conflicts of interest: The authors declare that they have no conflicts of interest.

Acknowledgments/Funding: PIBIC, CAPES e CNPq (307944/2022-0, 302922/2025-3).

https://doi.org/10.1016/j.htct.2026.106277

6

STRUCTURALLY MODIFIED IKAV PEPTIDES AS BIOLOGICALLY ACTIVE LIGANDS IN TRIPLE-NEGATIVE BREAST CANCER

André Vinicius Zolesi, Danielle Vieira Sobral,
Flávio Lopes Alves,
Fernanda Ferreira Mendonça,
Luciana Malavolta, Leonardo Lima Fuscaldi

Faculdade de Ciências Médicas da Santa Casa de São Paulo, São Paulo, SP, Brazil

Introduction/Justification: Breast cancer remains a public health challenge, and triple-negative breast cancer (TNBC) is its most aggressive subtype, characterized by high recurrence, early metastasis, and lack of hormone receptors and HER2 expression. TNBC cells overexpress molecular targets, such as integrins, which play a key role in adhesion, migration, and signaling. Laminin-111, enriched in the breast tumor microenvironment, generates bioactive fragments, such as IKVAV, that selectively interact with integrins a3ß1 and a6ß1 associated with aggressive tumor behavior. These fragments participate in tumor cell growth regulation, supporting IKVAV as a biologically active ligand for integrin-targeting strategies. Structural modification by histidine (H) insertion enables radiolabeling with Tc, reinforcing its potential application in molecular imaging. **Objectives:** To synthesize structurally modified IKVAV peptides incorporating a H residue and to evaluate their in vitro interaction as biologically active ligands in TNBC (MDA-MB-231) cells. **Materials and Methods:** IKVAV-NH2, HIKVAV-NH2, and N-acetyl-HIKVAV-NH2 were synthesized by solid-phase peptide synthesis using the Fmoc/tBu strategy and MBHAR resin. Purification and characterization were performed by RP-HPLC and mass spectrometry. For growth curve analysis, MDA-MB-231 cells were seeded in 6-well plates (5×104 cells/well) and treated with the respective peptides (IKVAV-NH2: 151.6 μM; HIKVAV-NH2: 90.3 μM; N-acetyl-HIKVAV-NH2: 113.2 μM). Viable cells were counted on days 1, 3, 5, and 7, comparing with non-treated control (CT). Data are presented as mean $\pm$ SD and the statistical analyses

were performed applying Student's t-test (significance set at $p < 0.05$). **Results:** IKVAV-NH2 presented a single, well-defined chromatographic peak and a compatible molar mass (528 g/mol), requiring no further purification. In contrast, HIKVAV-NH2 and N-acetyl-HIKVAV-NH2 initially showed two chromatographic peaks, with the minor peak corresponding to IKVAV-NH2, indicating incomplete H coupling. Co-injection and mass spectrometry confirmed this finding, necessitating additional purification. After purification, both peptides were obtained in pure form, with compatible molar masses (665 g/mol for HIKVAV-NH2 and 707 g/mol for N-acetyl-HIKVAV-NH2). Biological evaluation demonstrated that IKVAV-NH2 and HIKVAV-NH2 did not significantly affect MDA-MB-231 cell proliferation compared to CT: IKVAV-NH2 = $(2.2 \pm 0.7) \times 105$ versus CT = $(2.0 \pm 0.9) \times 105$ [day 7; $p = 0.6322$; $n = 6$]; HIKVAV-NH2 = $(3.5 \pm 0.4) \times 105$ versus CT = $(3.1 \pm 0.2) \times 105$ [day 7; $p = 0.1444$; $n = 6$]. In contrast, N-acetyl-HIKVAV-NH2 induced a significant increase in cell proliferation: N-acetyl-HIKVAV-NH2 = $(7.6 \pm 1.3) \times 105$ versus CT = $(5.3 \pm 0.9) \times 105$ [day 7; $p = 0.0020$; $n = 5$], indicating a distinct biological response following N-terminal acetylation. This effect may be associated with increased peptide stability in the biological environment, favoring prolonged cellular interaction. **Conclusion:** Under the evaluated conditions, only N-acetyl-HIKVAV-NH2 significantly modulated MDA-MB-231 cell growth, suggesting that N-terminal acetylation influences peptide stability and biological activity. These findings support the relevance of structural modifications in peptide-based tumor-targeting strategies and highlight the need for further functional and preclinical investigations, including ???Tc radiolabeling for molecular imaging applications.

Keywords: Triple-negative breast cancer, Peptides, Laminin-111, Integrins, Molecular imaging.

Conflicts of interest: Not declared.

Acknowledgments/Funding: Cancer Theranostics Innovation Center (CancerThera) / Centros de Pesquisa, Inovação e Difusão (CEPID) / Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP): grant number 2021/10265-8. Chamada CNPq/MCTI/FNDCT N° 22/2024 - Programa Conhecimento Brazil - Apoio a Projetos em Rede com Pesquisadores Brasileiros no Exterior / Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq): grant number 444492/2024-0. Bolsa de IC PIBIC/CNPq 2024-2025. Fundo de Amparo ao Pesquisador (FAP) / Fundação Arnaldo Vieira de Carvalho (FAVC) 2024/2026.

https://doi.org/10.1016/j.htct.2026.106278

7

SYNTHESIS, CHARACTERIZATION AND ANTIPROLIFERATIVE ACTIVITIES OVER MELANOMA (SK-MEL-28) CELLS OF A NOVEL CO(II) COMPLEX WITH A NUCLEOBASE ANALOG

Lucas Zanoni Davoli, Pedro Paulo Corbi, Leticia Pires de Oliveira, Carmen Silvia Passos Lima, Gilberto Carlos Franchi Júnior, Gabriele Pereira Menezes

Universidade Estadual de Campinas, Campinas, SP, Brazil

Introduction/Justification: The increase in cancer incidence together with acquired resistance to conventional treatments, reinforces the urgent need for new therapeutic approaches. Skin cancer is the most common malignant neoplasm globally, and nucleic acid analogues like 5-fluorouracil (5-FU) have been used clinically to treat patients affected by this disease. At the same time, coordination chemistry has been consolidating itself as a promising strategy in the development of new antitumor agents. Among the metals of interest, cobalt(II) remains as a particularly attractive candidate, still largely unexplored, but with high therapeutic potential. **Objectives:** The present work is dedicated to the synthesis and characterization of a novel cobalt(II) complex containing a nucleobase derivative, besides the evaluation of the in vitro antiproliferative activity of the compound over melanoma (SK-MEL-28) cells. **Materials and methods:** The Co(II) complex was synthesised by deprotonation of the nucleobase analog (6-trifluoromethyluracil, Merck, 97% purity) in alkaline aqueous medium; In another flask, Co(II) bipyridine was prepared and then added to the nucleobase aqueous solution. The synthesis was stirred for 2h. Red crystals were obtained and collected. Elemental analyses (CHN) were performed using the CHNS/O Perkin Elmer 2400 analyzer. Antiproliferative activity of the complex was evaluated against melanoma (SK-MEL-28) and immortalized keratinocyte (HaCaT) cell lines using a colorimetric assay. Cells were treated with the complex. Cisplatin and the free nucleobase were used as positive controls. Cell growth inhibition was determined by absorbance at 540nm and IC50 values were calculated by sigmoidal regression. **Results:** Elemental analysis confirmed the composition of the complex as C20H12CoF6N6O4. The cobalt(II) complex showed moderate antiproliferative activity over SK-MEL-28 cells, with IC50 ranging from 20 μM to 200 μM, while cisplatin showed IC50 value of 13.5 μM. Free nucleobase did not show antiproliferative effect even at the highest concentration tested. **Conclusion:** A new cobalt(II) complex with the nucleic acid analogue 6-trifluoromethyluracil with composition C20H12CoF6N6O4 was obtained. The cobalt(II) complex has presented modest antiproliferative activity against SK-MEL-28 cells, while the free ligand did not show activity even at the highest concentration. Further analyses are envisaged to determine the structural formula of the complex besides the evaluation of its antiproliferative activities over other skin cancer cells.

Keywords: Cobalt complex, Melanoma, Nucleic acid, Skin Neoplasms, Novel.

Conflicts of interest: The authors declare that they have no conflicts of interest.

Acknowledgments/Funding: FAPESP n°2025/01640-0 and 2021/10265-8 Cancer Theranostics Innovation Center CEPID CancerThera.

https://doi.org/10.1016/j.htct.2026.106279