Current Trends in Biotechnology and Pharmacy
Vol. 19 (Supplementary Issue 4), Oct-Dec 2025, ISSN 0973-8916 (Print)., 2230-7303 (Online)
10.5530/ctbp.2025.4s.3

Next-Generation Materials in Biophysical Chemistry: Nano and Bio Innovations

D Sai Pavani, A Sowmiya, S Sasikala, and N Usharani*

Department of Molecular Analytics, Saveetha School of Engineering, Saveetha Institute of Medical and Technical Sciences (SIMATS), Chennai-600124, Tamil Nadu, India

Corresponding author email id:usharannin.sse@saveetha.com

Abstract

Nanomaterials are revolutionizing biophysical chemistry through their applications in targeted drug delivery, diagnostics, and biosensing; however, a detailed understanding of their interactions with biological macromolecules is essential for effective therapeutic development. Ubiquitin (PDB ID: 1UBQ), a conserved 76-amino-acid protein central to protein degradation and intracellular signalling, serves as an ideal model for studying nano–bio interactions. In this study, silicon dioxide (SiO_2), sourced from PubChem as a representative nanomaterial-inspired ligand, was docked with ubiquitin to explore potential binding mechanisms. The protein structure was retrieved from the Protein Data Bank, and ligand optimization and docking were performed using AutoDock Vina, with blind docking employed to survey the entire protein surface. Analysis of docking scores, hydrogen bonds, and hydrophobic interaction profiles revealed moderate-affinity binding pockets involving β-sheet surfaces and flexible loop regions, suggesting that SiO_2 can interact with key polar and charged residues to stabilize or modulate protein function. Linking these interactions to practical applications, the SiO_2–ubiquitin contacts at the β-sheet regions could potentially enhance serum stability, increase circulation half-life and improving drug delivery efficiency. Furthermore, the interactions within flexible loop regions might facilitate endosomal escape, enabling targeted release in intracellular environments. These findings highlight the potential of silicon dioxide-based nanomaterials for biomedical applications such as targeted therapeutics, protein stabilization, and biosensor development, and provide a computational foundation for future experimental validation of nanomaterial–protein interactions.

Keywords: Nano objects, Silicon dioxide, Ubiquitin, nanocarriers, Next generation materials

Introduction

Nanotechnology is one of the most prominent technologies that has expanded its applications across all fields. In medicine, the approach of nanodevices, nanoobjects, and nanocarriers is employed for imaging, diagnostics, and therapeutics (1). Nanotechnology, which is involved in various fields, has numerous applications in medical practices. The site-directed cum targeted drug delivery with the sustainable release is achieved on a larger scale by the nanosized carrier system (2). The functionalized nanoobjects address therapeutic issues due to their high surface area, concentration, conductivity, resonance, and volume ratio (3). The polyfunctionality of nanomaterials prepared from metals (Au & Fe), oxides of metal (Zn, Fe, Ni, Cu, Cd, Co, and Al), synthetic polymers (Polyglycolic acid (PGA), polylactic acid (PLA), polylactic glycolic acid (PLGA), and polycaprolactone (PCL)), dendrimers, and aptamer, etc. are employed currently in clinical practices (4). For instance, Adjuvant therapy with metal-tagged nanoparticles is used for different clinical conditions such as diabetes, cancer, myocardial infections, asthma, Parkinson's, and Alzheimer's disease (5). Au Nps with greater affinity help in encapsulating the mRNA, DNA, and protein as a carrier for the targeted delivery system (6). Similarly, the silver nanoparticles possess microbicidal

Vol. 19 (Supplementary Issue 4), Oct-Dec 2025, ISSN 0973-8916 (Print)., 2230-7303 (Online)
10.5530/ctbp.2025.4s.3

activity and are effectively used to treat pathogens. Besides their polyfunctionality, they are used for cellular tracing and detection in imaging protocols (7). The oxides of metal nanoparticles are used as nanosensors for detecting pathogenic wounds and their associated infections.

Polymers such as PGA, PEG, and PLGA, as well as their composites, are used to prepare nanoparticles. The nature of polymeric nanoparticles is biodegradable, biocompatible, with enhanced bioavailability and prolonged retention (8). PLA or PLGA bio-functionalized nanoparticles, incorporating drugs such as doxorubicin, are used to treat brain cancer. The bioconjugates of polymers show better efficiency than free drugs (9). Dendrimers, being radially symmetric nanosized compounds, exhibit polyvalency, electrostatic interactions, stability, and low toxicity to the host. These also have a wide surface area for sustainable drug release (10). In the case of aptamers, oligonucleotide or peptide aptamers are selected for in vivo treatment protocols using techniques such as yeast two-hybrid, phage display, and ribosome display. Aptamers are highly specific, small in size, and exhibit low immunogenicity.

Additionally, APTA-nanosensors are utilized for detecting apoptotic cells. Metal layered hydroxides, such as zinc layered, zinc-aluminum layered, and magnesium-aluminum layered hydroxides, are used to carry para-aminosalicylic acid by the process of co-precipitation and ion exchange methods (11). These multi-layered hydroxides are released rapidly and circulated sustainably. Anti-TB drugs stabilized by metal hydroxides undergo electrostatic interactions between negatively charged drugs and the positively charged nanolayers (12). Immunoactivators loaded liposomes induce the release of cytokines and the antibody response in the host (13). This initiates a promising hope for the nano delivery carriers in the case of pulmonary tuberculosis.

Biophysical chemistry now relies heavily on nanotechnology, which provides novel methods for investigating molecular interactions at the nanoscale. For building next-generation biomedical tools, it is essential to understand how these nanomaterials interact with biological molecules (14). Ubiquitin is a small regulatory protein found in almost all eukaryotic cells, playing a crucial role in protein degradation and cellular regulation (15). It helps mark proteins for destruction by the proteasome, a process essential for maintaining cellular health and function. This mechanism is often referred to as the "molecular kiss of death" for proteins. Silicon dioxide nanoparticles are commonly used in biomedical applications, including targeted drug delivery and biosensing. Understanding how ubiquitin interacts with silicon dioxide for nanoparticle-based therapeutic approaches for diseases such as cancer and neurodegenerative disorders (Fig. 1). This study aims to explore the molecular interaction between the human regulatory protein ubiquitin (PDB ID: 1UBQ) and a nanomaterial-inspired compound (PubChem CID: 24269) through computational molecular docking techniques.

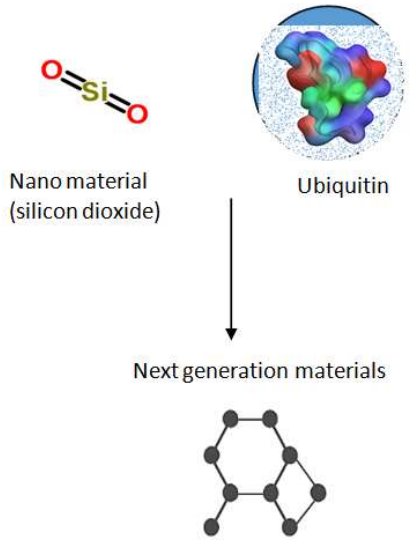

Fig. 1: Formation of next-generation materials

Vol. 19 (Supplementary Issue 4), Oct-Dec 2025, ISSN 0973-8916 (Print)., 2230-7303 (Online)
10.5530/ctbp.2025.4s.3

Predicting the binding affinity and identifying potential interaction sites between the nano compound and ubiquitin were the focus. Furthermore, to analyze the nature of interactions at the nano-bio interface, including hydrogen bonding and hydrophobic contacts. Hence in this study, the docking supports the design of next-generation nanomaterials with biomedical relevance, particularly in targeted drug delivery and biosensing applications.

Material and Methods

Protein and Ligand Preparation

The three-dimensional structure of ubiquitin (PDB ID: 1UBQ) was retrieved from the RCSB Protein Data Bank (PDB) in .pdb format. Due to its extensive cellular functions, ubiquitin serves as an ideal model system for docking analysis. Prior to docking, the protein structure was cleaned using AutoDock Tools (ADT). Non-essential heteroatoms, such as crystallographic water molecules and ions, were removed to prevent steric hindrance during the docking process (16). Polar hydrogen atoms were added to improve hydrogen-bonding accuracy, and Gasteiger charges were assigned to ensure proper electrostatic representation of the protein-ligand system. The prepared protein was then saved in the .pdbqt format, which is required for AutoDock-based docking protocols.

The ligand selected for this study was silicon dioxide (SiO_2) (Fig. 2B), obtained from the PubChem database in .sdf format. Since PubChem structures are not optimized for docking studies, the molecule was subjected to energy minimization and structural optimization using BIOVIA Discovery Studio. This step ensured that the ligand adopted a low-energy conformation suitable for interaction analysis.

Following optimization, hydrogen atoms were added where necessary, and Gasteiger charges were applied to maintain compatibility with AutoDock Vina. The optimized ligand was finally converted into the .pdbqt format for docking simulations.

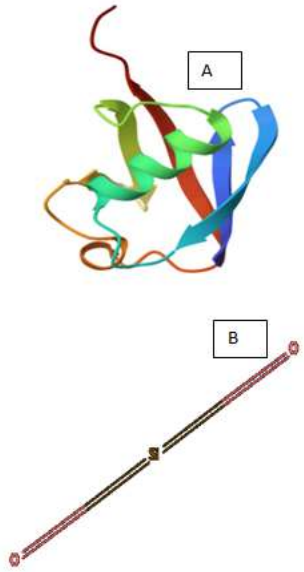

Fig. 2: Structure of Receptor Ubiquitin (A) Ligand SiO_2 (B)

Molecular Docking Setup

Molecular docking was conducted using AutoDock Vina, a widely used open-source docking engine known for its efficiency and accuracy in predicting ligand binding modes. The prepared protein and ligand files were imported, and docking grids were defined. The docking grid was carefully centered on ubiquitin's known functional and binding pocket regions, as reported in structural biology studies. This ensured that the ligand was probed against biologically relevant sites rather than non-specific surface regions. The grid box dimensions were optimized to allow sufficient conformational sampling of the ligand without being excessively large, thereby minimizing the potential reduction in docking accuracy.

In parallel, the docking experiment was also performed on the CB-Dock2 server, an advanced blind docking platform that automatically identifies potential binding cavities on the protein surface. CB-Dock2 employs cavity detection algorithms to generate docking sites and integrates them

Vol. 19 (Supplementary Issue 4), Oct-Dec 2025, ISSN 0973-8916 (Print)., 2230-7303 (Online)
10.5530/ctbp.2025.4s.3

with the AutoDock Vina scoring function. This allowed for a comparative docking approach: while AutoDock Vina focused on experimentally known binding regions, CB-Dock2 explored additional possible binding pockets to validate and cross-check interaction hotspots (17).

Docking results were obtained in terms of binding affinity scores (kcal/mol) and predicted ligand conformations. The top-ranked binding poses were selected based on docking scores, interaction patterns, and their location within functional regions of ubiquitin. Further visualization and interaction analysis (hydrogen bonds, hydrophobic interactions, van der Waals contacts) were carried out using BIOVIA Discovery Studio and PyMOL to assess the structural basis of binding.

Results

Docking Results Overview

Nanomaterials are transforming biophysical chemistry through their applications in targeted drug delivery, diagnostics, and biosensing; yet, understanding their molecular interactions with proteins is essential for the safe and effective design of therapeutics (18). Ubiquitin (PDB ID: 1UBQ), a small regulatory protein central to protein degradation and cell signaling, was used as a model to explore nano–bio interactions (Figure 2A). In this study, silicon dioxide (SiO_2), retrieved from PubChem as a nanomaterial-inspired ligand, was docked with ubiquitin using AutoDock Vina to predict binding affinity, interaction residues, and potential biomedical relevance (Fig. 3). Docking simulations revealed a best binding energy of −1.7 kcal/mol, with five stable conformations (C2: −1.7 kcal/mol, C4: −1.6 kcal/mol, C1: −1.5 kcal/mol, C3: −1.5 kcal/mol, C5: −1.4 kcal/mol).

Key interaction residues included K27, Q41, Q49, L50, E51, D52, and R72, forming hydrogen bonds and electrostatic interactions with the ligand. These findings suggest that SiO_2 interacts primarily with ubiquitin's β-sheet and flexible loop regions, potentially influencing protein stability and

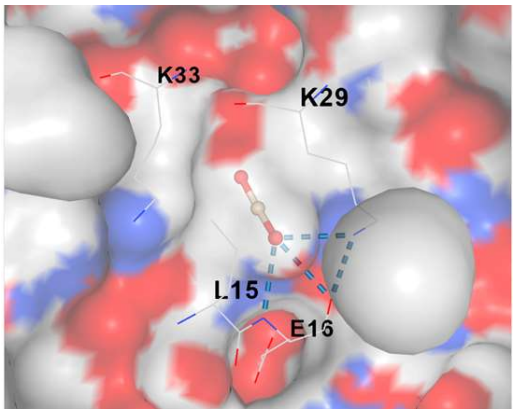

Fig. 3: Interaction between ligand (SiO2) and protein(1UBQ)

functional modulation. This computational study highlights the promise of silicon dioxide for biomedical applications in drug delivery, biosensing, and protein surface engineering, providing a molecular foundation for future experimental validation of nanomaterial–protein interactions.

Binding Sites and their Interactions moieties

The present docking study provides insights into the molecular interactions between ubiquitin (1UBQ) and silicon dioxide (SiO_2), highlighting the structural basis of protein–nanoparticle recognition. Docking simulations performed with AutoDock Vina and CB-Dock2 consistently identified pocket C2 as the most favorable binding site, with a docking score of –1.7 kcal/mol. While the absolute binding affinity is relatively weak compared to organic drug-like ligands, this is not unexpected for an inorganic ligand such as SiO_2, which lacks conventional aromatic and heteroatomic functional groups. Nevertheless, the identification of consistent interaction residues underscores the reproducibility of the methodology and the biological relevance of the observed binding site.

Residue-Level Insights

The binding analysis revealed several ubiquitin residues involved in stabilizing the

Vol. 19 (Supplementary Issue 4), Oct-Dec 2025, ISSN 0973-8916 (Print)., 2230-7303 (Online)
10.5530/ctbp.2025.4s.3

interaction with SiO_2. Key residues included K27, Q41, Q49, L50, E51, D52, and R72, forming a cluster of polar and charged amino acids within the binding pocket. Lysine (K27, K29, K33, K48) and arginine (R72) residues contribute positively charged side chains that may form hydrogen bonds or electrostatic contacts with the negatively polarized surface of SiO_2. In contrast, glutamate (E16, E34, E51) and aspartate (D39, D52) residues provide negatively charged functionalities that may participate in ionic balance and hydrogen-bonding interactions. The involvement of polar residues, such as Q41, Q49, and H68, further suggests that hydrogen-bond networks play a crucial role in mediating the adsorption of silica at the protein interface.

Hydrophobic contacts were observed with residues such as LEU15, ILE44, LEU50, and PRO38, suggesting that although SiO_2 is primarily polar, its surface heterogeneity allows van der Waals stabilization through hydrophobic patches. Importantly, residues around the ILE44-centered hydrophobic patch (ILE44, PHE45, ALA46, GLY47, K48), a well-characterized ubiquitin recognition site, also engaged in ligand interactions. This suggests that nanoparticle binding could overlap with functional protein–protein interaction interfaces, potentially perturbing ubiquitin's biological role.

Types of Interactions and Stabilization

The predicted binding modes reveal a mixture of interaction types:

- Hydrogen bonding dominated the interaction landscape, particularly with Q41, Q49, E51, and D52.
- π–π stacking interactions, though weak, were observed with PHE45, highlighting possible stabilization via SiO_2's surface silanol groups interacting with aromatic residues.
- Hydrophobic interactions provided additional stabilization through contacts with LEU and ILE residues.

This interplay of hydrophilic and hydrophobic forces supports ubiquitin adsorption onto nanoparticle surfaces, which is coordinated through electrostatics, hydrogen bonding, and van der Waals effects.

Proof reading mechanism

The results summarize the ability of ubiquitin, which can readily interact with nanoparticle surfaces, forming part of the protein corona that dictates the fate of nanoparticles in biological systems. Prior reports indicate that ubiquitin binds strongly via its lysine and glutamate/glutamine-rich regions, which aligns well with our identified residues. The recurring involvement of lysine side chains (K27, K29, K48) is particularly noteworthy, as these residues are also critical for ubiquitination reactions and protein–protein signalling. This suggests that nanoparticle binding could potentially interfere with ubiquitin's physiological functions, a point of significance for nanotoxicology.

Moreover, the relatively modest docking score (–1.7 kcal/mol) highlights the unique challenges of modelling inorganic–protein interactions. Unlike small-molecule ligands, inorganic surfaces present extended, less specific contact areas that yield lower affinity scores, but still result in meaningful binding. Our results, therefore, emphasize that binding affinity alone cannot capture the full biological impact of nanoparticle–protein interactions; instead, residue-level mapping and interaction profiling are essential for understanding binding modes.

Implications for Nano–Bio Interfaces

The identification of a consistent binding pocket (C2) and residues such as K27, Q41, D52, and R72 suggests potential adsorption hotspots where ubiquitin may anchor onto silica nanoparticles Table 1. Such adsorption could alter the protein's conformational flexibility, potentially masking or exposing key functional regions. This has significant implications for the formation of protein coronas on nanoparticle surfaces, a process that is known to influence nanoparticle biocompatibility, biodistribution, and immunogenicity.

Vol. 19 (Supplementary Issue 4), Oct-Dec 2025, ISSN 0973-8916 (Print)., 2230-7303 (Online)
10.5530/ctbp.2025.4s.3

Table 1: Comparison and Validation of Cur pockets

CurPocket ID	Vina score	Cavity volume (Å3)	Docking size (x, y, z)	Center (x, y, z)
C2	-1.7	79	14,14,14	34,38,18
C4	-1.6	39	14,14,14	32,25,24
C1	-1.5	33	14,14,14	41,32,27
C3	-1.5	23	14,14,14	36,29,6
C5	-1.4	23	14,14,14	26,39,19

From a methodological perspective, the congruence of results from both AutoDock Vina and CB-Dock2 validates the robustness of our docking workflow. The results also serve as a proof-of-concept for applying molecular docking tools to probe nano–bio interactions, which are increasingly relevant in the fields of nanomedicine, biosensing, and nanotoxicology.

Future interventions and proceedings

Future research should build upon this docking study of silicon dioxide with ubiquitin by integrating both computational and experimental approaches to validate and expand the findings. Molecular Dynamics (MD) simulations, using platforms such as GROMACS, AMBER, or CHARMM, can provide atomistic insights into the binding stability, hydrogen bond occupancy, and conformational dynamics of the ubiquitin–ligand complex over nanosecond to microsecond timescales, thereby replicating physiological conditions such as ionic strength, pH, and temperature. Laboratory-based validation could involve synthesizing silicon dioxide nanoparticles (SiNPs) or surface-functionalized analogs through sol–gel or vapor deposition methods, followed by surface plasmon resonance (SPR), isothermal titration calorimetry (ITC), or microscale thermophoresis (MST) to measure binding affinities and thermodynamic profiles with ubiquitin and related proteins. Comparative docking studies with a diverse library of nanomaterial-inspired ligands, such as gold nanoparticles (AuNPs), graphene oxide, carbon nanotubes, and titanium dioxide (TiO_2), would facilitate structure–activity relationship (SAR) analysis, potentially revealing physicochemical features (e.g., particle size, charge, surface groups) that enhance binding specificity and stability. Extending this computational pipeline to include other ubiquitin-binding proteins, such as E3 ubiquitin ligases, deubiquitinating enzymes (DUBs), or ubiquitin-conjugating enzymes, could help uncover network-level effects of nanomaterial interactions, guiding the development of precision nanomedicines. Together, these computational and experimental strategies could advance applications in targeted drug delivery, biosensor platforms, protein engineering, and controlled therapeutic release systems, thereby bridging molecular docking predictions with translational nanotechnology solutions.

Conclusion

This study demonstrated the effective use of molecular docking to analyze the interaction between the nanomaterial-inspired compound silicon dioxide and the regulatory protein ubiquitin (PDB ID: 1UBQ), a central component of cellular protein degradation and signaling pathways. The docking simulations revealed a favorable binding affinity of −1.7 kcal/mol and multiple stable conformations, highlighting consistent interaction between silicon dioxide and key residues including K27, Q41, Q49, L50, E51, D52, and R72.

Vol. 19 (Supplementary Issue 4), Oct-Dec 2025, ISSN 0973-8916 (Print)., 2230-7303 (Online)
10.5530/ctbp.2025.4s.3

These residues are primarily located within ubiquitin's β-sheet and flexible loop regions, suggesting that silicon dioxide nanoparticles can form hydrogen bonds, electrostatic interactions, and hydrophobic contacts with strategic surface-exposed sites, potentially influencing ubiquitin's stability or interaction network. The insights gained from this computational analysis underscore the promise of silicon dioxide as a bio-interactive nanomaterial with relevance in biomedical nanotechnology. By demonstrating how nanoscale materials can interface with essential regulatory proteins, this study contributes to the growing field of nano–bio interaction modeling, which is crucial for the rational design of advanced drug delivery systems, precision molecular targeting strategies, protein-surface functionalization, and biosensor development. Such findings illustrate the broader potential of integrating nanotechnology into biophysical chemistry to create next-generation therapeutic and diagnostic solutions, bridging computational predictions with translational applications.

Acknowledgement

The authors are thankfulManagement of Saveetha School of Engineering for providing (SSE) the facilities to carry the work.

Conflicts of Interest

The authors declare thatno conflicts of interest.

References

1. Addington, W.W. (1979) 'The Side Effects And Interactions Of Antituberculosis Drugs', Chest, 76(6), pp. 782–784.
2. Suri, S.S., Fenniri, H. and Singh, B. (2007) 'Nanotechnology-Based Drug Delivery Systems', Journal of Occupational Medicine and Toxicology, 2:16.
3. Gelperina, S., Kisich, K., Iseman, M.D. and Heifets, L. (2005) 'The Potential Advantages Of Nanoparticle Drug Delivery Systems In Chemotherapy Of Tuberculosis', American Journal of Respiratory and Critical Care Medicine, 172, pp. 1487–1490.
4. Dolez, P.I. (2015) 'Nanomaterials Definitions, Classifications, And Applications', in Nano Engineering Global Approaches To Health And Safety Issues, pp. 3–40.
5. Verma, H., Shivangi and Meena, L.S. (2018) 'Delivery Of Antituberculosis Drugs To Mycobacterium tuberculosis H37Rv Infected Macrophages Via Polylactide-Co-Glycolide (PLGA) Nanoparticles', International Journal of Molecular Biology Open Access, 3(5), pp. 235–238.
6. Pati, R., Shevtsov, M. and Sonawane, A. (2018) 'Nanoparticle Vaccines Against Infectious Diseases', Frontiers in Immunology, 9:2224.
7. Charbgoo, F., Nejabat, M., Abnous, K., Soltani, F., Taghdisi, S.M., Alibolandi, M. et al. (2018) 'Gold Nanoparticle Should Understand Protein Corona For Being A Clinical Nanomaterial', Journal of Controlled Release, 272, pp. 39–53.
8. Buxton, R.B. (2013) 'The Physics Of Functional Magnetic Resonance Imaging (fMRI)', Reports on Progress in Physics, 76(9):096601.
9. Lin, H., Yue, Y., Maidana De, Bouzika, P., Atik, A., Matsumoto, H., Miller, J.W. and Vavvas, D.G. (2016) 'Drug Delivery Nanoparticles: Toxicity Comparison In Retinal Pigment Epithelium And Retinal Vascular Endothelial Cells', Seminars in Ophthalmology, 31(1–2), pp. 1–9.
10. Alasvand Saied, N., Kargozar, S., Brouki, P., Chauhan, N.P.S. and Mozafari, M. (2019) 'Functionalized Polymers For Drug/Gene-Delivery Applications', in Advanced Functional Polymers For Biomedical Applications, pp. 275–299.
11. Tan, W., Wang, H., Chen, Y., Zhang, X., Zhu, H., Yang, C. et al. (2011) 'Molecular Aptamers For Drug Delivery', Trends in Biotechnology, 29(12), pp. 634–640.
12. Bullo, S., El Zowalaty, M., Arulselvan, P., Fakurazi, S., Webster, T.J., Geilich, B.M. et al. (2014) 'Antimycobacterial, Antimicrobial, And Biocompatibility Properties Of Para-Aminosalicylic Acid With Zinc Layered Hydroxide And Zn/Al Layered Double Hydroxide Nanocomposites', Drug Design,

Vol. 19 (Supplementary Issue 4), Oct-Dec 2025, ISSN 0973-8916 (Print)., 2230-7303 (Online)
10.5530/ctbp.2025.4s.3

Development and Therapy, 8, pp. 1029–1036.
13. Riccardi, G. and Pasca, M.R. (2014) 'Trends In Discovery Of New Drugs For Tuberculosis Therapy', The Journal of Antibiotics, 67, pp. 655–659.
14. Zhao, X. et al. (2021) 'Recent Advances in Nanomaterial–Protein Interactions: Mechanism and Applications', Journal of Nanobiotechnology, 19(1):1–22.
15. Zhou, L. et al. (2018) 'Silicon Dioxide Nanoparticles: Biomedical Applications and Toxicity', Regulatory Toxicology and Pharmacology, 98, pp. 115–123.
16. Komander, D. and Rape, M. (2012) 'The Ubiquitin Code', Annual Review of Biochemistry, 81, pp. 203–229.
17. Trott, O. and Olson, A.J. (2010) 'AutoDock Vina: Improving the Speed and Accuracy of Docking with a New Scoring Function, Efficient Optimization, and Multithreading', Journal of Computational Chemistry, 31(2), pp. 455–461.
18. Liu, Y. et al. (2020) 'CB-Dock2: Enhanced Protein–Ligand Blind Docking Powered by Cavity Detection and Structure-Based Deep Learning', Briefings in Bioinformatics, 23(1):bbab473.