INTERNATIONAL JOURNAL OF ADVANCE RESEARCH, IDEAS AND INNOVATIONS IN TECHNOLOGY

ISSN: 2454-132X
Impact Factor: 6.078
(Volume 11, Issue 3 - V11I3-1379)
Available online at: https://www.ijariit.com

Design of Peptide Inhibitors Targeting MYC Oncogenic Protein Complexes

Varshika Ram Prakash
varshika.ramprakash@gmail.com
Salem High School, Canton, MI, USA

ABSTRACT

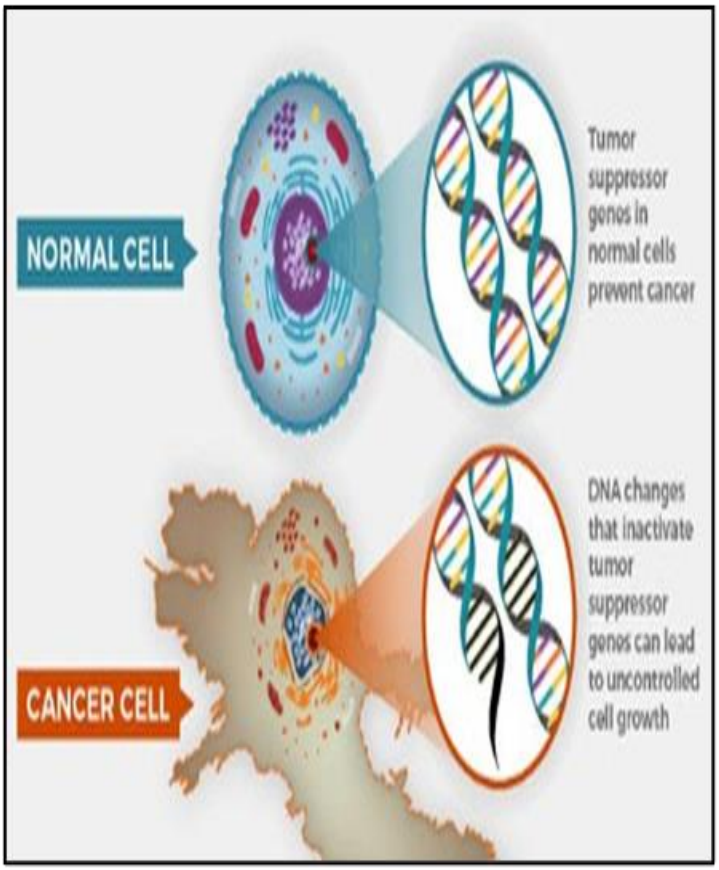
Cancer remains one of the leading causes of death worldwide, with the MYC oncogene being a key driver of tumor progression through its role in promoting uncontrolled cell growth. This study aims to design and evaluate peptide inhibitors targeting the interaction between MYC and DNA, which is essential for MYC's oncogenic function. Utilizing advanced computational methods, including RF diffusion, AlphaFold, and PyMOL, 30 potential peptide candidates were identified. These peptides were assessed based on their IPAE values, which ranged from 6.151 to 9.981, reflecting their effectiveness in disrupting MYC-DNA interactions. The use of AlphaFold enabled accurate prediction of the 3D structures of the MYC-MAX-DNA complex, while PyMOL provided visualization and structural analysis to confirm binding sites and key hotspots where the peptides interact. This detailed analysis confirmed that the peptides effectively target critical regions within the complex. Our findings underscore the potential of these peptides as novel inhibitors of MYC-driven cancer progression. The promising results suggest that these peptides could serve as the basis for new targeted cancer therapies. Moving forward, experimental validation of the peptide candidates will be conducted to confirm their binding affinity and biological activity. Additionally, structural refinement and optimization of the peptide designs will be pursued to enhance their therapeutic potential. Preclinical studies will be essential to evaluate the efficacy and safety of these peptide inhibitors in vivo. This research provides a foundation for developing innovative treatments aimed at targeting MYC-driven cancers.

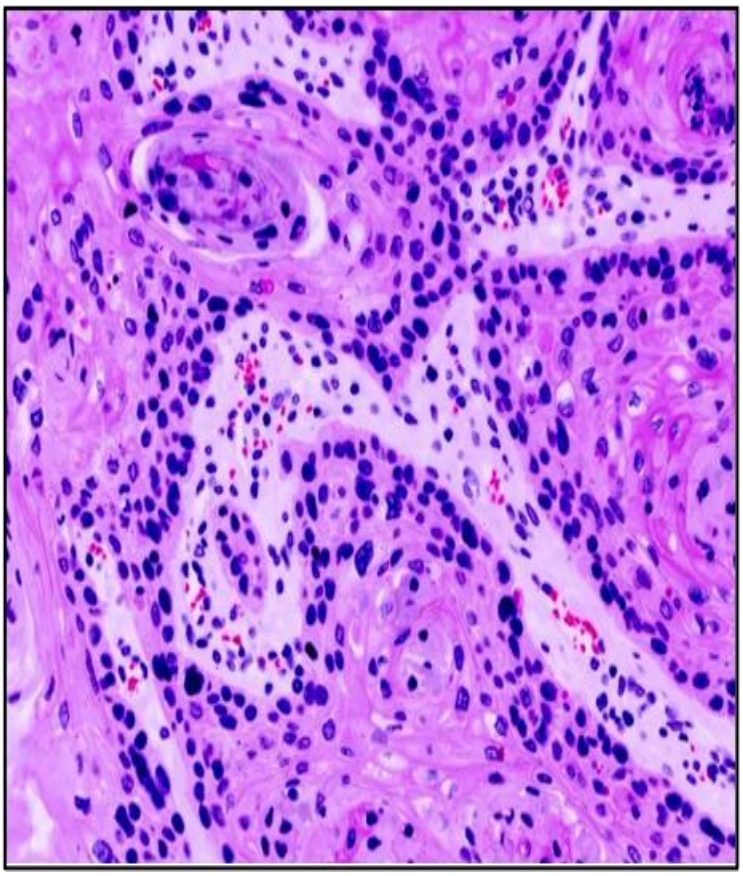
Keywords: *MYC Oncogene, Peptide Inhibitors, MYC-DNA Interaction, RF Diffusion*

INTRODUCTION

BACKGROUND

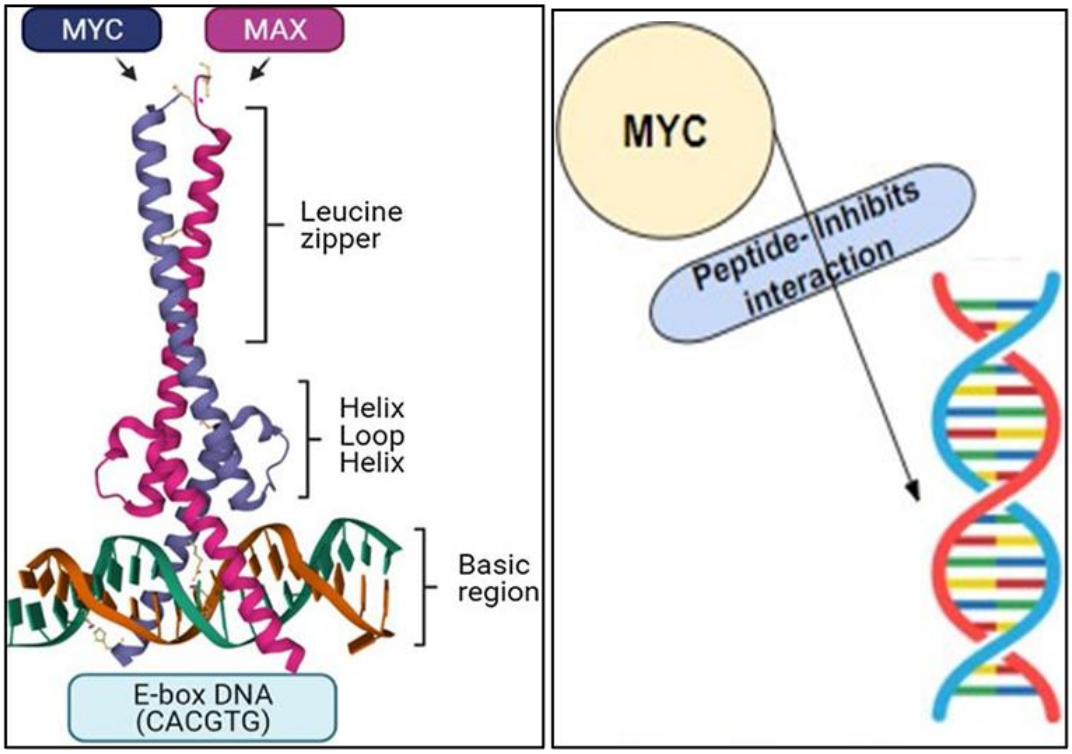
Cancer remains one of the leading causes of death worldwide, with approximately 20 million new cases diagnosed each year. The disease is primarily driven by genetic mutations that lead to uncontrolled cell growth. Among the various types of cancer, lung, breast, prostate, colorectal, and skin cancers are the most common. Diagnosis typically involves imaging tests, biopsies, and lab tests, while treatment options include surgery, radiation therapy, chemotherapy, and immunotherapy. Preventive measures focus on avoiding carcinogens and undergoing regular check-ups to detect the disease early. Cancer remains one of the leading causes of death worldwide, with approximately 20 million new cases diagnosed each year. The disease is primarily driven by genetic mutations that result in uncontrolled cell growth. Among the most prevalent types of cancer are lung, breast, prostate, colorectal, and skin cancers. Diagnostic methods typically involve imaging tests, biopsies, and lab tests, while treatment options include surgery, radiation therapy, chemotherapy, and immunotherapy. Preventive strategies emphasize avoiding carcinogens, such as UV rays and certain viruses, and undergoing regular check-ups for early detection.





Oncogenes play a crucial role in cancer by promoting the survival and spread of cancer cells. Targeting these oncogenes is essential to mitigate their harmful effects. Peptides, which are chains of two or more linked amino acids, have many functions. In the context of cancer, peptide offers a promising approach to inhibit oncogenes by blocking the activity of specific proteins involved in cancer progression. This study employs computational biology to design peptides that bind to and disrupt oncogenes, aiming to develop novel therapeutic agents that can hinder cancer cell proliferation and metastasis. Oncogenes are crucial in cancer development as they promote the survival and spread of cancer cells. Targeting these oncogenes is essential to counteract their detrimental effects. Peptides, which are chains of linked amino acids, show promise in this regard. In the context of cancer, peptides can inhibit oncogenes by targeting and blocking specific proteins involved in cancer progression. This study utilizes computational biology to design peptides that bind to and disrupt oncogenes, with the goal of creating novel therapeutic agents to hinder cancer cell proliferation and metastasis.

A key focus of this research is the MYC oncogene, a transcription factor that drives uncontrolled cell division by binding to specific DNA sequences through its partner, MAX. The interaction between MYC and DNA is crucial for the transcription of genes that promote cancer cell growth and is implicated in 60-70% of human cancers. I hypothesize that combining RF diffusion and advanced computational modeling will effectively produce novel inhibitors capable of disrupting MYC function in cancer cells. By targeting the MYC-DNA interaction with specially designed peptides, this study seeks to advance cancer therapies and offer new strategies for combating the disease. A primary focus of this research is the MYC oncogene, a transcription factor that drives uncontrolled cell division by interacting with specific DNA sequences through its partner, MAX. This MYC-DNA interaction is critical for the transcription of genes that facilitate cancer cell growth and is implicated in 60-70% of human cancers. We hypothesize that combining RF diffusion with advanced computational modeling will effectively produce novel inhibitors capable of disrupting MYC function in cancer cells. The aim is to inhibit the MYC-DNA interaction using specially designed peptides, thereby advancing cancer therapies and offering new strategies for combating the disease.



OBJECTIVES

The primary objective of this research is to employ advanced computational tools to design and evaluate peptide candidates aimed at inhibiting the interaction between the MYC oncogene and DNA. To achieve this, the study will utilize RF diffusion, AlphaFold, PyMOL, and the RCSB Browser for the design and analysis of peptides. These computational tools will be instrumental in predicting peptide binding sites and interaction interfaces, which are crucial for effective inhibition of the MYC-DNA complex. The primary objective of this research is to utilize advanced computational tools to design and evaluate peptide candidates aimed at inhibiting the MYC-DNA interaction. The study will employ RF diffusion, AlphaFold, PyMOL, and the RCSB Browser for peptide design and analysis. These tools will help predict peptide binding sites and interaction interfaces, which are crucial for effective inhibition of the MYC-DNA complex.

Understanding the role of peptide design in blocking oncogene interactions is a key focus of this research. By designing peptides that target specific regions of the MYC-DNA interaction, the study aims to elucidate how these peptides can disrupt oncogenic activity. This involves investigating the structural and functional significance of peptide interactions with MYC and DNA, which could lead to the development of novel therapeutic agents. Understanding how peptide design can block oncogene interactions is a key focus. The study aims to elucidate how peptides targeting specific regions of the MYC-DNA interaction can disrupt oncogenic activity. This involves investigating the structural and functional significance of peptide interactions with MYC and DNA to develop novel therapeutic agents.

Accurately determining the positions of MYC, DNA, and the peptides within the complex is essential for the success of this research. The study will focus on evaluating the spatial arrangements and hotspot interactions between these components, ensuring that the peptides are effectively positioned to disrupt the MYC-DNA interaction. Determining the spatial positions of MYC, DNA, and the peptides within the complex is essential. The research will assess the spatial arrangements and hotspot interactions between these components to ensure effective peptide positioning to disrupt the MYC-DNA interaction.

Finally, the research will assess the therapeutic implications of the designed peptides. By analyzing their potential to interfere with MYC-DNA interactions, the study aims to advance cancer therapies and provide new strategies for improving treatment outcomes for cancer patients. Finally, the study will evaluate the therapeutic implications of the designed peptides. By analyzing their potential to interfere with MYC-DNA interactions, the research seeks to advance cancer therapies and provide new strategies for improving treatment outcomes.

MATERIALS & METHODS

For this research, several computational tools and databases were utilized to design and analyze peptide candidates aimed at inhibiting the MYC-DNA interaction. The tools employed include Google Colab, RF Diffusion, AlphaFold server, RCSB Browser, and PyMOL.

The peptide design and screening process began with the use of Google Colab and RF Diffusion. Python scripts were utilized within Google Colab to process protein sequences and structures. The PDB file for MYC was input to facilitate the design of peptide binders that could potentially block the MYC-DNA interaction. The RF Diffusion tool was used to predict the binding affinity and stability of these peptide candidates. Peptides with IPAE scores below 10 were selected, as these scores indicated an accurate prediction of the spatial interactions necessary for effective inhibition. The research employed several computational tools and databases for peptide design and analysis, including Google Colab, RF Diffusion, AlphaFold, RCSB Browser, and PyMOL.

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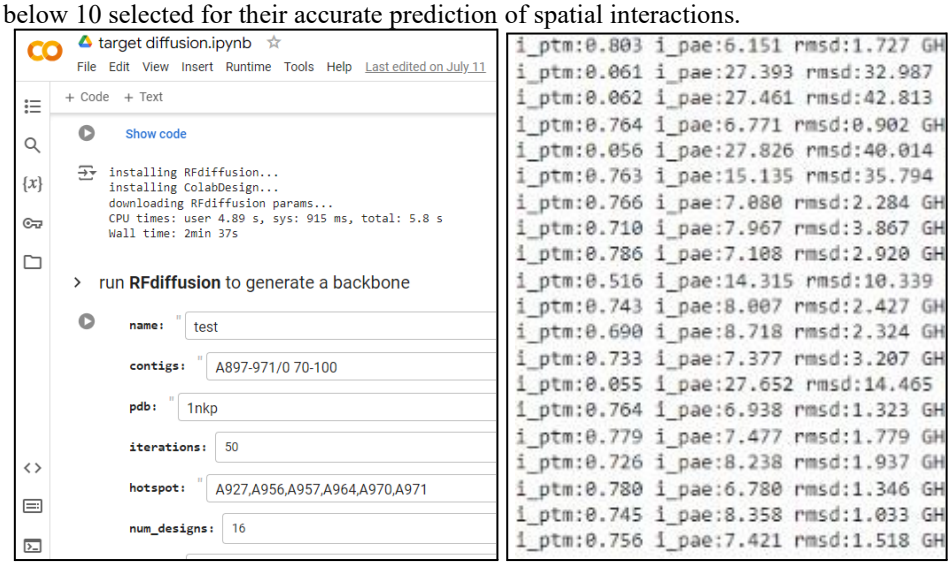
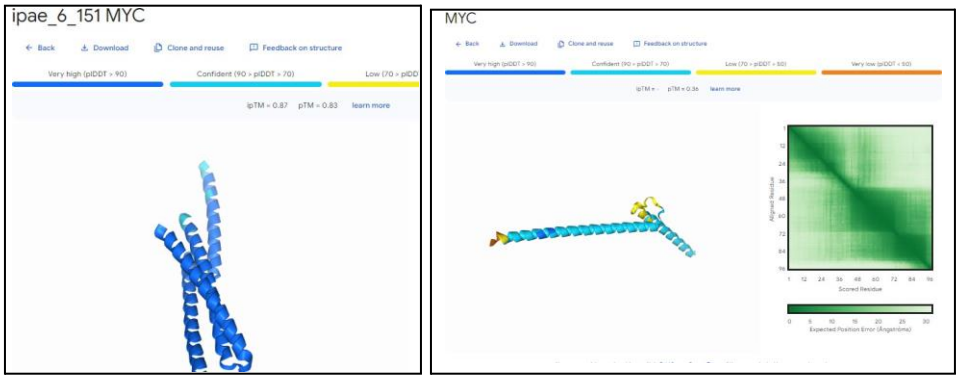
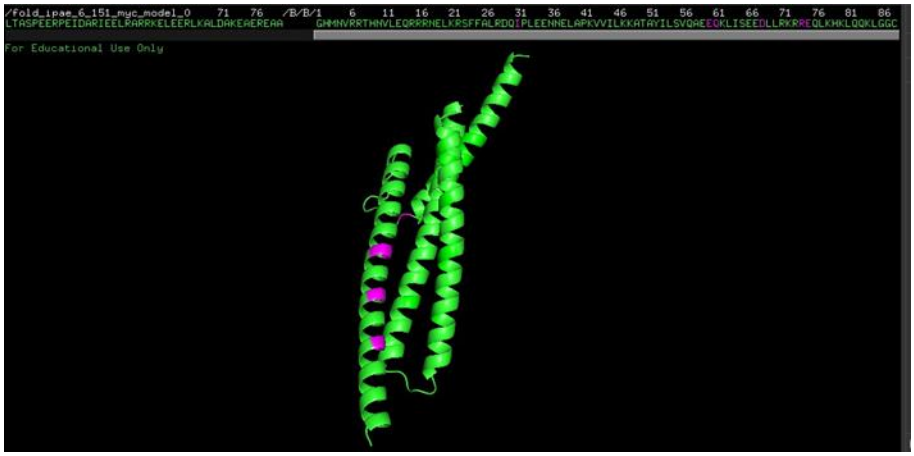
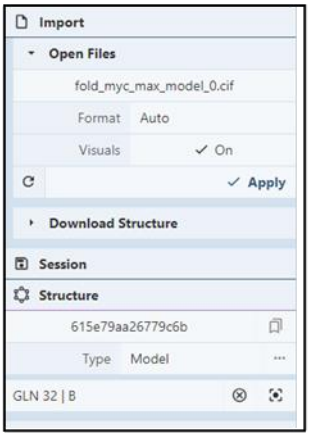


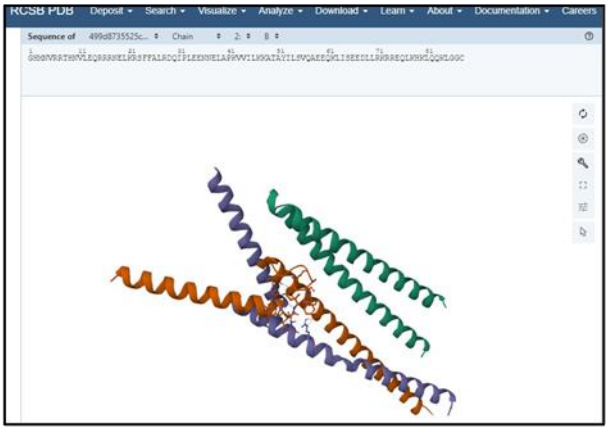
Protein structure prediction was conducted using the AlphaFold server. This tool was employed to predict the 3D structures of MYC in complex with the designed peptides. The aim was to gain insights into the binding regions and interaction interfaces of the peptides with MYC. For this purpose, combinations of MYC with each of the 30 designed peptides were analyzed, and the results were downloaded for further examination. Protein structure prediction was performed using the AlphaFold server, which predicted the 3D structures of MYC in complex with the designed peptides. This provided insights into the binding regions and interaction interfaces of the peptides with MYC. Analysis included combinations of MYC with each of the 30 designed peptides, and results were downloaded for further examination.



Structural analysis and visualization were performed using the RCSB Browser and PyMOL. High-resolution structures of MYC and DNA were retrieved from the RCSB PDB to validate the predictions made by AlphaFold. PyMOL was then used to visualize the interactions between MYC, DNA, and the peptides. Key hotspot sites were identified through PyMOL analysis, providing valuable information on how the peptides interact with MYC-DNA complexes. Structural analysis and visualization were carried out using the RCSB Browser and PyMOL. High-resolution structures of MYC and DNA from the RCSB PDB validated AlphaFold predictions. PyMOL was used to visualize interactions between MYC, DNA, and the peptides, identifying key hotspot sites.

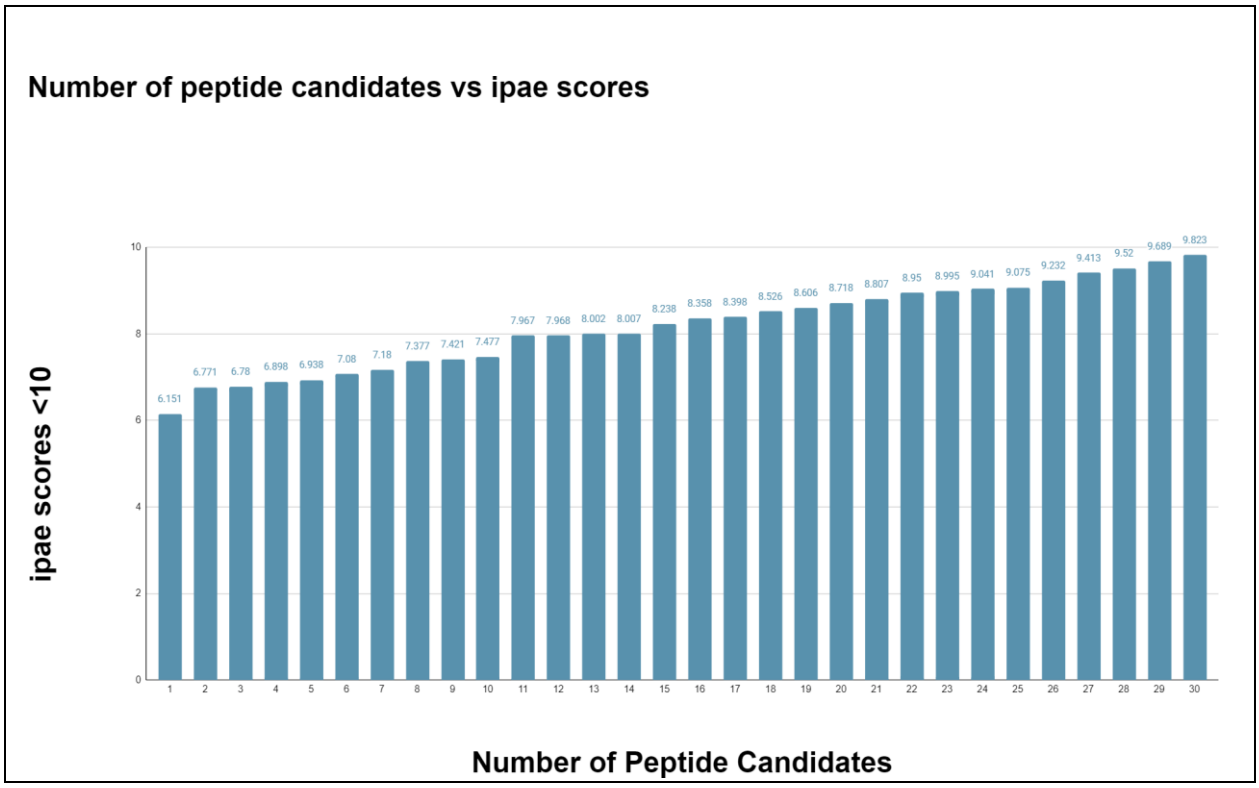






RESULTS

The research identified 30 potential peptide candidates designed to disrupt the MYC-DNA interaction. The IPAE values for these peptides ranged from 6.151 to 9.981, with all values falling below the threshold of 10. This range indicates that the predicted interactions between the peptides and the MYC-DNA complex are highly accurate. The research identified 30 potential peptide candidates designed to disrupt the MYC-DNA interaction. The IPAE values for these peptides ranged from 6.151 to 9.981, all below the threshold of 10, indicating highly accurate predicted interactions with the MYC-DNA complex.



The peptides were evaluated based on their predicted binding affinity and stability. The low IPAE values suggest that these peptides have a strong potential to bind effectively to the MYC-DNA interaction sites, disrupting the oncogenic activity of MYC. The precise identification of key hotspot sites where the peptides interact with MYC and DNA was achieved through the use of advanced computational modeling tools. The peptides were evaluated for their binding affinity and stability. The low IPAE values suggest strong potential for effective binding at MYC-DNA interaction sites, potentially disrupting MYC's oncogenic activity. Structural analysis confirmed that the peptides could interfere with the MYC-DNA complex, with key hotspot sites identified.

Structural analysis confirmed that the designed peptides could potentially interfere with the MYC-DNA complex. The peptides were visualized in the context of their interactions with MYC and DNA, and key hotspot sites were identified. These findings underscore the effectiveness of the peptide design and computational methods employed in predicting and validating potential inhibitors of MYC-driven oncogenesis.

Overall, the results highlight the promise of the designed peptides as candidates for further experimental validation, aiming to advance therapeutic strategies targeting MYC in cancer treatment. The findings highlight the effectiveness of the peptide design and computational methods in predicting and validating potential inhibitors of MYC-driven oncogenesis. The designed peptides show promise as candidates for further experimental validation.

DISCUSSION

This research successfully identified 30 peptide candidates with IPAE values ranging from 6.151 to 9.981, indicating their potential to effectively inhibit the MYC-DNA interaction. The low IPAE values achieved demonstrate the accuracy of the computational models used and the precision of the peptide design process. The peptides' ability to disrupt the MYC-DNA interaction highlights the effectiveness of integrating RF diffusion and advanced computational modeling in designing inhibitors for oncogene-targeted therapy. This research successfully identified 30 peptide candidates with IPAE values ranging from 6.151 to 9.981, reflecting their potential to effectively inhibit the MYC-DNA interaction. The low IPAE values demonstrate the accuracy of the computational models and the peptide design process. The peptides' ability to disrupt the MYC-DNA interaction underscores the effectiveness of integrating RF diffusion and advanced computational modeling in designing oncogene-targeted inhibitors.

The use of RF diffusion in conjunction with other computational tools, such as AlphaFold, PyMOL, and the RCSB Browser, enabled the precise prediction of peptide binding sites and interaction interfaces. These tools provided valuable insights into the structural dynamics of the MYC-DNA complex, allowing for the identification of key hotspot sites where peptides could potentially bind and exert their inhibitory effects. The successful design and validation of these peptides underscore the potential of computational approaches in developing targeted cancer therapies. The combination of RF diffusion with tools like AlphaFold, PyMOL, and the RCSB Browser allowed precise prediction of peptide binding sites and interaction interfaces. This approach provided valuable insights into the structural dynamics of the MYC-DNA complex and the identification of hotspot sites for peptide binding. The successful design and validation of these peptides highlight the potential of computational approaches in developing targeted cancer therapies.

The findings support the hypothesis that advanced computational modeling can produce effective inhibitors capable of disrupting MYC oncogene function. By utilizing these peptides, it may be possible to develop novel therapeutic strategies that specifically target MYC-driven oncogenesis. The results suggest that further experimental validation and in vivo studies are warranted to confirm the efficacy and safety of these peptide inhibitors in cancer treatment. The findings support the hypothesis that advanced computational modeling can generate effective inhibitors of MYC oncogene function. The peptides could lead to novel therapeutic strategies targeting MYC-driven oncogenesis, though further experimental validation studies are needed to confirm their efficacy and safety.

Overall, the research provides a promising avenue for advancing cancer therapies through the design of peptide inhibitors. Future work will focus on validating these findings through experimental methods and exploring their potential applications in clinical settings.

CONCLUSION

This research successfully identified 30 peptide candidates with high accuracy in disrupting the MYC-DNA interaction. By leveraging advanced computational tools, including RF diffusion, AlphaFold, and PyMOL, the design of peptides with precise binding interactions and pinpointing key hotspots within the MYC-DNA complex was possible. This research effectively identified 30 peptide candidates with high accuracy in disrupting the MYC-DNA interaction. By utilizing advanced computational tools such as RF diffusion, AlphaFold, and PyMOL, precise binding interactions and key hotspots within the MYC-DNA complex were pinpointed.

The effectiveness of these peptides, as indicated by their low IPAE values, underscores their potential for targeting critical interaction sites involved in MYC-driven oncogenesis. The confirmation of these interactions through structural analysis highlights the promising potential of these peptides for the development of novel cancer therapies. The peptides' effectiveness, indicated by

low IPAE values, highlights their potential for targeting critical interaction sites involved in MYC-driven oncogenesis. Structural analysis supports the promising potential of these peptides for developing novel cancer therapies.

Overall, the research advances the understanding of peptide-based inhibition strategies and offers a promising approach to developing targeted treatments aimed at inhibiting MYC-driven tumor progression. Future research will focus on experimental validation and exploring the clinical applicability of these peptide inhibitors to further enhance cancer treatment options. The study advances understanding of peptide-based inhibition strategies and offers a promising approach to developing targeted treatments for MYC-driven tumor progression. Future research will focus on experimental validation and exploring the clinical applicability of these peptide inhibitors.

FUTURE DIRECTIONS

The next steps in this research involve identifying the single peptide most suited for inhibiting the MYC-DNA interaction, based on binding affinity and stability. This peptide will be selected from the 30 identified candidates, focusing on the one with the highest efficacy in disrupting the MYC-DNA complex. The next phase involves identifying the most effective peptide for inhibiting the MYC-DNA interaction from the 30 candidates, based on binding affinity and stability. This peptide will undergo cell-based in vitro assays to evaluate its effectiveness in biological systems, including its impact on MYC-driven transcriptional activity and cancer cell proliferation.

Following the selection of the most promising peptide, cell-based in vitro assays will be conducted to assess its effectiveness in biological systems. These assays will evaluate the peptide's ability to inhibit MYC-driven transcriptional activity and its impact on cancer cell proliferation. Additionally, the peptide design will be refined based on the results of these in vitro experiments to enhance its efficacy and specificity. Following these in vitro tests, in vivo studies will be conducted to assess the peptide's biodistribution, pharmacokinetics, and safety. These studies are crucial for understanding the peptide's behavior in living organisms and its potential as a therapeutic agent.

Subsequently, in vivo studies will be performed to evaluate the biodistribution, pharmacokinetics, and overall safety of the selected peptide. These studies will provide critical information on how the peptide behaves in a living organism and its potential as a therapeutic agent.

By progressing through these stages, the research aims to validate the peptide's therapeutic potential and advance its development into a viable treatment option for MYC-driven cancers. Advancing through these stages seeks to validate the peptide's therapeutic potential and progress its development into a viable treatment option for MYC-driven cancers.

ACKNOWLEDGEMENT

The author gratefully acknowledges the opportunity to conduct this research at the Department of Oncology, Wayne State University, under the Biomedical Career Advancement Program (BCAP). The author expresses sincere gratitude to Dr. Benjamin Kidder support throughout the course of this project. Appreciation is also extended to the faculty, staff, and BCAP coordinators for their continuous support and for providing a stimulating research environment.

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