D J Med Sci 2026;12(1):36-43
doi: 10.5606/fng.btd.2026.215

Original Article

In silico molecular docking analysis of chlorotoxin-derived peptide interaction with MMP-2

Alper Demirezen

Department of Medical Biology and Genetics, Kocaeli University, Kocaeli, Türkiye

ABSTRACT

Objectives: This study aimed to investigate the interaction between chlorotoxin (CTX) and matrix metalloproteinase-2 (MMP-2) using *in silico* molecular docking.

Materials and methods: The three-dimensional structures of human MMP-2 (PDB ID: 1CK7) and CTX (PDB ID: 1CHL) were retrieved from the Protein Data Bank and prepared for docking analysis. Molecular docking was performed with AutoDock Vina version 1.2, focusing on the catalytic region of MMP-2. The resulting docking poses were analyzed for predicted binding affinity, spatial orientation, and residue-level interactions.

Results: Docking analysis identified several energetically favorable CTX binding poses on the MMP-2 surface. The top-ranked pose had a predicted binding affinity of –9.1 kcal/mol, with additional conformations showing affinities of –8.5, –8.2, and –7.9 kcal/mol. The most favorable binding mode was localized near the catalytic region of MMP-2, including residues adjacent to the zinc-binding pocket, but it did not clearly occupy the catalytic center. Key putative interactions involved Glu404, Asp410, His403, Glu412, Leu399, and Val400, suggesting stabilization through hydrogen bonding, electrostatic interactions, and hydrophobic contacts.

Conclusion: The present findings support the structural feasibility of CTX association with MMP-2 and suggest a surface-associated binding mode near the catalytic region rather than a classical deep active-site inhibitory interaction. These results provide a useful structural framework for future biochemical and cellular studies aimed at clarifying the role of CTX-MMP-2 recognition in glioma-associated systems.

Keywords: Chlorotoxin, glioblastoma, *in silico* analysis, MMP-2, molecular docking, tumor targeting.

Chlorotoxin (CTX) is a 36-amino-acid, disulfide-rich peptide originally isolated from the venom of *Leiurus quinquestriatus* and initially characterized as a chloride channel ligand. Its compact conformation and stable tertiary structure have since attracted considerable interest for cancer-targeting applications, particularly in glioma research. A pivotal development in this field came when CTX was shown to inhibit glioma cell invasion through a mechanism involving matrix metalloproteinase-2 (MMP-2), thereby shifting CTX from a neurotoxin of biochemical interest to a promising scaffold for tumor-targeted applications.[1-3]

Matrix metalloproteinase-2 remains a biologically plausible target in glioblastoma due to its established role in extracellular matrix degradation, tumor cell dissemination, and local tissue invasion, all of which are hallmarks of malignant glioma progression. Experimental studies have shown that modulation of the tissue inhibitor of matrix metalloproteinases 2/MMP-2 axis can directly influence MMP-2 activation and glioblastoma cell invasiveness, while clinicopathological analyses have associated elevated MMP-2 expression with higher astrocytoma grade and poorer patient prognosis. Beyond its prognostic significance, MMP-2 is also relevant as it has historically been linked to the anti-invasive effects of CTX in glioma models. Together, these observations support

Received: March 10, 2026
Accepted: April 28, 2026
Published online: June 09, 2026

Correspondence: Alper Demirezen.
E-mail: alperdemirezen766@gmail.com

Cite this article as:
Demirezen A. *In silico* molecular docking analysis of chlorotoxin-derived peptide interaction with MMP-2. D J Med Sci 2026;12(1):36-43. doi: 10.5606/fng.btd.2026.215.

the continued importance of MMP-2-centered approaches in the development of targeted glioma therapies.[4,5]

At the same time, the molecular basis of CTX selectivity appears more complex than a simple single-receptor interaction model. In addition to MMP-2-related mechanisms, annexin A2 has been identified as a molecular target for TM601, a CTX-derived peptide with tumor-targeting and anti-angiogenic properties. More recently, structural studies demonstrated that CTX can bind neuropilin-1 (NRP1), and subsequent biochemical evidence suggested that CTX may interact with both MMP-2 and NRP1. Collectively, these findings imply that CTX tumor tropism likely arises from a broader, context-dependent recognition pattern rather than from interaction with a single receptor alone.[6-8]

This expanding mechanistic understanding has facilitated the translational development of CTX-based platforms. Chlorotoxin-derived agents have been investigated clinically for imaging applications, including tozuleristide for fluorescence-guided glioma surgery, while CTX-directed chimeric antigen receptor (CAR) T-cell strategies further highlight the potential of CTX as a targeting domain in glioblastoma. Nevertheless, residue-level details of CTX-MMP-2 recognition remain incompletely defined, and further structural clarification is still needed to support rational optimization of CTX-based targeting strategies.[9,10]

In this context, *in silico* molecular docking provides a practical and mechanistically informative framework for evaluating peptide-protein interactions prior to experimental validation. An earlier computational study proposed plausible interaction models between CTX-related scorpion peptides and MMP-2; however, the precise binding interface of CTX with MMP-2 still warrants further structural investigation.[11] Therefore, the present study aimed to analyze the interaction between CTX and MMP-2 by molecular docking, with particular emphasis on predicted binding affinity, spatial orientation, and residue-level contacts that may underlie tumor-associated molecular recognition.

MATERIALS AND METHODS

Retrieval and preparation of the MMP-2 structure

The structural data and sequences used in this study were retrieved from the Protein Data Bank and UniProt databases in April 04, 1999. The three-dimensional structure of human MMP-2 was obtained from the Protein Data Bank (PDB ID: 1CK7). The catalytic domain of MMP-2 was selected for docking analysis due to its central role in substrate recognition and tumor-associated proteolytic activity. Prior to docking, the receptor structure was prepared by removing crystallographic water molecules and heteroatoms not directly involved in catalysis, while preserving the catalytic zinc-containing active-site environment. Hydrogen atoms were added using UCSF Chimera version 1.16 (Resource for Biocomputing, Visualization, and Informatics at the University of California, San Francisco). The receptor was then processed in AutoDockTools (The Scripps Research Institute), where Gasteiger charges were assigned, and the final receptor structure was converted to PDBQT format for docking calculations.

Retrieval and preparation of the chlorotoxin structure

The three-dimensional structure of CTX was retrieved from the Protein Data Bank (PDB ID: 1CHL). The amino acid sequence of CTX was cross-checked against the UniProt database (UniProt ID: P45639) to confirm sequence identity, as shown in Table 1. The ligand structure was prepared in AutoDockTools by adding hydrogen atoms, assigning Gasteiger charges, and defining rotatable bonds where applicable. The processed ligand was then saved in PDBQT format for subsequent docking analysis.

Molecular docking procedure

Molecular docking simulations were performed with AutoDock Vina version 1.2 (The Scripps Research Institute) to assess the potential interaction between CTX and MMP-2. The docking grid was set to encompass the catalytic region of MMP-2, including residues surrounding the zinc-binding pocket. The grid center was set to x = 12.5, y = –6.3, and

Table 1. Sequence motifs of chlorotoxin peptide and their characteristics

Amino acid position	Amino acid	Properties
1	M	Methionine functions as the starting amino acid and is hydrophobic.
2	C	Cysteine stabilizes the three-dimensional morphology of proteins by forming disulfide bridges.
4	P	Proline affects the structural integrity of proteins with its cyclic structure.
6	F	Phenylalanine has a hydrophobic and aromatic structure.
7	T	Threonine is polar and hydrophilic, can be found at phosphorylation sites, and may play a role in intracellular signaling.
9	D	Aspartic acid is a negatively charged (acidic) and polar amino acid.
10	H	Histidine is pH-sensitive, has a basic structure, and plays a role in enzyme activation.
11	Q	Glutamine is a polar amino acid that is important for cell growth and metabolism.
13	A	Alanine, a building block of proteins, is a hydrophobic amino acid.
14	R	Arginine is an important amino acid in wound healing and immune function.
15	K	Lysine, a basic and hydrophilic amino acid, plays an important role in protein-protein interactions.

The data was obtained from the UniProt database. (UniProt ID: P45639).

z = 22.1, with a grid box size of 25 × 25 × 25 Å. Docking was performed with an exhaustiveness of 8, producing 10 output binding modes and an energy range of 3 kcal/mol. The docking grid parameters used in the analysis are summarized in Table 2.

Visualization and interaction analysis

Docking results were visualized and analyzed using UCSF Chimera and PyMOL version 2.5 (Schrödinger, LLC). An overall structural representation of MMP-2 and CTX generated in UCSF Chimera is shown in Figure 1. The top-ranked binding pose was evaluated with particular emphasis on its spatial orientation relative to the catalytic region of MMP-2. Putative intermolecular interactions, including hydrogen bonds, electrostatic contacts, and hydrophobic interactions, were examined to identify residues potentially involved in ligand binding. Special attention was given to residues near the catalytic zinc-binding pocket to assess whether CTX preferentially occupied catalytically relevant regions of the enzyme surface.

Table 2. Parameter value and coordinates of CTX-MMP-2 molecular docking generated using AutoDock Vina version 1.2

Center X	12.5
Center Y	−6.3
Center Z	22.1
Grid size	25 × 25 × 25 Å

CTX, chlorotoxin; MMP-2, matrix metalloproteinase-2.

Evaluation of docking output

The docking outcome was interpreted primarily on the basis of predicted binding affinity and residue-level interaction patterns. Binding poses near the catalytic domain that showed energetically favorable interaction profiles were considered structurally relevant. Given that this study relied solely on molecular docking, the results were regarded as predictive and hypothesis-generating, providing a structural framework for future experimental validation.

RESULTS

Molecular docking of chlorotoxin to MMP-2

The potential interaction between CTX and MMP-2 was evaluated by molecular docking using AutoDock Vina. The docking analysis identified several energetically favorable binding poses on the surface of the MMP-2 catalytic domain. Among these, the top-ranked pose showed a predicted binding affinity of –9.1 kcal/mol, suggesting a stable interaction

Figure 1. Molecular modeling of MMP-2 and CTX using Chimera. The blue-colored molecule represents CTX, whereas the yellow-colored molecule represents MMP-2. The model was used to visualize the overall three-dimensional structures of the molecules and to support subsequent docking interpretation.
MMP-2, matrix metalloproteinase-2; CTX, chlorotoxin.

between CTX and MMP-2 under the selected docking conditions. Additional poses also demonstrated favorable predicted affinities, with values of –8.5, –8.2, and –7.9 kcal/mol, indicating that CTX may adopt more than one plausible binding orientation on the MMP-2 surface, as shown in Table 3.

Localization of the predicted binding region

Examination of the docking poses showed that the most favorable CTX conformation was positioned in proximity to the catalytic region of MMP-2, including residues surrounding the zinc-binding pocket. Although the docking model did not indicate direct occupation of the catalytic zinc center itself, the peptide was predicted to interact with residues located adjacent to this functionally important region. This spatial arrangement suggests that CTX binds near the catalytic pocket in a surface-accessible manner rather than deeply occupying the active-site cleft, as shown in Figure 2.

Residue-level interaction profile

Residue-level analysis of the top-ranked docking complex revealed several putative intermolecular contacts between CTX and MMP-2. Predicted hydrogen bond interactions were observed with Glu404 and His403, while Asp410 and Glu412 contributed predominantly to electrostatic contacts. In addition, Leu399 and Val400 appeared to participate in hydrophobic interactions that may further stabilize the ligand-protein complex. The predicted interaction distances were within a plausible range for non-covalent molecular recognition, including approximately 2.8 Å for Glu404, 2.9 Å for His403, 3.1 Å for Asp410, and 3.3 Å for Glu412, as shown in Table 4.

Distribution of binding poses

Comparison of the docking poses indicated that the predicted binding modes were not identical but clustered around regions corresponding to the catalytic domain and

Table 3. Binding affinity values and interaction residues of chlorotoxin with MMP-2 obtained by AutoDock Vina

Docking pose	Binding affinity (kcal/mol)	Hydrogen bond residues	Electrostatic interaction residues	Binding region
Pose 1	–9.1	Glu404, Asp410	His403, Glu412	Catalytic domain
Pose 2	–8.5	Glu404	Asp410	Surface region
Pose 3	–8.2	His403	Glu412	Catalytic pocket
Pose 4	–7.9	Asp410	His403	Surface region

MMP-2, matrix metalloproteinase-2.

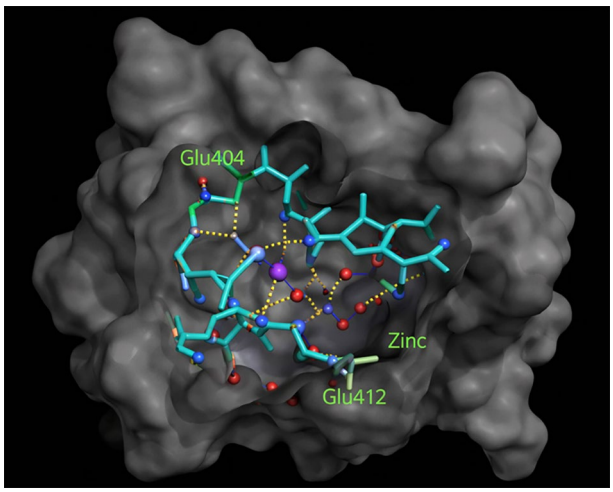

Figure 2. Structural model of the docking complex between MMP-2 and CTX generated using AutoDock Vina. Chlorotoxin is shown as a cyan stick model, whereas MMP-2 is represented as a gray molecular surface highlighting the binding pocket region. Glu404 and Glu412, two residues implicated in ligand binding, are labeled. Dashed yellow lines indicate putative hydrogen-bond interactions between CTX and nearby residues, and the purple sphere represents the catalytic zinc ion within the active-site region. This docking model supports a binding mode in which CTX interacts with residues located adjacent to the catalytic region of MMP-2.

MMP-2, matrix metalloproteinase-2; CTX, chlorotoxin.

nearby surface-exposed areas of MMP-2. The highest-affinity pose was associated with the catalytic domain, whereas lower-ranked poses were distributed between the catalytic pocket and adjacent surface regions. This distribution suggests that CTX may interact with MMP-2 through a set of related but not fully identical conformations, with the most favorable pose exhibiting the strongest predicted structural complementarity to catalytically relevant residues (Table 3).

Structural interpretation of the top-ranked complex

Visualization of the best-scoring docking model showed that CTX aligned along the outer surface of MMP-2 in a manner compatible with surface recognition near the enzyme's catalytically relevant region. The docking model suggested that negatively charged residues on the MMP-2 surface, particularly Glu404 and Asp410, may contribute to peptide recognition through electrostatic attraction and hydrogen bonding. In parallel, hydrophobic contacts involving Leu399 and Val400 appeared to support local stabilization of the complex. Taken together, these findings indicate that CTX has the potential to form a stable docking conformation near the catalytic region of MMP-2, with multiple non-covalent interactions contributing to the predicted binding pattern (Figure 2, Table 4).

DISCUSSION

The present study explored the potential interaction between CTX and MMP-2 by molecular docking and showed that CTX can adopt energetically favorable conformations in proximity to the catalytic region of MMP-2. The top-ranked pose displayed a predicted binding affinity of –9.1 kcal/mol, while additional lower-ranked poses also showed favorable interaction energies. Taken together, these findings suggest that CTX may associate with the MMP-2 surface through more than one plausible orientation rather than through a single rigid binding mode.

Table 4. Summary of the ligand-protein interactions identified between MMP-2 and chlorotoxin

MMP-2 residue	Interaction type	Distance (Å)	Interaction role
Glu404	Hydrogen bond	2.8	Binding stabilization
Asp410	Hydrogen bond/electrostatic	3.1	Catalytic region interaction
His403	Hydrogen bond	2.9	Zinc-binding region interaction
Glu412	Electrostatic	3.3	Surface interaction
Leu399	Hydrophobic	-	Binding pocket stabilization
Val400	Hydrophobic	-	Surface contact

MMP-2, matrix metalloproteinase-2.

In this respect, our data support the structural feasibility of CTX-MMP-2 association under the selected *in silico* conditions and are consistent with the broader view that CTX functions as a surface-recognizing tumor-targeting peptide rather than a simple small-molecule active-site ligand.[11,12]

One of the most relevant observations in the present study was that the best-scoring docking pose localized near the catalytic region of MMP-2, including residues adjacent to the zinc-binding area, without clearly occupying the catalytic center itself. This point is important since the relationship between CTX and MMP-2 has remained controversial. Early work by Deshane *et al.*[3] proposed that CTX inhibits glioma invasion through MMP-2 and reported both reduced surface expression and inhibition of MMP-2 activity. In contrast, a recent study by Blaney *et al.*[13] showed that, although CTX and its fragments can bind MMP-2, they do not measurably inhibit MMP-2 enzymatic activity, supporting a non-catalytic or allosteric interaction model. Our docking results appear to align more closely with this latter interpretation, as the predicted CTX pose was positioned adjacent to, rather than deeply within, the catalytic zinc-containing pocket. Accordingly, the present findings support the possibility that CTX may modulate MMP-2-associated biology through surface recognition or conformational influence rather than through direct catalytic blockade.[3,13]

At the residue level, the predicted CTX-MMP-2 complex was stabilized by a combination of hydrogen bonding, electrostatic interactions, and hydrophobic contacts. In particular, Glu404, Asp410, His403, and Glu412 emerged as putative contact residues, while Leu399 and Val400 appeared to contribute to local hydrophobic stabilization. This interaction profile is structurally plausible given the basic character of CTX and the presence of positively charged residues that can interact favorably with acidic patches on the MMP-2 surface. Interestingly, Dastpeyman *et al.*[14] showed that a short C-terminal fragment of CTX retained anti-migratory bioactivity even in the absence of the full native fold, suggesting that discrete structural motifs may be sufficient for at least part of CTX function. This observation is compatible with our docking model, in which localized residue-level complementarity may be more important than complete insertion into the catalytic pocket.

The biological interpretation of the CTX-MMP-2 interaction should also be considered within the broader context of CTX target selectivity. Although MMP-2 has long been regarded as one of the principal CTX-associated molecules in glioma, later work demonstrated that CTX tumor recognition is likely multifactorial. Lyons *et al.*[12] showed that CTX selectively binds gliomas and other tumors of neuroectodermal origin, thereby establishing the tumor-targeting phenotype experimentally. More recently, McGonigle *et al.*[15] identified NRP1 as a driver of tumor-specific CTX uptake, while Farkas *et al.*[8] demonstrated that CTX can bind both MMP-2 and NRP1. Together, these findings suggest that CTX tumor tropism is unlikely to depend on a single receptor alone. In this framework, our results do not imply that MMP-2 is the exclusive target of CTX; rather, they support the idea that MMP-2 remains one structurally and biologically relevant component of a broader recognition network.

From a translational standpoint, the present findings are of interest, as CTX has already advanced beyond basic biochemical characterization into diagnostic and therapeutic development. Mamelak *et al.*[16] reported the safety and biodistribution of intracavitary TM-601 in adults with recurrent high-grade glioma, providing early clinical evidence for CTX-based targeting. Subsequently, Butte *et al.*[17] demonstrated that BLZ-100 showed high affinity for glioma tissue in near-infrared imaging studies, supporting the utility of CTX-derived fluorescent guidance during tumor resection. More recently, Barish *et al.*[18] reported interim clinical experience with CTX-directed CAR T-cell therapy in recurrent glioblastoma, highlighting the continued translational relevance of CTX-based targeting strategies. These studies collectively indicate that CTX retains practical interest as a targeting scaffold even though its exact molecular binding mechanisms remain incompletely resolved.

The translational literature also suggests that CTX may be particularly valuable as a delivery ligand rather than solely as a direct

therapeutic effector. Costa et al.[19] developed CTX-coupled nanoparticles for nucleic acid delivery to glioblastoma cells and showed their promise as targeted nanocarriers. Wang and Guo[20] reported that a CTX-conjugated onconase construct had anti-glioma potential, supporting the use of CTX in conjugate-based therapeutic strategies. More recently, Mundžić et al.[21] described CTX-functionalized mesoporous silica nanoparticles for pH-responsive paclitaxel delivery to glioblastoma multiforme, further illustrating the continuing development of CTX-guided nanoplatforms. In light of these studies, our docking data may be particularly relevant for understanding how CTX-based systems achieve tumor-associated recognition, even if direct inhibition of MMP-2 catalytic activity is not the principal biological outcome.

Several limitations should nevertheless be acknowledged. First, molecular docking provides a static approximation of peptide-protein recognition and does not fully account for receptor flexibility, solvent effects, ionic strength, or time-dependent conformational rearrangements. Second, docking-derived affinity values do not directly establish biochemical inhibition or cell-based functional activity. Third, as CTX may interact with multiple binding partners, including MMP-2 and NRP1, MMP-2-centered docking cannot fully explain the entirety of CTX biology in glioma.[8,13,15] Therefore, the present findings should be regarded as hypothesis-generating and should be complemented by molecular dynamics simulations, mutational analyses, enzymatic assays, biophysical binding experiments, and cellular migration or invasion studies.

In conclusion, the present docking analysis suggests that CTX can form a structurally favorable complex near the catalytic region of MMP-2 through multiple non-covalent contacts involving residues surrounding the zinc-binding area. Rather than supporting a simple active-site inhibition model, our findings are more consistent with a surface-associated binding pattern that may contribute to tumor-related molecular recognition. When interpreted together with recent experimental and translational studies, these results support the view that the CTX-MMP-2 interaction remains biologically relevant but is likely to represent only one component of the broader and more complex targeting behavior of CTX in glioma-associated systems.

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

Conflict of Interest: The author declared no conflicts of interest with respect to the authorship and/or publication of this article.

Funding: The author received no financial support for the research and/or authorship of this article.

AI Disclosure: The author declare that artificial intelligence (AI) tools were not used, or were used solely for language editing, and had no role in data analysis, interpretation, or the formulation of conclusions. All scientific content, data interpretation, and conclusions are the sole responsibility of the author. The author further confirm that AI tools were not used to generate, fabricate, or 'hallucinate' references, and that all references have been carefully verified for accuracy.

REFERENCES

1. DeBin JA, Maggio JE, Strichartz GR. Purification and characterization of chlorotoxin, a chloride channel ligand from the venom of the scorpion. Am J Physiol 1993;264:C361-9. doi: 10.1152/ajpcell.1993.264.2.C361.
2. Lippens G, Najib J, Wodak SJ, Tartar A. NMR sequential assignments and solution structure of chlorotoxin, a small scorpion toxin that blocks chloride channels. Biochemistry 1995;34:13-21. doi: 10.1021/bi00001a003.
3. Deshane J, Garner CC, Sontheimer H. Chlorotoxin inhibits glioma cell invasion via matrix metalloproteinase-2. J Biol Chem 2003;278:4135-44. doi: 10.1074/jbc.M205662200.
4. Lu KV, Jong KA, Rajasekaran AK, Cloughesy TF, Mischel PS. Upregulation of tissue inhibitor of metalloproteinases (TIMP)-2 promotes matrix metalloproteinase (MMP)-2 activation and cell invasion in a human glioblastoma cell line. Lab Invest 2004;84:8-20. doi: 10.1038/labinvest.3700003.
5. Ramachandran RK, Sørensen MD, Aaberg-Jessen C, Hermansen SK, Kristensen BW. Expression and prognostic impact of Matrix Metalloproteinase-2 (MMP-2) in astrocytomas. PLoS One 2017;12:e0172234. doi: 10.1371/journal.pone.0172234.
6. Kesavan K, Ratliff J, Johnson EW, Dahlberg W, Asara JM, Misra P, et al. Annexin A2 is a molecular target for TM601, a peptide with tumor-targeting and anti-angiogenic effects. J Biol Chem 2010;285:4366-74. doi: 10.1074/jbc.M109.066092.

7. Sharma G, Braga CB, Chen KE, Jia X, Ramanujam V, Collins BM, et al. Structural basis for the binding of the cancer targeting scorpion toxin, ClTx, to the vascular endothelia growth factor receptor neuropilin-1. Curr Res Struct Biol 2021;3:179-86. doi: 10.1016/j.crstbi.2021.07.003.
8. Farkas S, Cioca D, Murányi J, Hornyák P, Brunyánszki A, Szekér P, et al. Chlorotoxin binds to both matrix metalloproteinase 2 and neuropilin 1. J Biol Chem 2023;299:104998. doi: 10.1016/j.jbc.2023.104998.
9. Patil CG, Walker DG, Miller DM, Butte P, Morrison B, Kittle DS, et al. Phase 1 safety, pharmacokinetics, and fluorescence imaging study of tozuleristide (BLZ-100) in adults with newly diagnosed or recurrent gliomas. Neurosurgery 2019;85:E641-9. doi: 10.1093/neuros/nyz125.
10. Wang D, Starr R, Chang WC, Aguilar B, Alizadeh D, Wright SL, et al. Chlorotoxin-directed CAR T cells for specific and effective targeting of glioblastoma. Sci Transl Med 2020;12:eaaw2672. doi: 10.1126/scitranslmed.aaw2672.
11. Othman H, Wieninger SA, ElAyeb M, Nilges M, Srairi-Abid N. In Silico prediction of the molecular basis of ClTx and AaCTx interaction with Matrix Metalloproteinase-2 (MMP-2) to inhibit glioma cell invasion. J Biomol Struct Dyn 2017;35:2815-29. doi: 10.1080/07391102.2016.1231633.
12. Lyons SA, O'Neal J, Sontheimer H. Chlorotoxin, a scorpion-derived peptide, specifically binds to gliomas and tumors of neuroectodermal origin. Glia 2002;39:162-73. doi: 10.1002/glia.10083.
13. Blaney E, Demeke M, Kamayirese S, Monga L, Hansen LA, Watts CR, et al. Chlorotoxin does not target matrix metalloproteinase-2 in glioblastoma. PLoS One 2026;21:e0328964. doi: 10.1371/journal.pone.0328964.
14. Dastpeyman M, Giacomin P, Wilson D, Nolan MJ, Bansal PS, Daly NL. A C-terminal fragment of chlorotoxin retains bioactivity and inhibits cell migration. Front Pharmacol 2019;10:250. doi: 10.3389/fphar.2019.00250.
15. McGonigle S, Majumder U, Kolber-Simonds D, Wu J, Hart A, Noland T, et al. Neuropilin-1 drives tumor-specific uptake of chlorotoxin. Cell Commun Signal 2019;17:67. doi: 10.1186/s12964-019-0368-9.
16. Mamelak AN, Rosenfeld S, Bucholz R, Raubitschek A, Nabors LB, Fiveash JB, et al. Phase I single-dose study of intracavitary-administered iodine-131-TM-601 in adults with recurrent high-grade glioma. J Clin Oncol 2006;24:3644-50. doi: 10.1200/JCO.2005.05.4569.
17. Butte PV, Mamelak A, Parrish-Novak J, Drazin D, Shweikeh F, Gangalum PR, et al. Near-infrared imaging of brain tumors using the Tumor Paint BLZ-100 to achieve near-complete resection of brain tumors. Neurosurg Focus 2014;36:E1. doi: 10.3171/2013.11.FOCUS13497.
18. Barish ME, Aftabizadeh M, Hibbard J, Blanchard MS, Ostberg JR, Wagner JR, et al. Chlorotoxin-directed CAR T cell therapy for recurrent glioblastoma: Interim clinical experience demonstrating feasibility and safety. Cell Rep Med 2025;6:102302. doi: 10.1016/j.xcrm.2025.102302.
19. Costa PM, Cardoso AL, Mendonça LS, Serani A, Custódia C, Conceição M, et al. Tumor-targeted chlorotoxin-coupled nanoparticles for nucleic acid delivery to glioblastoma cells: A promising system for glioblastoma treatment. Mol Ther Nucleic Acids 2013;2:e100. doi: 10.1038/mtna.2013.30.
20. Wang X, Guo Z. Chlorotoxin-conjugated onconase as a potential anti-glioma drug. Oncol Lett 2015;9:1337-42. doi: 10.3892/ol.2014.2835.
21. Mundžić M, Ultimo A, Mladenović M, Pavlović A, Gobbo OL, Ruiz-Hernandez E, et al. Chlorotoxin-functionalized mesoporous silica nanoparticles for pH-responsive paclitaxel delivery to Glioblastoma multiforme. Heliyon 2024;11:e41151. doi: 10.1016/j.heliyon.2024.e41151.