Computational Simulations of CD19-targeted Chimeric Antigen Receptor (CAR) T Cells Therapy in Autoimmune Disease

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ABSTRACT Chimeric Antigen Receptor (CAR) T-cell therapy involves genetically engineering a patient's T cells to enhance their ability to target and eliminate specific cells in the body. This approach has emerged as a promising treatment strategy for various cancers, particularly B-cell malignancies. In addition to its application in cancer, CAR T-cell therapy can potentially treat autoimmune diseases where autoreactive B cells are implicated. Severe Myositis and Systemic Sclerosis are autoimmune diseases that affect different body parts, with B cells playing a significant role in triggering and maintaining autoimmunity. CD19, a surface receptor in the B cells, presents an attractive target for CAR T-cells to eliminate these autoreactive B cells to the specific binding site on the surface of CD19 receptors, facilitating effective targeting by CAR T-cells. The structure of the CD19 receptors was predicted using AlphaFold 3, a machine learning-based method. The P2Rank web server was employed to identify binding sites on the surface of receptors. The single-chain variable fragment (ScFv) was retrieved from the Protein Data Bank (PDB), a global repository of 3D structures of biological macromolecules. The HDOCK software was effectively utilized to simulate docking interactions between antibodies and CD19 receptors. Results showed that receptor complexes formed strong interactions at the binding site predicted by the graph neural network, confirming the docked results. Antibodies were selected based on visual inspection, binding energy calculation, and hydrogen bond analysis. This research will provide valuable advancements and insights into creating more effective CAR T-cells targeting autoimmune diseases, such as severe myositis and systemic sclerosis.

1. INTRODUCTION

Chimeric Antigen Receptor (CAR) T-cell therapy represents a novel approach in immunotherapy, involving the genetic modification of a patient's T-cells to express synthetic receptors capable of recognizing specific antigens on target cells. Through this process, T-cells are engineered to identify and attack cancer cells, particularly those associated with blood malignancies such as leukemia and lymphoma. The core mechanism relies on the introduction of CARs, which combine the specificity of an antibody with the cytotoxic potential of T-cells, thereby directing immune responses against malignant cells. Although initially designed for hematological cancers, ongoing investigation is evaluating the application of CAR T-cell therapy to solid tumors and autoimmune diseases. By adapting CARs to selectively target autoreactive immune cells, researchers aim to address the pathological immune responses characteristic of conditions like rheumatoid arthritis and lupus, potentially offering new strategies for disease management.

Fundamentally, CAR T-cell therapy operates by extracting a patient's own T-cells and genetically modifying them to express chimeric antigen receptors, which are synthetic proteins engineered to recognize and bind to surface antigens present on diseased cells. This engineered receptor allows T-cells to detect malignant targets independently of traditional antigen presentation pathways, enabling them to locate and eradicate cancer cells that may otherwise evade immune detection (Mohanty et al., 2019). CARs themselves are composed of several integrated domains: an antigen-binding region, a hinge, a transmembrane domain, and intracellular signaling elements, each essential for promoting targeted immune responses while striving to limit adverse effects (Sterner & Sterner, 2021). In clinical practice, the approach has primarily targeted blood cancers such as leukemia and lymphoma, where surface antigens like CD19 are readily accessible for CAR-mediated recognition and destruction. The therapy's methodology, while promising for hematological malignancies, establishes the foundation for ongoing exploration in other disease settings, including solid tumors and autoimmune conditions.

In addition to blood malignancies, CAR T-cell therapy is currently being investigated for its applicability to solid tumors and

autoimmune diseases, where immune targets are distinct and present unique challenges. For solid tumors, the identification of appropriate antigens has enabled preclinical and early clinical studies in breast cancer and other malignancies, yet obstacles such as limited T-cell infiltration and immunosuppressive tumor microenvironments persist and require further optimization of CAR design strategies (Yang et al., 2022). In the context of autoimmune disorders, researchers are engineering CAR T-cells to selectively eliminate autoreactive immune cells, including B-cell clones and autoreactive T-cells, which are responsible for attacking healthy tissue. This approach has sparked interest in diseases such as pemphigus vulgaris, type 1 diabetes, and multiple sclerosis, where the elimination or regulation of autoreactive cells offers potential for long-lasting disease remission (Zmievskaya et al., 2021). Ultimately, the ongoing adaptation of CAR technology to these new domains seeks to harness precise immune targeting while managing safety and efficacy concerns inherent to these complex disease settings.

Moreover, CAR T-cell therapy holds distinct promise for reprogramming the immune system in autoimmune diseases such as rheumatoid arthritis and lupus by directly targeting and eliminating the cells responsible for aberrant immune activity. Unlike classic immunosuppressive strategies, engineered CAR T-cells can precisely identify autoreactive B lymphocytes or other immune cells contributing to the self-directed immune response, thereby aiming to restore immunological balance with minimal impact on protective immunity (Liu et al., 2024). Clinical investigations in conditions like systemic lupus erythematosus have yielded rapid and sustained remission following anti-CD19 CAR T-cell administration, demonstrating a comprehensive resetting of the B-cell compartment and a pronounced decrease in disease-driving autoantibodies (Blache et al., 2023). Furthermore, novel approaches including CAR-modified regulatory T cells and chimeric autoantibody receptor T cells are being developed to induce targeted immune tolerance, reducing the risk of global immunosuppression by sparing healthy immune components. Such strategies illustrate the therapeutic potential of CAR T-cell therapy to correct underlying immune misdirection in autoimmune pathologies while potentially avoiding the limitations of conventional treatments.

Early preclinical studies have laid the groundwork for understanding how CAR T-cells may be harnessed to treat autoimmune diseases by eliminating autoreactive immune populations. Experimental models in mice have been instrumental in evaluating CD19-targeted CAR T-cells, which were found to deplete pathogenic B-cell and plasma cell reservoirs and disrupt established pools of disease-driving autoantibodies, thereby suggesting the potential for substantial immune system reset (Schett et al., 2023). These findings encouraged further investigations into the mechanisms and durability of remission, along with assessments of safety profiles in animal systems prior to clinical translation (Li et al., 2024). Nevertheless, the application of CAR T-cells in autoimmune contexts remains experimental; both preclinical models and early clinical studies emphasize the ongoing necessity for long-term observation to address concerns such as late-onset toxicities and relapse. As such, the current stage is characterized by careful monitoring and iterative refinement, highlighting both the promise and the outstanding challenges of adapting CAR T-cell therapy beyond oncology.

Within the immune system, CD19 plays a pivotal role as a surface glycoprotein on B cells, facilitating their maturation, activation, and participation in immune responses through signal transduction. Serving as both a developmental marker and a functional modulator, CD19 enables the identification and classification of B-cell populations across different stages, which is instrumental for targeted therapies. In CAR T-cell therapy, CD19 is the most widely used target antigen, permitting the selective elimination of malignant B cells in hematologic cancers such as acute lymphoblastic leukemia and diffuse large B-cell lymphoma (Anagnostou et al., 2020). This specificity allows engineered T-cells to engage and destroy both cells with high and dim levels of CD19 expression, addressing tumor heterogeneity while minimizing off-target effects (Pillai et al., 2019). In addition, emerging research demonstrates that targeting CD19 can also aid in the removal of autoreactive B cells implicated in autoimmune disorders, potentially achieving immune reset and disease amelioration within experimental and clinical settings.

In CAR T-cell design, the use of single-chain variable fragments (ScFv) retrieved from the Protein Data Bank (PDB) has contributed greatly to therapeutic specificity by providing CARs with robust antigen recognition capabilities. These ScFv domains, derived from high-affinity antibodies, serve as the extracellular targeting regions that bind directly to surface antigens such as CD19 on disease-associated B cells. Figure 1 illustrates the molecular interactions underlying these therapies: panel (a) depicts an antigen-presenting cell (APC) activating a T-cell receptor, culminating in downstream B-cell activation and release of autoantibodies, while panel (b) demonstrates how engineered CAR T-cells employ their ScFv domain to bind B cells and induce apoptosis, effectively reducing autoreactive populations. The inclusion of well-characterized ScFv fragments from structural databases has advanced the rational design of CARs, optimizing target selectivity and reducing off-target activity (Zhang et al., 2020). Consequently, these molecular tools are critical in translating structural insights into safe and effective cell-based immunotherapies.

In parallel with advances in molecular engineering, recent breakthroughs in computational biology have greatly impacted the field of immunotherapy through innovations such as AlphaFold 3, molecular docking, and the characterization of immune cell markers like CD81. AlphaFold 3, a deep-learning system, provides highly accurate three-dimensional predictions for proteins and a range of biomolecular complexes, greatly facilitating the structural analysis of antigens, receptors, and other molecular targets integral to drug discovery and mechanistic research (Abramson et al., 2024). This capability improves identification of binding sites and aids in the rational design of therapies by modeling complex interactions relevant to immune modulation (Krokidis et al., 2025). Complementing structure prediction, molecular docking simulations enable researchers to forecast how small molecules interact with specific protein targets, critical for screening new candidate therapies and optimizing drug binding efficacy at the atomic level. Finally, CD81, a surface protein abundantly expressed on immune cells, plays a role in cell signaling, adhesion, and immune activation, further serving as a focus in the study of disease mechanisms and therapeutic intervention.

2. METHOD

The amino acid sequence of the CD19 protein was retrieved from the UniProt database, a comprehensive resource providing detailed information on protein sequences and functional annotations. To obtain the 3D structure of the CD19 receptor, the AlphaFold 3 model was used, a deep-learning system that predicts protein structures from amino acid sequences. The downloaded

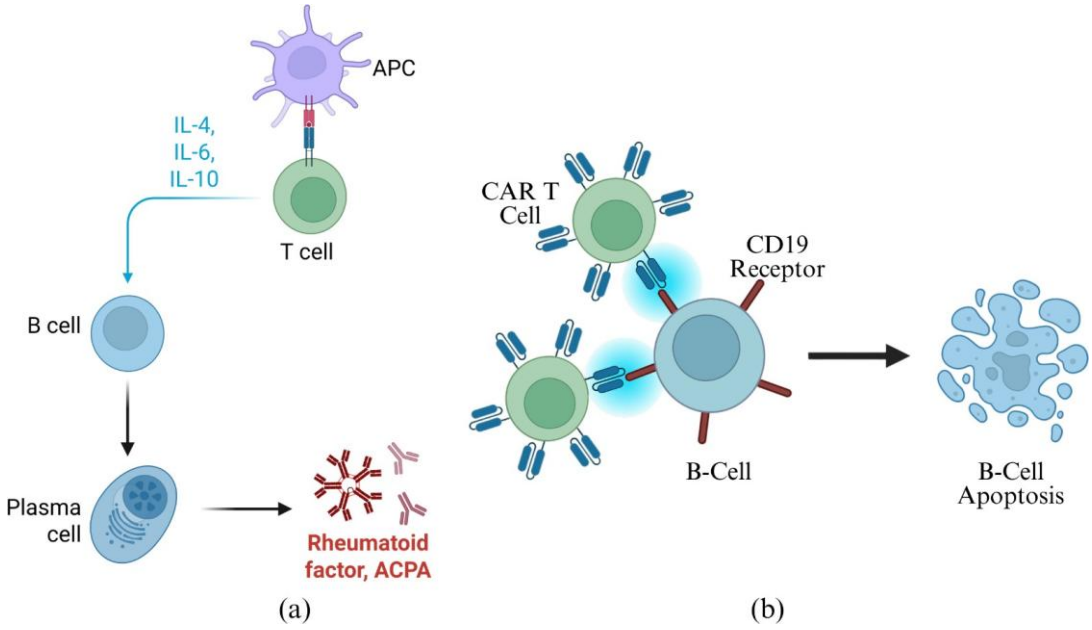

Fig. 1. Mechanism of autoimmune B-cell activation and CAR T-cell–mediated targeting of CD19 receptors. (a) Illustration of the autoimmune pathway in which antigen-presenting cells (APCs) activate T cells, leading to the release of cytokines such as IL-4, IL-6, and IL-10. These cytokines stimulate B cells to differentiate into plasma cells that produce autoantibodies, including rheumatoid factor and anti-citrullinated protein antibodies (ACPA), contributing to autoimmune disease progression. (b) Schematic representation of CD19-targeted CAR T-cell therapy. Engineered CAR T cells recognize and bind to CD19 receptors expressed on B cells, leading to targeted immune attack and induction of B-cell apoptosis.

CD19 receptor structure was then truncated to remove unnecessary features such as swirls. For binding site prediction, the ScanNet tool was employed to identify regions on the protein where ligands or other molecules could bind, potentially influencing the receptor's function. The single-chain variable fragment (ScFv) was retrieved from the Protein Data Bank (PDB), a global repository of 3D structures of biological macromolecules. To predict how the CD19 receptor and single-chain variable fragment (ScFv) interact, molecular docking simulations were performed using HDOCK software, a computational method that predicts the preferred orientation and interaction of the two molecules when binding occurs. Finally, binding energy calculations were carried out using PRODIGY, which estimates the strength and stability of the protein-ligand interaction by determining the energy required for binding.

3. RESULTS

Surface properties of CD19 receptors

ScanNet was a computational tool used to predict the binding sites on a protein's surface by analyzing its 3D structure. The tool identified potential regions where ligands or antibodies might bind based on structural features and electrostatic properties. By using ScanNet, the most likely binding sites for drug molecules, antibodies, or other interacting partners were identified, aiding in the design of therapeutic interventions or understanding molecular interactions. In the context of CD19, ScanNet was used to predict the regions where an antibody would most effectively bind, helping to guide the selection of optimal therapeutic candidates. Figure 2 (a) shows the electrostatic surface potential (ESP) charge, which visualizes the distribution of positive and negative charges on the protein's surface, influencing molecular interactions. The electrostatic surface potential (ESP) charge represented the distribution of electric charge on the surface of a molecule, typically a protein, based on its atomic composition and the environment. The ESP helped visualize areas of positive or negative charge on the molecular surface, which influenced how the molecule interacted with other charged entities (like antibodies or single-chain variable fragments (ScFv)). This was crucial for understanding how proteins might attract or repel each other based on their charge distribution, providing insights into the protein's binding behavior and interaction preferences. Figure 2 (b) depicts the predicted binding site identified by Scannet.

Figure 2 shows two key elements in protein interaction analysis. Panel (a) displayed the electrostatic surface potential (ESP) charge, which mapped the distribution of positive and negative charges on the protein's surface, crucial for understanding how the protein interacted with other charged molecules. Panel (b) presented the predicted binding site identified by ScanNet, a tool that analyzed the protein's 3D structure to pinpoint regions where ligands, single-chain variable fragments (ScFv), or antibodies might bind. Together, these visualizations helped identify potential interaction sites, guiding therapeutic design and molecular studies.

Molecular Docking simulations

For the molecular docking simulations, HDOCK was used, a tool that predicted the preferred orientation and interaction of two molecules, such as a protein and a ligand (in this case, the CD19 receptor and an antibody).

Molecular docking is a computational technique used to predict how two molecules, like a protein and a ligand, interact and bind to each other. It helped determine the optimal binding orientation and the strength of the interaction, providing valuable insights for drug design and molecular interactions. In Figure 3, the structures of the CD19 receptor and single-chain variable fragment (ScFv) antibody were selected based on the predicted binding site obtained from ScanNet, and the antibody was shown to bind to this site in the molecular docking simulation.

Figure 3 shows the molecular docking structures of CD19 and antibodies using HDOCK, with the antibody binding to the predicted binding site on CD19. The predicted binding site was obtained from ScanNet, a computational tool that analyzed the 3D structure of the protein to identify regions likely to interact with ligands, single-chain variable fragments (ScFv), or antibodies. This docking simulation helped visualize how the antibody interacted with the CD19 receptor at the identified binding site.

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Antibody Selection Criteria: The following antibody steps were used to select the most appropriate antibody: (a) Visual inspection: ChimeraX software, the antibody should bind to the predicted binding site shown in Figure 2b. ChimeraX was used to visualize the 3D structures of molecules, including proteins and antibodies. By inspecting the docking results, it was ensured that the antibody bound to the predicted binding site of the CD19 receptor, as shown in Figure 2b. This step helped confirm that the antibody interacted with the correct region of the target protein. Based on the visual inspection, antibodies 1B4J, 1F8T, and 4A6Y were selected (b) Binding energy: PRODIGY calculated the binding energy of the antibody–CD19–single-chain variable fragment (ScFv) complex, where a more negative binding energy indicated a stronger, more stable interaction. A lower (more negative) binding energy suggested that the antibody bound more effectively to CD19, making it a better candidate for further studies or therapeutic applications. Among the above three antibodies, 4A6Y showed the strongest binding energy of -16.6 kcal/mol.

4. DISCUSSION: CD19 PROTEIN SEQUENCE RETRIEVAL AND STRUCTURAL PREDICTION

The amino acid sequence of the CD19 protein was first obtained from the UniProt database, providing the foundational data necessary for in-depth structural and functional analyses. This sequence was then used as input for AlphaFold 3, a deep learning framework that generates highly accurate three-dimensional (3D) protein structure predictions essential for immunological research (Jann et al., 2025). Accurate structural data from AlphaFold 3 not only addresses the scarcity of experimentally determined structures, but also allows researchers to examine conformational epitopes and potential interaction interfaces more thoroughly (Jiang et al., 2024). The robustness of AlphaFold 3 output enables detailed characterization of antigenic regions, which is particularly critical for rational therapeutic design targeting CD19. Incorporating these computational approaches streamlines the initial stages of drug discovery by rapidly providing structural insights that inform subsequent experimental and engineering efforts.

Structural Preparation and Binding Site Prediction

After obtaining the initial AlphaFold 3-predicted structure, the CD19 receptor underwent structural refinement by truncating extraneous regions, including flexible swirls, to produce a streamlined model more appropriate for interaction analysis. This structural preparation removes segments that might otherwise obscure or distort critical surface features relevant for binding investigations. Subsequently, ScanNet was applied to the refined 3D structure to systematically predict potential protein-protein and protein-antibody binding sites, utilizing its geometric deep learning capabilities to learn from the spatiochemical environments of neighboring residues (Tubiana et al., 2022). The adoption of ScanNet facilitates the identification of functional regions, bridging the gap between abundant high-quality structural data from frameworks like AlphaFold and the paucity of experimentally annotated binding sites (Tubiana et al., 2022). Through this combined approach, the resulting CD19 model becomes better suited for downstream tasks such as molecular docking and therapeutic antibody design, ensuring that interaction studies are based on accurate and functionally relevant protein representations.

ScFv Structure Acquisition and Docking Methodology

To advance the molecular analysis of CD19 interactions, the structure of a single-chain variable fragment (ScFv) was retrieved from the Protein Data Bank (PDB), leveraging its repository of experimentally resolved antibody configurations. This selection was strategically informed by previous computational modeling that demonstrates the crucial role of ScFv structure in achieving high affinity and specificity toward CD19 targets, exemplified by the H8_L1 variant, which exhibits notable binding properties and stability in silico (Krishnan et al., 2025). Using the refined CD19 receptor model, molecular docking simulations were conducted with HDOCK, a platform known for effective protein–protein docking irrespective of the biological context, allowing comprehensive exploration of possible interaction conformations (Krishnan et al., 2025). The rationale behind employing both the PDB for structural sourcing and HDOCK for simulation lies in their combined ability to ensure both structural fidelity and predictive accuracy in modeling ScFv–CD19 complexes, thus supporting reliable therapeutic design. These systematic computational approaches provide a robust platform for analyzing antigen–binder interactions prior to experimental validation, establishing a foundation for further optimization and screening of novel antibody candidates (He et al., 2023).

Binding Energy Calculation and Interaction Analysis

Furthermore, quantifying the interaction strength between the CD19 receptor and ScFv requires evaluating their binding energy, a parameter directly linked to therapeutic efficacy. Utilizing PRODIGY, a web-based tool for predicting binding affinities from structural models, the binding energy of the CD19–ScFv

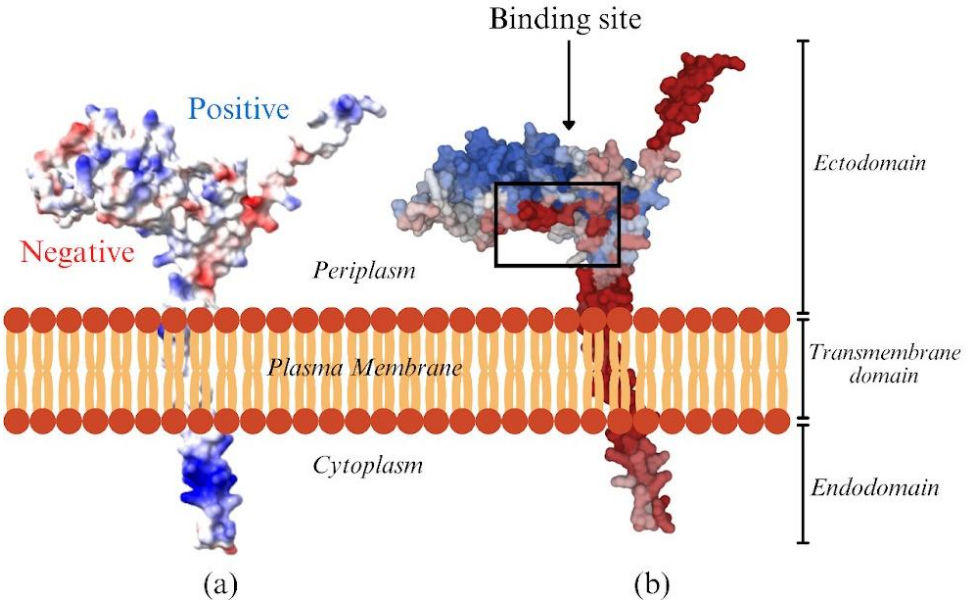

Fig. 2. Electrostatic surface representation and membrane localization of the target protein. (a) Electrostatic potential map of the protein showing positively charged regions (blue) and negatively charged regions (red), highlighting charge distribution across the structure. (b) Structural orientation of the protein relative to the plasma membrane, illustrating the extracellular ectodomain, transmembrane region, and intracellular endodomain. The predicted ligand binding site is indicated by the boxed region within the ectodomain. The lipid bilayer represents the plasma membrane separating the periplasmic/extracellular space from the cytoplasm.

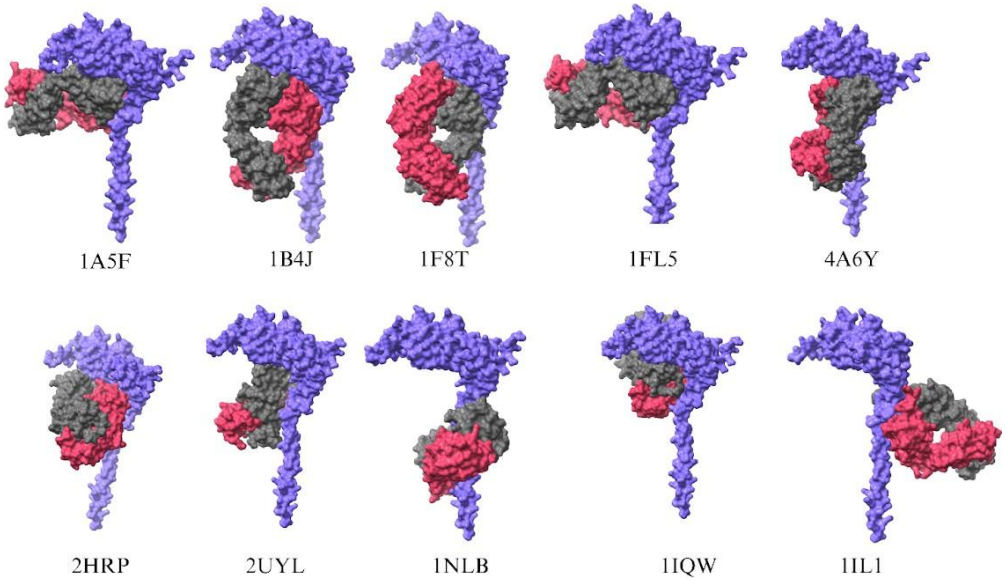

Fig. 3. Structural comparison of selected antibodies targeting the receptor binding region. Three-dimensional surface representations of ten antibodies obtained from the Protein Data Bank (PDB IDs: 1A5F, 1B4J, 1F8T, 1FL5, 4A6Y, 2HRP, 2UYL, 1NLB, 1IQW, and 1IL1). The structures are shown in surface representation to highlight their binding interfaces. The heavy chain is shown in purple, the light chain in gray, and the antigen-binding regions (complementarity determining regions, CDRs) are highlighted in red. These antibodies were analyzed to identify suitable candidates for interaction with the target receptor and to evaluate their structural compatibility with the predicted binding site.

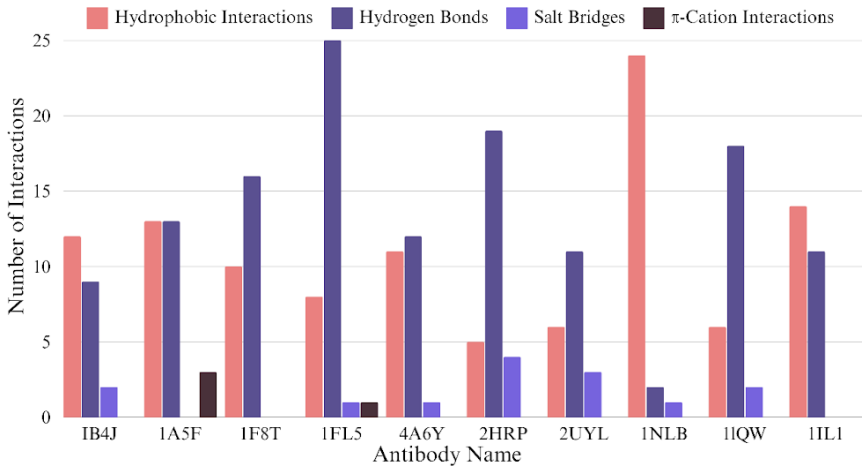

Fig. 4. Number of interactions between CD19–single-chain variable fragment (ScFv). PLIP Figure 4 illustrates the number of interactions between CD19 and the antibody, as analyzed using PLIP (Protein-Ligand Interaction Profiler). PLIP was a tool that identified and quantified various types of molecular interactions, such as hydrogen bonds, hydrophobic interactions, salt bridges, and pi-cation interactions between the protein and the antibody. This figure highlights the specific interactions that contribute to the binding affinity and stability of the CD19–single-chain variable fragment (ScFv) complex.

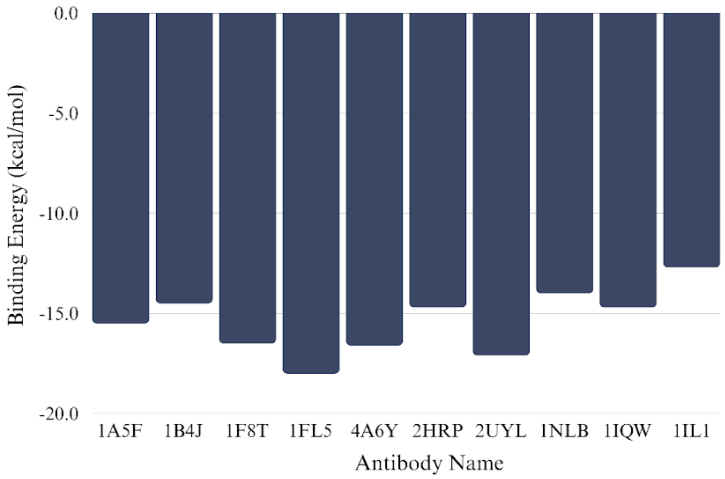

Fig. 5. Binding energy comparison of candidate antibodies. Bar graph showing the predicted binding energies (kcal/mol) of ten antibodies (1A5F, 1B4J, 1F8T, 1FL5, 4A6Y, 2HRP, 2UYL, 1NLB, 1IQW, and 1IL1) after molecular docking with the target protein. The x-axis represents the antibody PDB IDs, while the y-axis indicates the calculated binding energy in kcal/mol. More negative binding energy values correspond to stronger predicted binding affinity between the antibody and the target protein. Among the evaluated antibodies, structures such as 1FL5 and 2UYL exhibit relatively stronger binding interactions, suggesting their potential suitability for further analysis and optimization.

complex was calculated based on the input generated from prior docking simulations. This computational assessment estimates the thermodynamic stability of the antigen–antibody assembly, providing a predictive measure for how likely the interaction is to persist under physiological conditions (Jann et al., 2025). Importantly, interpreting these binding energy values in the context of immunotherapy helps differentiate candidate antibodies with favorable binding characteristics, while also guiding the subsequent design of molecules tailored for optimal affinity. As a result, integrating methods such as PRODIGY further enhances analytical pipelines established by deep learning-based structural modeling and binding site prediction, ensuring the prioritization of biologically relevant therapeutic candidates (Tubiana et al., 2022).

Current Treatments for Autoimmune Diseases

Amid advances in protein characterization and molecular docking, the prevailing management options for autoimmune diseases remain anchored in the administration of immunosuppressive drugs and biologics. These therapies, although capable of reducing pathological immune responses, often expose patients to recurring infections, organ toxicity, and impaired immune surveillance, revealing substantial safety and efficacy challenges for long-term disease management (Schett et al., 2023). Furthermore, conventional immunosuppressive regimens do not selectively target autoreactive immune cells, frequently resulting in generalized immunosuppression that fails to address the fundamental pathogenic mechanisms driving autoimmunity. To compound these shortcomings, treatment durability is frequently undermined by adverse events, secondary loss of response, or the need for continuous therapy, leaving a portion of patients refractory or inadequately controlled (Schett et al., 2023). Given these substantial drawbacks, there is mounting clinical interest in developing more precise strategies that disrupt disease-promoting pathways while minimizing collateral risk, thereby emphasizing the demand for therapies anchored in targeted molecular insights.

CAR T-cell Therapy Targeting CD19:

In light of the limitations faced by current therapies, CD19-targeted chimeric antigen receptor (CAR) T-cell therapy offers a novel strategy for addressing underlying immune dysregulation in autoimmune diseases. By engineering patient-derived T cells to express a receptor specific for CD19, this approach achieves rapid and profound depletion of pathogenic B cells responsible for autoantibody production and disease persistence (Schett et al., 2024). Notably, patients with refractory conditions such as systemic lupus erythematosus, idiopathic inflammatory myositis, and systemic sclerosis have exhibited either complete remission or marked improvement following CAR T-cell administration, accompanied by restoration of immune homeostasis and drug-free remission, even after B-cell reconstitution with nontargeted, naive cells (Müller et al., 2024). Clinical studies also demonstrate that safety risks, including cytokine release syndrome, are consistently mild, with an absence of immune effector cell–associated neurotoxicity limiting concerns regarding adverse immunologic effects. Consequently, CAR T-cell therapy targeting CD19 demonstrates considerable promise as a targeted intervention aiming to eliminate autoreactive B cells and achieve sustained disease control through immune system reset.

5. LIMITATIONS AND FUTURE DIRECTIONS

Despite the compelling advancements offered by computational modeling and CAR T-cell developments, there remains a critical necessity for rigorous in vitro and in vivo experimental validation to confirm the therapeutic potential of predicted interactions and mechanisms. At present, a major restriction of these studies is the relatively small pool of antibodies evaluated, which can constrain the breadth and generalizability of findings regarding CD19 antibody binding and clinical utility. Expanding future research to include a wider spectrum of antibody candidates will not only improve the robustness of computational predictions, but also facilitate the identification of molecules with distinct functional and pharmacokinetic profiles (Beck et al., 2025). Additionally, recent investigations into biomarkers, such as changes in liver FDG uptake post-therapy, underscore the importance of integrating complementary clinical parameters to refine treatment response assessment and stratification (Beck et al., 2025). Ongoing and future studies should prioritize comprehensive validation and the diversification of antibody libraries to advance next-generation CD19-targeted therapies tailored for varied autoimmune disease contexts.

6. CONCLUSION

This study used computational methods to eval- uate antibodies targeting the CD19 receptor for potential appli- cation in CAR T-cell therapy for autoimmune diseases such as severe myositis and systemic sclerosis. The CD19 protein struc- ture was predicted using AlphaFold 3, and potential binding regions were identified using ScanNet. Molecular docking simulations using HDOCK demonstrated that several antibodies could successfully bind to the predicted CD19 binding site. Interaction analysis using PLIP and binding energy calculations using PRODIGY showed that antibody 4A~~6~~Y had the strongest binding affinity, with a binding energy of 16.6 kcal/mol, suggesting a stable and favorable interaction with the CD19 receptor. These findings indicate that computational modeling can effectively identify promising antibody candidates for CAR T-cell design targeting autoreactive B cells. Although the results are promising, further experimental validation and testing of a larger set of antibodies will be necessary to confirm their therapeutic potential for treating autoimmune diseases.

7. REFERENCES

Abramson, J., Adler, J., Dunger, J., Evans, R., Green, T., Pritzel, A., Ronneberger, O., Willmore, L., Ballard, A. J., Bambrick, J., Bodenstein, S. W., Evans, D. A., Hung, C.-C., O'Neill, M., Reiman, D., Tunyasuvunakool, K., Wu, Z., Žemgulytė, A., Arvaniti, E., … Jumper, J. M. (2024). Accurate structure prediction of biomolecular interactions with AlphaFold 3. Nature, 630(8016), 493–500.

Anagnostou, T., Riaz, I. B., Hashmi, S. K., Murad, M. H., & Kenderian, S. S. (2020). Anti-CD19 chimeric antigen receptor T-cell therapy in acute lymphocytic leukaemia: a systematic review and meta-analysis. The Lancet Haematology, 7(11), e816–e826.

Beck, M., Blumenberg, V., Bücklein, V. L., Bundschuh, R. A., Harrer, D. C., Hirschbühl, K., Jung, J., Kunz, W. G., Menhart, K., Winkelmann, M., Yakushev, I., Illert, A. L., Eckstein, M., Völkl, S., Claus, R., Hansmann, L., Hecker, J. S., Kuwert, T., Mackensen, A., … Müller, F. (2025). Liver-FDG-uptake augments early PET/CT prognostic value for CD19-targeted CAR-T cell therapy in diffuse large B cell lymphoma. EJNMMI Research, 15(1), 25.

Blache, U., Tretbar, S., Koehl, U., Mougiakakos, D., & Fricke, S. (2023). CAR T cells for treating autoimmune diseases. RMD Open, 9(4).

He, C., Mansilla-Soto, J., Khanra, N., Hamieh, M., Bustos, V., Paquette, A. J., Angus, A. G., Shore, D. M., Rice, W. J., Khelashvili, G., Sadelain, M., & Meyerson, J. R. (2023). CD19 CAR antigen engagement mechanisms and affinity tuning. Science Immunology, 8(81), eadf1426.

Jann, A., Perez, M. A. S., & Zoete, V. (2025). Rapid and Reliable Structural Modeling of Adaptive Immune Receptors Using an Optimized AlphaFold3 workflow. bioRxiv.

Jiang, F., Guo, Y., Ma, H., Na, S., An, W., Song, B., Han, Y., Gao, J., Wang, T., & Huang, J. (2024). AlphaEpi: enhancing B cell epitope prediction with AlphaFold 3. Proceedings of the 15th ACM International Conference on Bioinformatics, Computational Biology and Health Informatics, 1–8.

Krishnan, K., Chugh, A., Rajaram, R., Setlur, A. S., K, C., Uttarkar, A., & Niranjan, V. (2025). Computational modeling and optimization of peptide-based CAR-T cell receptors targeting CD19 for enhanced efficacy and minimized toxicity. Research Square.

Krokidis, M. G., Koumadorakis, D. E., Lazaros, K., Ivantsik, O., Exarchos, T. P., Vrahatis, A. G., Kotsiantis, S., & Vlamos, P. (2025). AlphaFold3: an overview of applications and performance insights. International Journal of Molecular Sciences, 26(8), 3671.

Li, Y.-R., Lyu, Z., Chen, Y., Fang, Y., & Yang, L. (2024). Frontiers in CAR-T cell therapy for autoimmune diseases. Trends in Pharmacological Sciences, 45(9), 839–857.

Liu, Y., Dong, M., Chu, Y., Zhou, L., You, Y., Pang, X., Yang, S., Zhang, L., Chen, L., Zhu, L., Xiao, J., Wang, W., Qin, C., & Tian, D. (2024). Dawn of CAR-T cell therapy in autoimmune diseases. Chinese Medical Journal, 137(10), 1140–1150.

Mohanty, R., Chowdhury, C., Arega, S., Sen, P., Ganguly, P., & Ganguly, N. (2019). CAR T cell therapy: A new era for cancer treatment. Oncology Reports, 42(6), 2183–2195.

Müller, F., Taubmann, J., Bucci, L., Wilhelm, A., Bergmann, C., Völkl, S., Aigner, M., Rothe, T., Minopoulou, I., Tur, C., Knitza, J., Kharboutli, S., Kretschmann, S., Vasova, I., Spoerl, S., Reimann, H., Munoz, L., Gerlach, R. G., Schäfer, S., … Schett, G. (2024). CD19 CAR T-cell therapy in autoimmune disease—a case series with follow-up. New England Journal of Medicine, 390(8), 687–700.

Pillai, V., Muralidharan, K., Meng, W., Bagashev, A., Oldridge, D. A., Rosenthal, J., Van Arnam, J., Melenhorst, J. J., Mohan, D., DiNofia, A. M., Luo, M., Cherian, S., Fromm, J. R., Wertheim, G., Thomas-Tikhonenko, A., Paessler, M., June, C. H., Prak, E. T. L., Bhoj, V. G., … Rheingold, S. R. (2019). CAR T-cell therapy is effective for CD19-dim B-lymphoblastic leukemia but is impacted by prior blinatumomab therapy. Blood Advances, 3(22), 3539–3549.

Schett, G., Müller, F., Taubmann, J., Mackensen, A., Wang, W., Furie, R. A., Gold, R., Haghikia, A., Merkel, P. A., Caricchio, R., D'Agostino, M.-A., Locatelli, F., June, C. H., & Mougiakakos, D. (2024). Advancements and challenges in CAR T cell therapy in autoimmune diseases. Nature Reviews Rheumatology, 20(9), 531–544.

Schett, G., Schett, G., Mackensen, A., Mougiakakos, D., & Mougiakakos, D. (2023). CAR T-cell therapy in autoimmune diseases. The Lancet, 402(10416), 2034–2044.

Schett, G., Schett, G., Mackensen, A., Mougiakakos, D., & Mougiakakos, D. (2023). CAR T-cell therapy in autoimmune diseases. The Lancet, 402(10416), 2034–2044.

Sterner, R. C., & Sterner, R. M. (2021). CAR-T cell therapy: current limitations and potential strategies. Blood Cancer Journal, 11(4), 69.

Tubiana, J., Schneidman-Duhovny, D., & Wolfson, H. J. (2022a). ScanNet: an interpretable geometric deep learning model for structure-based protein binding site prediction. Nature Methods, 19(6), 730–739.

Tubiana, J., Schneidman-Duhovny, D., & Wolfson, H. J. (2022b). Scannet: A web server for structure-based prediction of protein binding sites with geometric deep learning. Journal of Molecular Biology, 434(19), 167758.

Yang, Y.-H., Liu, J.-W., Lu, C., & Wei, J.-F. (2022). CAR-T cell therapy for breast cancer: from basic research to clinical application. International Journal of Biological Sciences, 18(6), 2609–2626.

Zhang, X., Lu, X.-A., Yang, J., Zhang, G., Li, J., Song, L., Su, Y., Shi, Y., Zhang, M., He, J., Song, D., Lv, F., Li, W., Wu, Y., Wang, H., Liu, H., Zhou, X., He, T., & Lu, P. (2020). Efficacy and safety of anti-CD19 CAR T-cell therapy in 110 patients with B-cell acute lymphoblastic leukemia with high-risk features. Blood Advances, 4(10), 2325–2338.

Zmievskaya, E., Valiullina, A., Ganeeva, I., Petukhov, A., Rizvanov, A., & Bulatov, E. (2021). Application of CAR-T cell therapy beyond oncology: autoimmune diseases and viral infections. Biomedicines, 9(1), 59.