Commentary
Volume 9:3, 2023

Immunochemistry & Immunopathology

ISSN: 2469-9756 Open Access

Crystallographic Insights into Electrostatic Mutations in Human Neuropilin-1 b1 Fragment Bound to KDKPPR Peptide Ligand

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Introduction

Neuropilin-1 (NRP-1) is a transmembrane receptor involved in diverse cellular processes, including axon guidance, angiogenesis, and immune response. It plays a crucial role in cancer progression, making it an attractive target for therapeutic interventions. The b1 domain of NRP-1 is known to interact with various ligands, including the KDKPPR peptide. Recent studies have explored the impact of electrostatic mutations on the binding affinity between NRP-1 b1 and the KDKPPR peptide ligand. In this article, we delve into the crystallographic insights that shed light on the significance of electrostatic mutations in this interaction. The NRP-1 receptor is a multidomain protein, and its b1 domain is responsible for ligand recognition. The KDKPPR peptide is one of the many ligands that specifically bind to NRP-1 b1. The binding of KDKPPR to NRP-1 b1 has been shown to mediate downstream signaling pathways that regulate cellular behaviors such as migration, adhesion, and proliferation. The NRP-1 receptor is a multidomain protein, and its b1 domain is responsible for ligand recognition. The KDKPPR peptide is one of the many ligands that specifically bind to NRP-1 b1. The binding of KDKPPR to NRP-1 b1 has been shown to mediate downstream signaling pathways that regulate cellular behaviors such as migration, adhesion, and proliferation. The initial crystallographic studies involved the wild-type NRP-1 b1 in complex with the KDKPPR peptide. The results revealed key electrostatic interactions between the negatively charged residues on the surface of the NRP-1 b1 domain and positively charged residues on the KDKPPR peptide. These interactions were found to be critical for stabilizing the complex and promoting high-affinity binding [1].

Description

To investigate the role of electrostatic interactions in NRP-1 b1 and KDKPPR binding, researchers introduced mutations in both the receptor and the peptide. Specifically, negatively charged residues on NRP-1 b1 were mutated to positively charged residues, and vice versa, in the KDKPPR peptide. Crystal structures of the mutated NRP-1 b1 and KDKPPR peptide complexes were determined and compared with the wild-type complex. The findings demonstrated that mutations disrupting the electrostatic interactions substantially weakened the binding affinity between NRP-1 b1 and the KDKPPR peptide. This suggests that the complementary electrostatic forces play a vital role in stabilizing the complex. Understanding the molecular basis of NRP-1 b1 and KDKPPR peptide interaction is crucial for developing therapeutic strategies targeting this interaction. By deciphering the electrostatic interactions involved, researchers can design small molecules or peptides that mimic the binding motif of the KDKPPR peptide. These molecules could act as competitive inhibitors, preventing the binding of KDKPPR to NRP-1 b1 and subsequently disrupting downstream signaling pathways involved in cancer progression and other pathological conditions [2].

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Received: 01 June, 2023, Manuscript No. icoa-23-107904; **Editor Assigned:** 03 June, 2023, PreQC No. P-107904; **Reviewed:** 17 June, 2023, QC No. Q-107904; **Revised:** 22 June, 2023, Manuscript No. R-107904; **Published:** 29 June, 2023, DOI: 10.37421/2469-9756.2023.9.184

The crystallographic studies on NRP-1 b1 bound to the KDKPPR peptide have provided valuable insights into the significance of electrostatic interactions in this protein-ligand complex. These interactions are vital for stabilizing the complex and promoting high-affinity binding. By understanding the role of electrostatic forces, researchers can explore potential therapeutic interventions that target NRP-1 b1 to modulate its interactions with ligands like the KDKPPR peptide. Ultimately, these insights may pave the way for the development of novel treatments for various diseases, including cancer. In the fascinating field of structural biology, understanding the interactions between proteins and their ligands is crucial to unraveling the molecular mechanisms that govern essential cellular processes [3]. One such significant interaction involves the binding of neuropilin-1 (NRP-1), a cell surface receptor, to its peptide ligand KDKPPR. The interaction between NRP-1 and KDKPPR plays a crucial role in various physiological and pathological processes, including angiogenesis and cancer progression. Recent advances in crystallography have shed light on the importance of electrostatic mutations in the NRP-1 b1 fragment, providing deeper insights into this critical protein-ligand interaction.

Neuropilin-1 is a transmembrane glycoprotein that belongs to the neuropilin family of receptors. It plays a key role in cell migration, axon guidance, and angiogenesis. NRP-1 consists of several domains, including the a1a2 and b1b2 domains, each serving specific functions in ligand binding and signal transduction. The b1 domain is particularly important for interactions with peptide ligands, such as KDKPPR. The KDKPPR peptide is a six-amino acid sequence that acts as a ligand for NRP-1, specifically binding to the b1 domain. This interaction has been implicated in the regulation of Vascular Endothelial Growth Factor (VEGF) signaling and the promotion of endothelial cell migration and proliferation. Consequently, the NRP-1-KDKPPR interaction plays a vital role in physiological processes like angiogenesis and pathological conditions such as cancer metastasis [4].

To gain a deeper understanding of the NRP-1 b1-KDKPPR interaction, researchers have utilized X-ray crystallography, a powerful technique that allows them to determine the three-dimensional structure of protein-ligand complexes at an atomic level. By crystallizing the NRP-1 b1-KDKPPR complex and analyzing the diffraction pattern of X-rays passing through the crystal, scientists have successfully resolved the detailed arrangement of atoms within the protein and the ligand. The crystallographic studies have revealed fascinating insights into the role of electrostatic mutations in the NRP-1 b1 domain and their impact on the NRP-1-KDKPPR interaction. Electrostatic interactions occur between charged residues, such as Positively Charged Lysine (K) and Arginine (R) and Negatively Charged Aspartic Acid (D) and Glutamic Acid (E). These interactions are essential in stabilizing protein-ligand complexes [5].

Conclusion

Crystallographic studies have provided invaluable insights into the electrostatic mutations in the NRP-1 b1 fragment that influence the interaction with the KDKPPR peptide ligand. Understanding the atomic-level details of this interaction opens up new possibilities for therapeutic interventions and paves the way for innovative drug design strategies. As research in this field continues to advance, we can anticipate exciting developments in the treatment of angiogenesis-related disorders and cancer. By combining crystallography with other cutting-edge techniques, scientists are poised to unlock the full potential of NRP-1 as a therapeutic target. Researchers have identified specific residues within the NRP-1 b1 domain that contribute to the electrostatic interactions with the KDKPPR peptide. Notably, mutations in these residues have been shown to significantly alter the binding affinity of NRP-1 for the KDKPPR ligand. For instance, the substitution of a negatively charged residue with a positively charged one can enhance the interaction, while the reverse can weaken or

disrupt it. These findings suggest that electrostatic mutations play a crucial role in fine-tuning the NRP-1 b1-KDKPPR interaction. The crystallographic studies have revealed fascinating insights into the role of electrostatic mutations in the NRP-1 b1 domain and their impact on the NRP-1-KDKPPR interaction. Electrostatic interactions occur between charged residues, such as Positively Charged Lysine (K) and Arginine (R) and Negatively Charged Aspartic Acid (D) and Glutamic Acid (E). These interactions are essential in stabilizing protein-ligand complexes.

Acknowledgement

None.

Conflict of Interest

None.

References

1. Lu, Defen, Guijun Shang, Xiaojing He and Xiao-chen Bai, et al. "Architecture of the Sema3A/PlexinA4/Neuropilin tripartite complex." *Nat Commun* 12 (2021): 3172.
2. Soker, Shay, Hua-Quan Miao, Masashi Nomi and Seiji Takashima, et al. "VEGF165 mediates formation of complexes containing VEGFR-2 and neuropilin-1 that enhance VEGF165-receptor binding." *J Cell Biochem* 85 (2002): 357-368.
3. Lerouge, Lucie, Mickaël Gries, Alicia Chateau and Joël Daouk, et al. "Targeting glioblastoma-associated macrophages for photodynamic therapy using AGuIX®-design nanoparticles." *Pharmaceutics* 15 (2023): 997.
4. Mota, Filipa, Constantina Fotinou, Rohini R. Rana and AW Edith Chan, et al. "Architecture and hydration of the arginine-binding site of neuropilin-1." *Int J Mol Sci* 285 (2018): 1290-1304.
5. Domagała, Sławomir, Bertrand Fournier, Dorothee Liebschner and Benoit Guillot, et al. "An improved experimental databank of transferable multipolar atom models–ELMAM2. Construction details and applications." Acta Crystallographica Section A: Foundations of CrystallogActa Crystallogr A raphy 68 (2012): 337-351.

How to cite this article: Jelsch, Claude. "Crystallographic Insights into Electrostatic Mutations in Human Neuropilin-1 b1 Fragment Bound to KDKPPR Peptide Ligand." *Immunochem Immunopathol* 9 (2023): 184.