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Review article

In silico methods for studying *ankylosing spondylitis*

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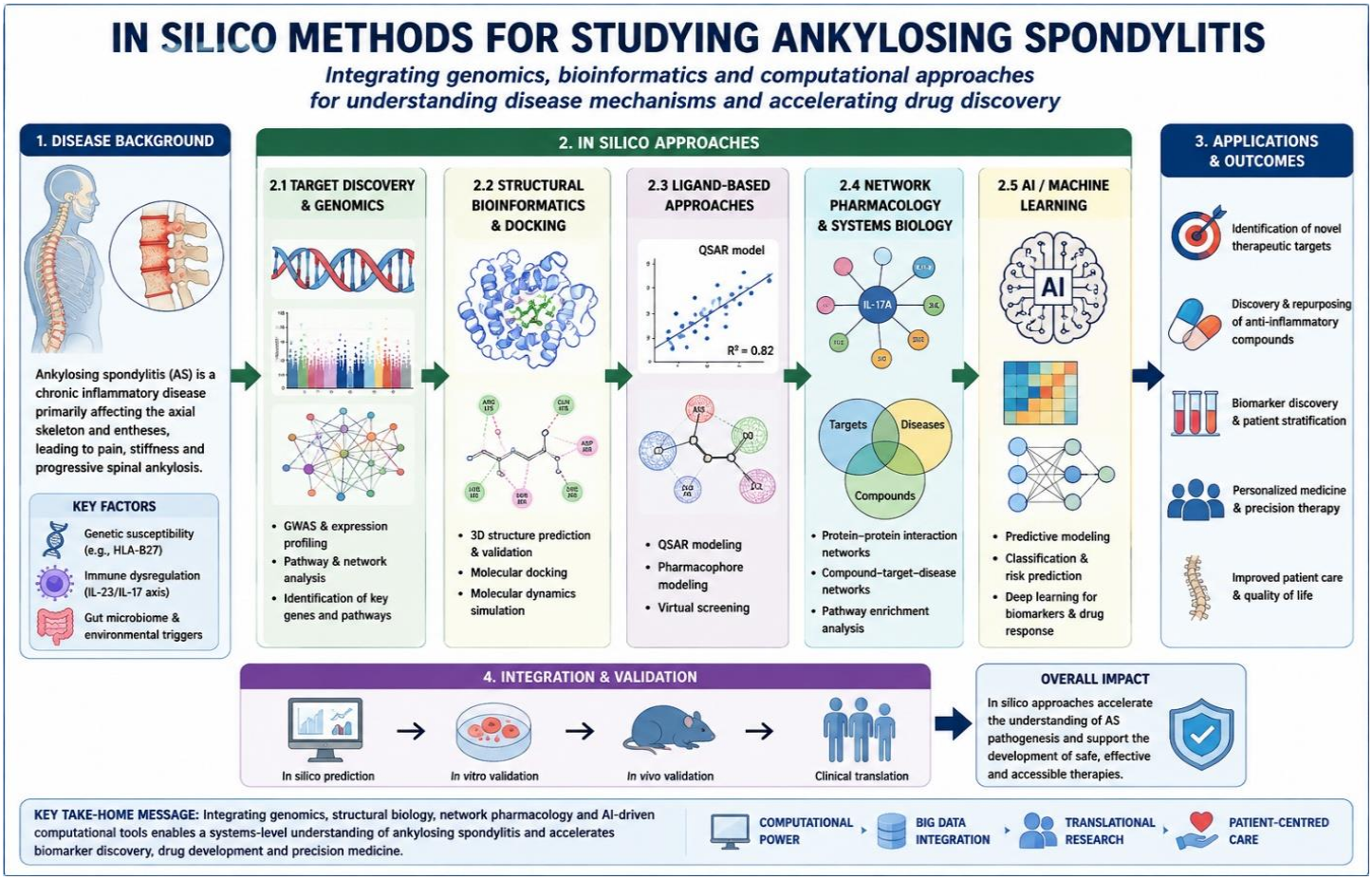
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ABSTRACT

The chronic inflammatory condition known as *ankylosing spondylitis* (AS) is an axial spondyloarthritis that causes pain, progressive spinal stiffness and, in advanced cases, ankylosis. Despite progress in clinical therapy (notably TNF and IL-17 inhibition), many patients have incomplete responses, side effects, or delayed diagnosis. In silico methods — spanning target discovery (genomics, GWAS), drug design based on structure (molecular docking, molecular dynamics), ligand-based methods (QSAR, pharmacophores), network pharmacology, and machine learning (ML)/AI approaches — are accelerating hypothesis generation, screening and translational research for AS.



This review summarizes the biology and genetic architecture of AS that underpin computational work, details current in silico methods, surveys representative applications (including network pharmacology and docking studies on anti-inflammatory phytochemicals and small molecules), highlights strengths and limitations, and outlines ethical and humanitarian considerations for deploying computational discoveries in patient care.

Keywords: *Ankylosing spondylitis, Axial spondyloarthritis, In silico* methods, Target discovery, Artificial intelligence.

INTRODUCTION

Quality of life is affected negatively, there is severe disability, and there is increased likelihood of other diseases such as osteoporosis and heart disease [1]. Limited awareness, delayed diagnosis, and poor access to therapies add to the humanitarian burden of the disease, particularly in low- and middle-income countries where diagnostic imaging or biologics are not accessible in low-resource environments; computational approaches could speed up biomarker discovery as well as enable repurposing of low-cost drugs [2]. By building a bridge between science and humanity, in silico research offers great potential to improve patient treatment and achieve equality in medicine.

Genetic predisposition to AS involves several genetic components; however, the most prevalent one appears to be HLA-B27, which is present in up to 90% of people with AS compared to only 6-8% in the general population. Although HLA-B27 is an important contributing factor, it is not the only cause because very few HLA-B27 positive individuals develop the disease [3]. The immune system, particularly the disruption of the IL-23/IL-17 pathway, may have a significant role in AS, according to genome-wide association scans. There is evidence to show that patients with AS have higher levels of IL-17 and IL-23, resulting in increased activation of the Th17 cells and increased neutrophils, hence resulting in inflammation in entheses and axial joints [4]. Additionally, innate immune mechanisms such as the activation of dendritic cells and natural killer cells further increase the inflammatory response [5]. Studies have shown that gut dysbiosis results in activation of the immune system, wherein bacterial antigens cause an inappropriate immune response in susceptible individuals. Animal models such as HLA-B27 transgenic rats are further proof of the gut-joint axis of AS, since these animals exhibit spontaneous colitis and spondyloarthritis.

Pathophysiology and molecular pathogenesis of *ankylosing spondylitis*

The inflammatory disorder *ankylosing spondylitis* (AS) is extremely complex because of the involvement of different factors such as genetics, the immune system, the environment and intestinal flora. The first manifestation of *ankylosing spondylitis* that demonstrates inflammation in entheses (tissue that connects tendons or ligaments with bone) is enthesitis. This leads to the development of bone tissue, syndesmophytes, ankyloses and dysfunction [6].

Genetic factors

There is significant evidence for genetic predisposition as one of the most important factors in AS onset. HLA-B27 is currently the most established genetic susceptibility locus for AS, but the distribution of this gene is extremely variable between different ethnicities and geographic regions [7]. It should be noted that HLA-B27 alone is not enough for AS onset, which means other factors play their role in AS pathogenesis. There were also discovered several non-HLA susceptibility loci through genome-wide association studies (GWAS). These include ERAP1, IL23R, and RUNX3 [8]. These genes play an important role in antigen processing, presentation, T-cell differentiation and regulation of immunity.

Gut microbiome and gut–joint axis

Intestinal dysbiosis was recently proven to be an essential step in the development of AS. Microbial community shifts, for instance, shifts in Prevotella and Dialister may influence the immune system response globally [10]. Inflammation in the intestine and its association with spondyloarthritis were proven by the use of HLA-B27 transgenic animal models [11]. Enhanced intestinal permeability can promote microbial products and antigen transfer into the bloodstream, leading to innate immune pathway activation and inflammation.

Cytokine network and inflammatory pathways

Cytokines play an integral part in the molecular mechanism of AS. TNF-α serves to be an important inflammatory mediator and the efficacy of TNF-α as an inhibitor in clinic settings makes it clear that it plays a significant part in the pathogenesis of AS. IL-23/IL-17 pathway is yet another important part of the molecular mechanism, wherein IL-17A acts as an important mediator for chronic inflammation and tissue remodelling. Efficacy of secukinumab and other IL-17A inhibitors proves the importance of the pathway [12]. Other mediators like IL-6, IL-22, GM-CSF may be involved as well [13].

Bone remodelling and ankylosis

One of the most important features of AS is the presence of inflammation, bone erosion, and abnormal bone formation. Inflammation causes the production of cytokines, which promote bone erosion through osteoclasts. However, the activation of osteogenic pathways simultaneously leads to bone formation. Thus, the outcome is syndesmophyte formation and spine fusion between vertebrae. Therefore, the interplay between immune and

mesenchymal cells and dysregulated bone-remodelling pathways constitutes an essential link between inflammation and ankylosis.

Genomic and bioinformatics strategies for *ankylosing spondylitis*

A lot of headway has been achieved in the investigation of the molecular mechanisms of *ankylosing spondylitis* through the use of next-generation sequencing and bioinformatics approaches. Genomic, transcriptomic, epigenomic, proteomic, and bioinformatics methods can be combined to find disease-related genes, conduct regulatory studies, find pathways, biomarkers, and drug targets. Notably, multi-omics methods have also been developed and have shown that combining genetics data with gene expression and regulation is beneficial for understanding the biological processes of statistical genetics [14,15].

Study of genome-wide associations

Genome-wide association studies have been important in understanding the genetics of AS. Besides the significance of HLA-B27 in AS, GWAS has also helped to discover many non-HLA susceptibility loci for AS, like ERAP1, IL23R, RUNX3, PTGER4, TYK2, and others involved in immune regulation. Large-scale multi-ancestry GWAS of large scale have played a vital role in discovering more and more susceptibility loci for AS and have helped to find biological mechanisms associated with immune regulation, intestinal biology, and other such mechanisms. The integration of GWAS findings with functional genomics can play an important part in the discovery of causative variants and their involvement in gene regulation [16].

Transcriptomics and gene expression profiling

Whereas the methods of genomics reveal the genetic foundation of susceptibility to disease, the methods of transcriptomics offer information about the functioning of genes in diseased cells and tissues. In AS, RNA sequencing and microarray experiments have identified alterations in gene expression linked to inflammation, immunity, bone metabolism, and cellular differentiation. By combining the results of transcriptomics and GWAS, one can discover the disease-related genes that may act downstream from the genetic risk factors. Tools commonly employed for differential gene expression analysis are DESeq2 and edgeR. [17].

Figure 1: Workflow for an *in-silico* approach for studying *ankylosing spondylitis*. Genomic, clinical and molecular data are analysed using bioinformatic methods to identify candidate genes, proteins, pathways and biomarkers. Functional and molecular modelling validation of predictions made by bioinformatics methods is used to study the biological significance of the predictions

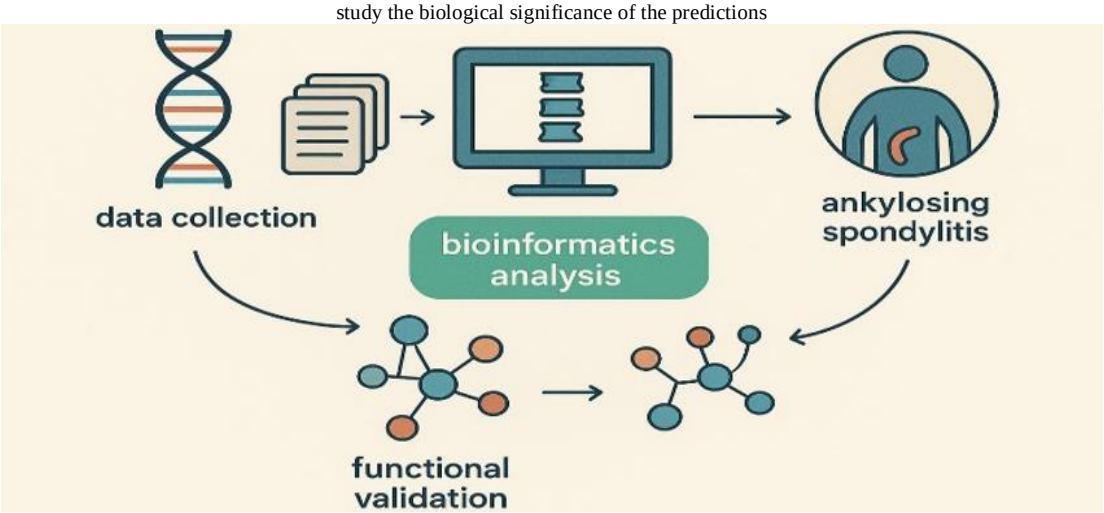
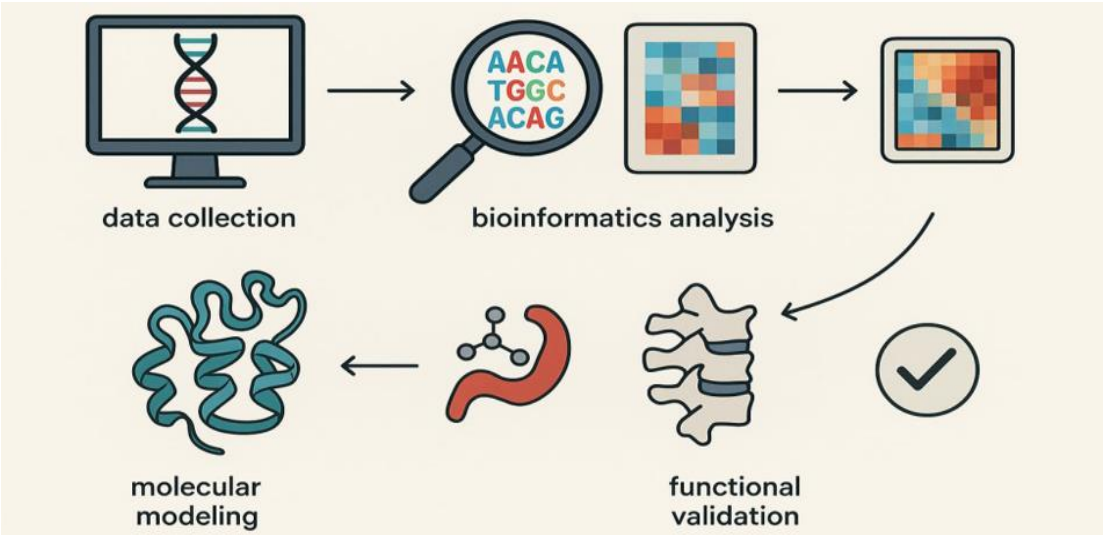


Figure 2. Workflow for in silico drug discovery in the case of *ankylosing spondylitis*. It includes data collection, bioinformatics analysis, target identification, molecular modelling, virtual screening, docking and functional validation



Epigenomics and regulator elements

DNA methylation, histone modification, chromatin accessibility, and other aspects of epigenetic regulation and enhancers, is yet another form of regulation within AS. EWAS and functional epigenomics tools have been used to search for regulation changes regulated by disease in immune cells and other cell types. Combining epigenomics data with GWAS will aid in finding out if the disease-regulated variants act through regulation of gene expression. Data available from resources such as ENCODE and the Roadmap Epigenomics project will be useful in understanding chromatin states, regulatory elements, transcription factor binding, and cell type-specific epigenetic marks. Recent studies of AS reveal that using integrated omics data makes it possible to connect disease-regulated variants to regulatory elements and target genes [18].

Databases and computation tools

Availability of freely available genomics and molecular biology databases is very important for the computation of AS. GWAS catalogue, dbSNP, and ClinVar contain information on genetic variations, disease association, and the clinical relevance of such mutations. Protein interaction databases, including STRING and BioGRID, can be used for the construction of protein-protein interaction networks and the determination of molecular hubs related to disease pathways [19].

Structural bioinformatics and in silico drug discovery

Apart from genomics, the application of structural bioinformatics reveals the protein structures and protein-ligand interactions associated with AS. The methods used include homology modelling, molecular docking, molecular dynamics simulation, virtual screening, and protein-ligand interaction studies. By combining the knowledge gained using these methods with the insights provided by genomics and transcriptomics, the disease genes can be related to proteins and therapeutic targets. Therefore, structural and multi-omics bioinformatics is a promising tool for understanding AS pathogenesis and the development of therapeutic drugs for AS [20].

Structural bioinformatics and molecular docking

Many AS-related proteins, including ERAP1, IL-23R, and RUNX3, lack experimentally determined crystal structures. Homology modelling provides a way to predict 3D protein structures based on sequence similarity with known templates. Tools like SWISS-MODEL, Phyre2, and I-TASSER are widely used to construct accurate structural models for AS-associated proteins [23]. These models enable visualization of key functional domains, protein -protein interfaces and ligand-binding pockets [21].

In vitro drug discovery through molecular docking forms the basic foundation of in silico drug discovery for AS. The molecular docking of the small molecules onto the target proteins provides a ranking and identification of the potential drugs. Some of the programs which enable the prediction of the binding affinity and residues in contact include AutoDock, Schrödinger Glide, and MOE. Molecular docking experiments on IL17A and IL-23R have indicated that natural compounds, such as flavonoids and alkaloids, having high binding affinities. This indicates that the natural compounds can be used as anti-inflammatory agents. Similarly, the docking experiments on TNF-α inhibitors have enabled the optimization of the biologics and biosimilars in the treatment of AS. Therefore, in silico screening reduces the dependency on expensive wet-lab experiments [22].

The proteomics data are increasingly being used in the protein-protein interaction (PPI) network formation through the use of software such as STRING, BioGRID, and Cytoscape. These PPI networks will provide the insight on the hub proteins and the pathways involved in the development of AS. For instance, TNF-α, STAT3, and NF-κB have been observed as the key nodes in these models.

Systems biology, network pharmacology and artificial intelligence in *ankylosing spondylitis*

AS is a multifactorial disease that involves gene-environment interactions along with immune response, bone remodeling, gut flora, and environmental factors. Classical reductionist research focusing on the study of individual genes or proteins gives mechanistic insights; however, it may not fully reflect the interconnected nature of these events. Systems biology tries to overcome this problem by combining different levels of biology and investigating networks and their interactions related to the disease. High-throughput genomics, transcriptomics, proteomics, metabolomics and clinical data provide opportunities for computational modelling of AS in a systems approach.

Multi-omics analysis can show coordinated regulation of immune signalling pathways, cytokine networks, metabolism and skeletal remodelling in AS. Computational studies of AS revealed interconnected inflammatory pathways such as TNF, IL-23/IL-17, NF-κB, JAK-STAT and cytokine-cytokine receptor signalling. Such approaches allow revealing how environmental factors and genetic susceptibility lead to convergence on the same pathways and identify the biological processes missed by single data analysis. Recently, multi-omics and single-cell studies identified molecular and cell heterogeneity in AS [23].

Network pharmacology: a multi-target approach

Network pharmacology makes use of system-level thinking in studying drug-targets and disease-related molecular networks. Instead of assuming a simplistic one-drug-one-target model, the approach considers how a certain therapeutic compound affects multiple interacting proteins and signalling pathways. This is especially applicable for AS because the disease pathogenesis

involves several interacting inflammatory and tissue remodelling pathways.

Tools like STRING, STITCH, Cytoscape, and NetworkAnalyst can be employed in constructing protein-protein interaction networks and drug-target networks, identifying hub proteins, and carrying out functional/pathway enrichment analysis. Some of the target genes of therapeutic compounds discovered through network pharmacology include TNF, IL-6, STAT3, PTGS2, and other components of NF-κB and JAK-STAT signalling. For instance, through network analysis of the effects of Salvia miltiorrhiza, TNF, IL-6, STAT3, PTGS2, and VEGFA were identified as potential targets, along with the TNF, NF-κB, JAK-STAT, PI3K-AKT, and MAPK signalling pathways [24].

Combining multi-omics

Because it incorporates information from genomes, transcriptomics, proteomics, metabolomics, epigenomics, and single cell analysis, this multi-omics integration offers a far more thorough explanation of AS. The computational tools will be able to establish connections between genetic variants and their impact on gene expression, protein levels, metabolism, and cell phenotype, thus allowing for the discovery of possible causative pathways and molecular subtypes.

Tools like iCluster and Multi-Omics Factor Analysis (MOFA) will enable researchers to uncover common molecular signatures across various omics layers. Recent research shows that the integration of proteomics, metabolomics, lipidomics, and single-cell analyses will be able to uncover disease pathways and possible biomarker candidates for AS [25].

Biomarker identification through networks and artificial intelligence

Systems biology and networks can help discover molecular hub genes and candidate biomarkers that can be further evaluated via machine learning techniques. Genes or proteins that have highly connected networks in diseases can become interesting candidates as potentially biologically important regulators and biomarkers. Machine learning methods like support vector machines, random forest, logistic regression, gradient boosting, and artificial neural networks can be used for their assessment.

Artificial intelligence (AI) allows for analysing heterogeneous clinical and molecular data that may be difficult to detect using traditional statistical methods. Machine learning models have been explored in AS for classifying patients and predicting the outcomes of treatment [26].

Polypharmacology and drug repurposing

The computational approach provided by network pharmacology is also useful in drug repurposing, in which approved drugs are investigated for their potential action against disease-related targets or pathways. Databases such as DrugBank and the Connectivity Map (CMap) can be used together with disease genes and networks to find candidate drugs.

Repurposing strategies using computations can also focus on molecules that affect AS-related pathways, such as AMPK, mTOR, JAK-STAT, NF-κB, and Th17 pathway signalling. Predictions made by computation can help reduce costs and time involved in drug discovery due to the presence of information regarding pharmacology and safety. However, computational predictions need to be validated through experiments and clinical trials [27].

Personalized systems medicine

A combination of systems biology, multi-omics, and AI forms the foundation of personalized systems medicine for AS. Patients suffering from AS show substantial diversity in relation to their genetic makeup, inflammatory status, clinical manifestation, course of the disease and drug response. The computational modelling approach can incorporate all these data to reveal subpopulations of patients and predict the response to treatment.

Machine learning analysis showed that it was possible to predict the response to TNF inhibitors using the baseline clinical data. In the future, using multi-omics profiles along with longitudinal data, it would become possible to make exact predictions about the disease course, therapeutic efficacy and the risk of complications.

Overall, systems biology, network pharmacology, multi-omics, and AI represent complementary approaches to studying the complex molecular structure of AS. Through combining genetic polymorphism, signalling pathways, molecular interactions and clinical manifestations, these approaches may substantially help in the discovery of biomarkers, therapeutic targets, drug repositioning and personalized treatment. However, problems related to heterogeneity of datasets, small sizes of cohorts, external validation, integration and interpretation of the AI models need to be addressed [28].

Drug discovery and repositioning in *ankylosing spondylitis*

Drug discovery for *ankylosing spondylitis* (AS) is a challenging task due to the complexity of the genetic background, heterogeneous clinical manifestations, and numerous inflammatory and skeletal mechanisms underlying the pathology. A bioinformatics approach can contribute to the acceleration of early drug discovery stages through the combination of data from genomics, transcriptomics, proteomics and structural studies to choose targets and compounds before experimental validation [29].

***In silico* selection of disease-related therapeutic targets**

Selection of disease-related therapeutic targets is an important step in the AS drug discovery process. A combination of the data obtained from the above-mentioned approaches such as GWAS, transcriptomics, proteomics and network analysis will aid in

identifying the disease-associated genes and proteins. Targets such as ERAP1, IL23R, TNF, and the components of the IL-17 pathway should be considered since their involvement in antigen presentation and inflammatory processes has particular importance [30]. Structural bioinformatics, molecular docking and molecular dynamics can help in analyzing the structure of the target protein and ligand-binding site.

***In silico* drug repurposing**

Drug repurposing implies investigation of already approved drugs for a new use. Computational approaches such as network pharmacology, molecular docking, transcriptomic signature matching, and similarity analysis via machine learning are capable of identifying those drugs that can have an effect on pathways associated with AS. Repurposed drugs can have several benefits since some information about their pharmacological and safety profile is available.

Pharmacophore modelling and QSAR

Pharmacophore modelling helps to define important chemical and geometrical aspects of interaction with the biological target, while quantitative structure–activity relationship (QSAR) study allows relating molecular properties with biological activity. This can be used to optimize compounds affecting inflammatory pathways and select active molecules. In addition, computational approaches have been applied to natural compounds such as flavonoids and alkaloids as inflammatory signalling pathway modulators [31]. Nevertheless, the medicinal value of these compounds should be further verified experimentally and clinically.

Computational ADMET prediction

ADMET prediction plays an important role in selecting potential drug targets since it allows one to estimate how effective the selected compounds will be in vivo and avoid time-consuming laboratory experiments with inappropriate candidates. Tools such as SwissADME, pkCSM, and ADMETlab allow the prediction of physicochemical, pharmacokinetic, and toxicity properties.

Figure 3: This image shows an in-silico drug discovery pipeline for *Ankylosing Spondylitis* (AS), where data is collected, potential drug targets are identified, molecules are designed and tested through simulations, toxicity is predicted, and finally candidate drugs are selected for experimental validation. In short, it is a step-by-step computer-based process to find and validate new treatments.

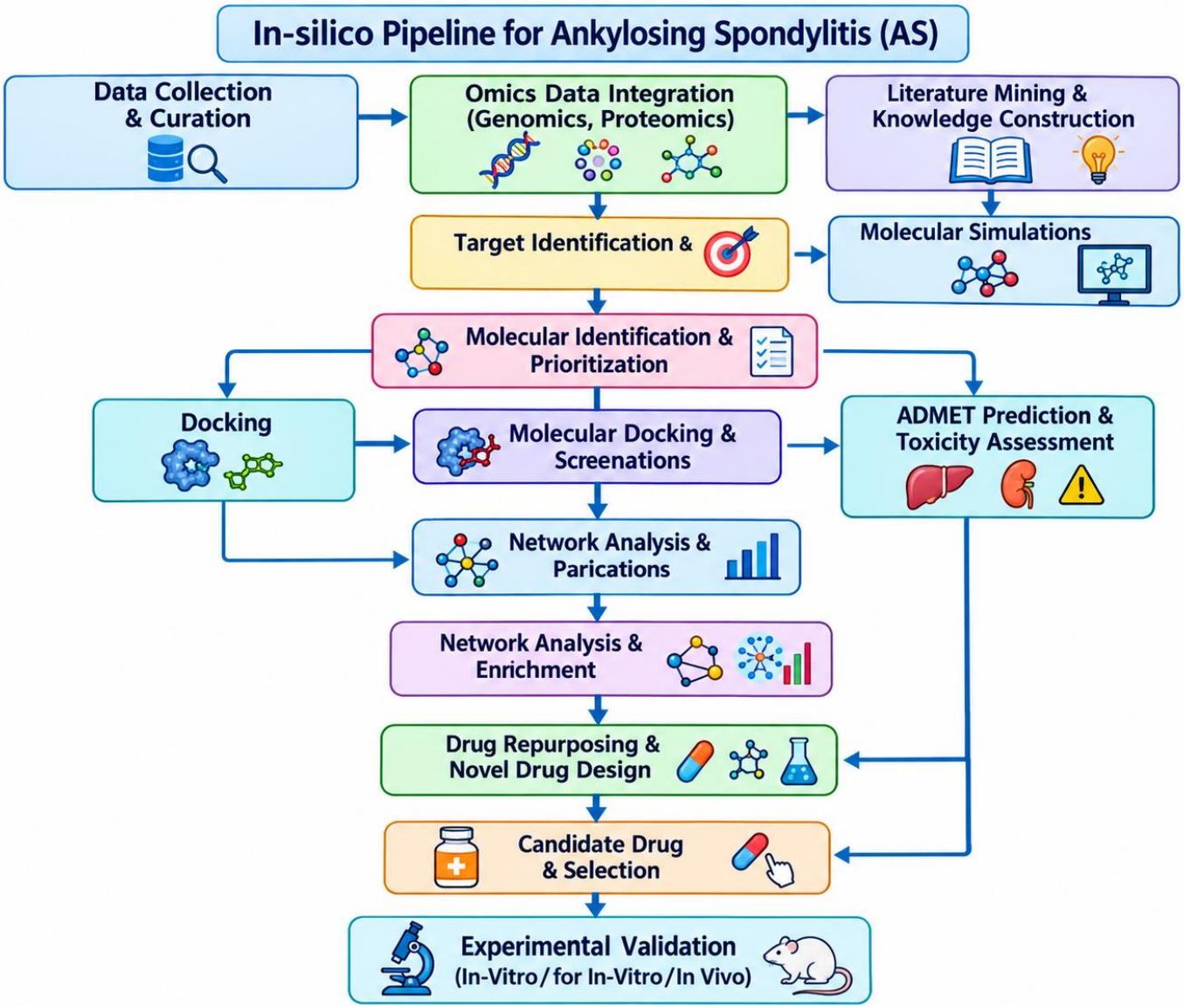


Table 1: Computational and In Silico strategies for *ankylosing spondylitis*

Computational approach	Application in AS	Potential contribution
Genomics & bioinformatics	Identification of disease-associated genes and pathways	Target and biomarker discovery
Proteomics & structural modelling	Protein characterization and target–ligand interactions	Drug discovery
Systems biology & network pharmacology	Integration of molecular pathways	Multi-target therapy and repurposing
Clinical translation & personalized medicine	Patient stratification and response prediction	Precision treatment
Ethical considerations	Privacy, consent and equity	Responsible translation

Systems pharmacology and polypharmacology

AS is related to the interaction of different pathways such as TNF, IL-17, JAK-STAT, NF-κB, and bone remodelling pathways. In this case, systems pharmacology and polypharmacology allow one to identify compounds that are able to regulate multiple disease-related targets [32].

Humanitarian & global health implications

The use of computational techniques in drug discovery and repurposing may help decrease the costs associated with early screening, select promising compounds, and possibly accelerate the process of developing new drugs. These potential advantages can contribute to the development of more accessible medicines, especially when resources are limited. Nonetheless, the results provided by computational methods should be viewed as an initial step and need to be proven experimentally as well as clinically. Therefore, combining computational methods with experiments and clinical trials is a promising approach [33].

DISCUSSION

Literature review reveals a change in approach from reductionism to systems biology regarding AS, in which genetics, immunity, environment, and microbiome interact to result in AS pathogenesis. The incorporation of different omics technologies, like genomics, transcriptomics, proteomics, etc., has resulted in the identification of pathways other than HLA-B27, including ERAP1, IL-23/IL-17, TNF, and NF-κB pathways. In silico methods like molecular docking, virtual screening, network pharmacology, and drug repositioning can potentially help in fast-tracking target identification and prioritization and save costs at the early stage of drug development. The application of artificial intelligence and machine learning in increasing numbers may aid biomarker discovery, patient stratification, and drug responsiveness prediction, and thus may contribute to the development of precision medicine. Still, the computer-based predictions should be subject to experimental and clinically validated testing, as well as be contingent on high-quality, representative, and interpretable data. Additionally, the aforementioned technologies may potentially help lower barriers in research in under-resourced settings, despite the necessity for the equitable availability of the resultant technologies and drugs. Finally, the rise of the use of genomic and clinical data is associated with many privacy, informed consent, algorithmic bias, and data governance issues. Future research in the field of AS will benefit from new technologies, such as digital twins, federated learning, and multi-omics data integration models, assuming that they will be developed in an ethical manner.

CONCLUSION

In silico techniques are vital for researching *ankylosing spondylitis* (AS) since they bridge molecular and clinical aspects. They apply genomics, proteomics, systems biology, molecular docking, and artificial intelligence, and aid in comprehension of complex AS mechanisms, expedite treatment development, and provide targeted treatment. Besides, they lower costs, reduce animal testing, and broaden access to healthcare in resource-limited countries.

Use of Digital twin modelling with advanced multi-omics may be optimized for AS by incorporating customized, algorithm-driven, privacy-preserving systems for therapy response prediction and flexible switching. Global validation, validation against diverse datasets, and patient confidentiality are critical challenges. The data ecosystems for trustworthy, responsible use with fair-just collaborations, equitable benefit-sharing, and resolution of these challenges are essential. The continued development of in silico methods reflects scientific evolution and ethical responsibility.

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Authorship

Bidisha Das- Original draft, original writing and formal analysis

Rojina Khatun-Resources, writing and editing

Malavika Bhattacharya-Supervisor

Declaration

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REFERENCES

1. Ward LM, Weber DR, Munns CF, et al, 2020. A Contemporary View of the Definition and Diagnosis of Osteoporosis in Children and Adolescents. J Clin Endocrinol Metab. 105(5), Pages e2088–97. Doi: 10.1210/clinem/dgz294.

2. Henares O, Pflimlin A, Romand X, 2022. Urolithiasis in *ankylosing spondylitis*: A meta-analysis. Joint Bone Spine. 89(5), Page 105388. Doi: 10.1016/j.jbspin.2022.105388.

3. Colbert R A, DeLay M L, Layh-Schmitt G, et al, 2009. HLA-B27 misfolding and spondyloarthropathies. Prion. 3(1), Pages 15–26. Doi: https://doi.org/10.4161/pri.3.1.8072.

4. Bowness P, 2015. HLA-B27. Annu Rev Immunol. 33, Pages 29-48. Doi: 10.1146/annurev-immunol-032414-112110.

5. Chen Y, Li Y, Xu Y, et al, 2025. Revealing the role of natural killer cells in *ankylosing spondylitis*: identifying diagnostic biomarkers and therapeutic targets. Ann Med. 57(1), Pages 2457523. Doi: 10.1080/07853890.2025.2457523.

6. Sharip A, Kunz J, 2020. Understanding the Pathogenesis of Spondyloarthritis. Biomolecules. 10(10), Pages 1461. Doi: 10.3390/biom10101461.

7. Brown MA, Kenna T, Wordsworth BP, 2016. Genetics of *ankylosing spondylitis*--insights into pathogenesis. Nat Rev Rheumatol. 12(2), Pages 81-91. Doi: 10.1038/nrrheum.2015.133.

8. Kenyon M, Maguire S, Rueda Pujol A, et al, 2022. The genetic backbone of *ankylosing spondylitis*: how knowledge of genetic susceptibility informs our understanding and management of disease. Rheumatol Int. 42, Pages 2085–2095. Doi: https://doi.org/10.1007/s00296-022-05174-5.

9. Ranganathan V, Gracey E, Brown MA, et al, 2017. Pathogenesis of *ankylosing spondylitis* - recent advances and future directions. Nat Rev Rheumatol. 13(6), Pages 359-367. Doi: 10.1038/nrrheum.2017.56.

10. Tito RY, Cypers H, Joossens M, et al, 2017. Brief Report: Dialister as a Microbial Marker of Disease Activity in Spondyloarthritis. Arthritis Rheumatol. 69(1), Pages 114-121. Doi: 10.1002/art.39802.

11. Gilis E, Mortier C, Venken K, et al, 2018. The Role of the Microbiome in Gut and Joint Inflammation in Psoriatic Arthritis and Spondyloarthritis. J Rheumatol Suppl. 94, Pages 36-39. Doi: 10.3899/jrheum.18013.

12. Baeten D, Sieper J, Braun J, et al, 2015. Secukinumab, an interleukin-17A inhibitor, in *ankylosing spondylitis*. N Engl J Med. 373, Pages 2534–2548. Doi:10.1056/NEJMoa1505066.

13. Reinhardt A, Yevsa T, Worbs T, et al, 2016. Interleukin-23-Dependent γ/δ T Cells Produce Interleukin-17 and Accumulate in the Enthesis, Aortic Valve, and Ciliary Body in Mice. Arthritis Rheumatol. 68(10), Pages 2476-86. Doi: 10.1002/art.39732.

14. Gao Y, Li X. Luo F, et al, 2025. Integrative mass spectrometry-driven multi-omics and single cell technologies in *ankylosing spondylitis*: insights into pathogenesis, biomarker discovery, and precision medicine. Journal of translational autoimmunity. 11, Page 100319. Doi: https://doi.org/10.1016/j.jtauto.2025.100319.

15. Dai L, Xia L, Su G, et al, 2024. Identifying prioritization of therapeutic targets for *ankylosing spondylitis*: a multi-omics Mendelian randomization study. J Transl Med. 22(1), Pages 1115. Doi: 10.1186/s12967-024-05925-x.

16. Dehghan A, 2018. Genome-Wide Association Studies. Methods Mol Biol. 1793, Pages 37-49. Doi: 10.1007/978-1-4939-7868-7_4.

17. Yang L, Bo C, Chen M, et al, 2025. Multiomics Identifies Potential Biomarkers in *Ankylosing Spondylitis* Bone Formation. Hum Mutat. 2025 Aug 2025, Pages 8771129. Doi: 10.1155/humu/8771129.

18. Jing X, Fan L, Wang Y, et al, 2025. DNA methylation and transcriptome signatures of the FOXO1 gene in *ankylosing spondylitis*. Immunol Invest. 54(7), Pages 1152-1166. Doi: 10.1080/08820139.2025.2517814.

19. Song X, Reif J, 2019. Nucleic Acid Databases and Molecular-Scale Computing. ACS Nano. 13(6), Pages 6256-6268. Doi: 10.1021/acsnano.9b02562.

20. Li X, Li X, Wang H, 2023. Exploring hub pyroptosis-related genes, molecular subtypes, and potential drugs in *ankylosing spondylitis* by comprehensive bioinformatics analysis and molecular docking. BMC Musculoskelet Disord. 24(1), Page 532. Doi: 10.1186/s12891-023-06664-8.

21. Swati Chaudhary, Sobinder Singh, Rashmi Gupta, 2026. Role of Artificial Intelligence in bioinformatics: Revolutionizing molecular docking and DNA tokenization. Comput. Biol. Chem. 124, Doi: https://doi.org/10.1016/j.compbiolchem.2026.109217

22. Patel KN, Chavda D, Manna M, 2024. Molecular Docking of Intrinsically Disordered Proteins: Challenges and Strategies. Methods Mol Biol. 2780, Pages 165-201. Doi: 10.1007/978-1-0716-3985-6_11.

23. Yarıcı M, Karabekmez ME, 2026. Systems Biology of Metabolic Dysregulation in *Ankylosing Spondylitis* Using scRNA-Seq Data. OMICS. 30(3), Pages 146-157. Doi: 10.1177/15578100261424002.

24. Wang X, Wu L, Yu M, et al, 2025. Exploring the molecular mechanism of Epimedium for the treatment of *ankylosing spondylitis* based on network pharmacology, molecular docking, and molecular dynamics simulations. Mol Divers. 29(1), Pages 591-606. Doi: 10.1007/s11030-024-10877-x.

25. Gao Y, Li X, Luo F, et al, 2025. Integrative mass spectrometry-driven multi-omics and single cell technologies in *ankylosing spondylitis*: insights into pathogenesis, biomarker discovery, and precision medicine. J Transl Autoimmun. 11, Pages 100319. Doi: 10.1016/j.jtauto.2025.100319.

26. Adams LC, Bressem KK, Poddubnyy D, 2024. Artificial intelligence and machine learning in axial spondyloarthritis. Curr Opin Rheumatol. 36(4), Pages 267-273. Doi: 10.1097/BOR.0000000000001015.

27. Cousins HC, Nayar G, Altman RB, 2024. Computational Approaches to Drug Repurposing: Methods, Challenges, and Opportunities. Annu Rev Biomed Data Sci. 7(1), Pages 15-29. Doi: 10.1146/annurev-biodatasci-110123-025333.

28. Wang R, Dasgupta A, Ward MM, 2022. Predicting probability of response to tumor necrosis factor inhibitors for individual patients with *ankylosing spondylitis*. JAMA Netw Open. 5(3), Pages e222312. Doi: 10.1001/jamanetworkopen.2022.2312.

29. Zhang H, Fan Q, Zhang Y, et al, 2026. Prediction and in vitro validation of potential indications for ginkgolide B based on network pharmacology strategies. Chinese. 55(3), Pages 267-277. Doi: 10.3724/zdxbyxb-2025-0696.

30. You W, Lin Y, Liu M, et al, 2024. Investigating potential novel therapeutic targets and biomarkers for *ankylosing spondylitis* using plasma protein screening. Front Immunol. 15, Page 1406041. Doi: 10.3389/fimmu.2024.1406041.

31. Wang M, Liu B, Ren J, et al, 2025. Identification of plasma protein biomarkers for *ankylosing spondylitis* by integrating proteome with genome. Clinical rheumatology, 44(12), Pages 4921–4930. Doi: https://doi.org/10.1007/s10067-025-07726-z.

32. Dan X, Guan X, Hu H, et al, 2026. Multi-Omics Integration Identifies a Six-Gene Diagnostic Signature for *Ankylosing Spondylitis* via Metabolic-Immune Crosstalk. International journal of molecular sciences. 27(9), Page 3860. Doi: https://doi.org/10.3390/ijms27093860.

33. Du K, Zhang C Y, Li A, et al, 2025. Unraveling new therapeutic targets in *ankylosing spondylitis*: Multi-omics Mendelian randomization on immune cells, metabolites, and inflammation proteins. Medicine. 104(16), Page e42177. Doi: https://doi.org/10.1097/MD.0000000000042177.

34. Venerito V, Gupta L, Mileto S, et al, 2025. Ethical challenges and regulatory pathways for artificial intelligence in rheumatology. Rheumatology advances in practice. 9(2), Page rkaf035. Doi: https://doi.org/10.1093/rap/rkaf035.