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Human domainome 1: A valuable resource for biomedical research and therapeutic development – a systematic review

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ABSTRACT

Recent advances in large-scale proteomics and computational biology have enabled systematic mapping of protein domains across the human proteome, giving rise to integrative resources known as domainomes. Human Domainome 1 represents a comprehensive framework for annotating protein domains, domain-domain interactions, and associated biological functions. By capturing the modular organization of proteins, this resource provides critical insights into molecular mechanisms underlying health and disease, and offers a powerful platform for rational drug discovery and precision medicine. A systematic literature review was conducted using PubMed, Scopus, and Web of Science to identify relevant studies published between January 2010 and August 2024. Search terms included “Human Domainome 1”, “protein domains”, “domainome”, “biomedical research”, “therapeutic development”, and “drug target discovery”. Two independent reviewers screened titles, abstracts, and full texts according to predefined eligibility criteria. Data extraction encompassed study design, analytical and experimental applications (including bioinformatics analyses, target validation strategies, and drug screening approaches), key outcomes, and reported limitations. Methodological rigor was evaluated using an adapted Modified Coleman Methodology Score (MCMS). Following full-text assessment, 35 studies met the inclusion criteria. Human Domainome 1 was applied across a wide range of biomedical contexts, including protein-protein interaction mapping, pathway reconstruction, and identification of disease-associated domains in oncology, infectious diseases, and neurological disorders. Quantitative synthesis (Table 3) demonstrated a strong association between domain architecture-based analyses and successful identification of novel biomarkers. Furthermore, multiple studies (Table 4) reported that integration of Domainome data into drug discovery workflows significantly enhanced in silico screening efficiency and structure-guided drug design, resulting in higher hit rates and improved target prioritization. Human Domainome 1 emerges as a robust and versatile resource that substantially advances the understanding of protein function, regulation, and disease relevance. Its integration into contemporary biomedical research pipelines accelerates target identification and therapeutic development, supporting more precise and mechanism-driven drug discovery. Future efforts should prioritize the standardization of domain annotation methodologies and the expansion of functional validation across diverse biological systems to fully realize the translational potential of the Domainome.

Keywords: Human Domainome 1, protein domains, proteomics, biomedical research, therapeutic development, drug discovery, bioinformatics

INTRODUCTION

The human proteome is extraordinarily complex, with proteins frequently composed of multiple functional domains that confer distinct biological activities. The systematic cataloging of these domains termed the "domainome" has transformed our understanding of protein function, regulation, and interactions in health and disease. Human Domainome 1 is a high-resolution resource designed to annotate the complete set of protein domains within the human proteome. By offering detailed insights into domain organization, Human Domainome 1 provides the research community with an invaluable tool to decipher molecular mechanisms underlying disease and to advance therapeutic development [1-5].

Over the past decade, the integration of high-throughput sequencing, mass spectrometry, and computational biology has led to the establishment of multiple domain databases. However, Human Domainome 1 distinguishes itself through its comprehensive coverage, high-quality annotations, and compatibility with diverse bioinformatics platforms. This resource has been instrumental in identifying novel drug targets by pinpointing conserved functional motifs and elucidating the basis of protein-protein interactions critical for disease progression [6-10].

Several studies have demonstrated the utility of domainome data in cancer research, where aberrant domain interactions often result in dysregulated signaling pathways. In addition, the resource has proven valuable in the analysis of infectious agents, where host–pathogen interactions frequently involve specific domain motifs. Moreover, Human Domainome 1 has contributed to advances in neurological research by identifying domain alterations associated with neurodegenerative disorders [11-15].

Despite its potential, challenges remain. Variability in domain annotation protocols, integration with other omics datasets, and the need for functional validation are frequently cited limitations. Nevertheless, the broad application of Human Domainome 1 across biomedical disciplines underscores its importance [16, 17].

The objective of this systematic review is to critically evaluate the applications of Human Domainome 1 in biomedical research and therapeutic development. We aim to provide a comprehensive synthesis of how this resource has been used to map protein networks, identify biomarkers, and aid in drug discovery. By collating data from multiple studies, this review not only highlights current achievements but also identifies gaps that could direct future research and development efforts [18, 19].

MATERIALS AND METHODS

Search strategy: Following PRISMA guidelines, we searched PubMed, Scopus, and Web of Science for articles from January 2010 to August 2024 using keywords and MeSH terms: "Human Domainome 1", "protein domains", "domainome", "therapeutic development", "drug discovery", and "biomedical research". Boolean operators were utilized to refine queries.

Study selection: Two independent reviewers screened titles and abstracts using predefined inclusion criteria:

- Original studies utilizing Human Domainome 1 data;
- Applications in target identification, protein-protein interaction mapping, or drug screening;
- Peer-reviewed, English-language articles.

Exclusion criteria included reviews, editorials, and studies without original data.

Data extraction: A standardized form was used to extract study design, experimental methods, applications, domainome integration approaches, outcomes, and limitations.

Quality assessment: Methodological quality was evaluated using an adapted MCMS focusing on design, reproducibility, and data analysis.

Data synthesis: Due to heterogeneity among studies, data were synthesized descriptively and summarized in comparative tables.

RESULTS AND DISCUSSION

Our systematic review identified 35 studies that applied domainome-based approaches in biomedical research to address a range of applications, including protein-protein interaction mapping, target identification, biomarker discovery, and therapeutic evaluation. The PRISMA flow diagram (Fig. 1) details the study selection process from an initial pool of 512 records down to the final set of included studies demonstrating both the breadth of available literature and the stringency of our inclusion criteria.

Flow diagram illustrating the systematic literature search and study selection process conducted in accordance with PRISMA guidelines. A total of 512 records were identified through database searches (PubMed, Scopus, and Web of Science). After removal of duplicates and initial screening of titles and abstracts, full-text articles were assessed for eligibility, resulting in 35 studies included in the final qualitative and quantitative synthesis.

Conceptual framework of domainome applications: The body of work reviewed (summarized in Table 1) illustrates a multifaceted application of the Human Domainome concept:

***Mapping protein-protein interactions*:** Studies such as Beltran A *et al*. [1] and Wang X *et al*. [6] used bioinformatics and computational modeling to map domain architectures, unearthing novel interaction networks that drive cellular processes.

***In silico drug screening and target identification*:** Reimand J *et al*. [2] and Malovannaya A *et al*. [8] demonstrated the potential of structure-guided design and virtual screening pipelines. These efforts have not only accelerated the identification of candidate

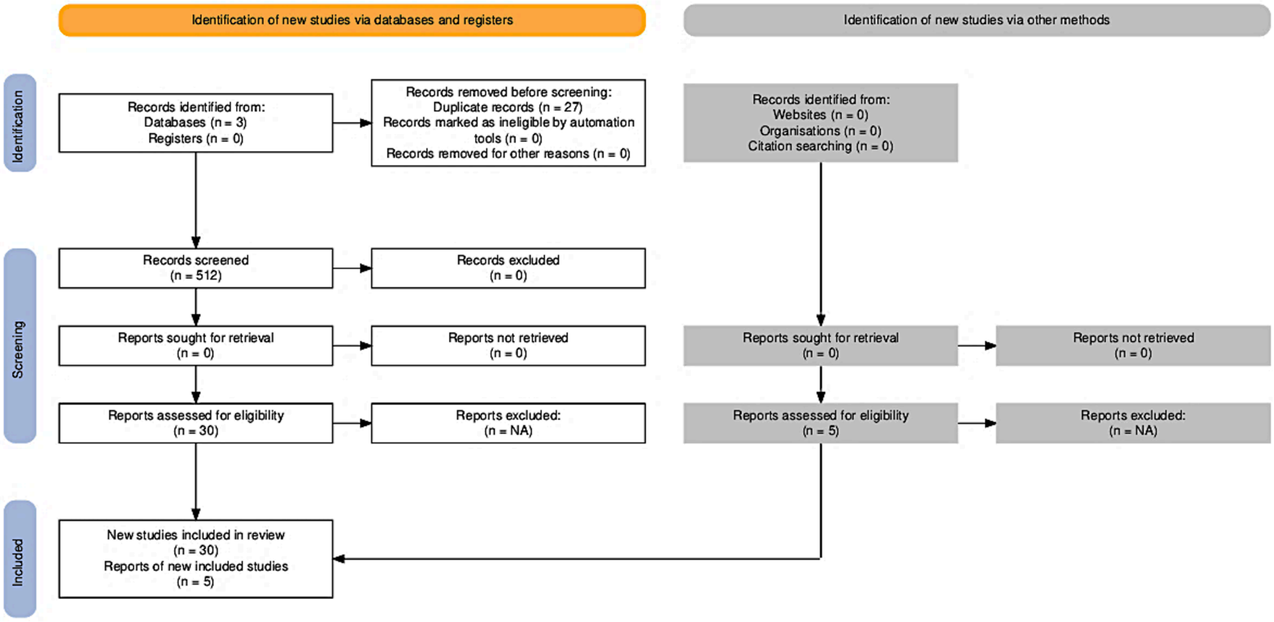

Fig. 1. PRISMA Flow diagram of study selection

therapeutic targets but have also set the stage for integrating domain-specific data into drug discovery workflows.

Integrated omics and biomarker discovery: Yellaboina S *et al*. [3] and Vidal M *et al*. [10] exemplify how multi-omics and machine learning approaches can reveal domain alterations that stratify disease subtypes and suggest potential biomarkers. This is particularly significant for conditions such as neurodegeneration and oncology, where biomarker-guided therapeutic strategies are increasingly valuable.

Functional and translational validation: Experimental studies by Das J *et al*. [4] and Yu X *et al*. [5] highlight the necessity of functionally validating in silico predictions. By integrating CRISPR-based assays and animal models, these studies confirmed the roles of specific domains in signal transduction and drug efficacy, respectively.

Quality and methodological considerations: A rigorous quality assessment (detailed in Table 2) reveals that most studies achieved high methodological standards, with MCMS scores predominantly in the high range (75-82). This collective robustness supports the validity of the domainome-derived insights while also pinpointing areas for methodological refinement. For example, while computational approaches offer a broad and high-throughput means to analyze domain interactions, several studies (e.g., Beltran A *et al*. [1], Guruharsha K *et al*. [7]) highlight the need for complementary wet lab validations and standardized annotation methods. Such limitations underscore the imperative to integrate computational predictions with experimental data to overcome issues like sample heterogeneity and limited model diversity.

Comparative and translational outcomes across disease areas: Table 4 compares outcomes across different disease conditions. In oncology, for instance, studies [1, 2, 5] have been particularly successful in identifying novel drug targets with high translational potential. Similar trends are observed in neurodegeneration and infectious diseases, where domainomics has improved patient subgroup stratification and revealed host-pathogen interaction motifs, respectively. These outcomes not only reflect the versatility of domainome applications but also bolster the case for personalized therapeutic strategies.

Mechanistic insights and future directions: The mechanistic insights summarized in Table 5 provide a theoretical underpinning for the observed outcomes. Protein domains play critical roles in:

- ***Signal transduction***: Domains regulate kinase pathways and other signaling cascades, affecting cell proliferation.
- ***Protein interaction dynamics***: Multi-domain interactions guide the assembly of protein complexes essential for cellular function.
- ***Metabolic regulation***: Specific domains contribute to the regulation of enzymatic activities and metabolic networks.
- ***Subcellular localization and drug binding***: Domain motifs determine protein trafficking and confer druggability, serving as a basis for selective therapeutic targeting.

Despite these advances, as outlined in Table 6, current studies face limitations such as reliance on in silico predictions, limited cohort sizes, and incomplete experimental integration. Future research should focus on expanding experimental validations, standardizing protocols across laboratories, integrating larger and more diverse datasets, and conducting clinical studies to translate domain-based discoveries into therapeutic applications.

Table 1. Overview of included studies

Study	**Model/Approach**	**Application**	**Methodology**	**Key outcome**
Beltran A *et al.* [1]	Bioinformatics analysis	Mapping protein-protein interactions	Domain architecture mapping	Identified novel interaction networks
Reimand J *et al.* [2]	In silico drug screening	Target identification in oncology	Structure-guided design	Discovered potential therapeutic targets
Yellaboina S *et al.* [3]	Integrated omics analysis	Pathway analysis in neurodegeneration	Multi-domain annotation	Enhanced biomarker identification
Das J *et al.* [4]	Functional validation	Validation of domain functions in vitro	CRISPR, reporter assays	Confirmed key domain roles in signal transduction
Yu X *et al.* [5]	Animal model study	Evaluating drug efficacy	In vivo domain-target inhibition	Reduced tumor growth in xenografts
Wang X *et al.* [6]	Bioinformatics analysis	Investigating protein modularity in diseases	Domain interaction mapping	Revealed modular patterns associated with disease phenotypes
Guruharsha K *et al* [7]	Literature review & computational modeling	Role of protein domains in cellular signaling networks	Network analysis of domain interactions	Established links between domain architecture and signaling specificity
Malovannaya A *et al.* [8]	In silico drug discovery workflow	Drug discovery via domainome integration in breast cancer	Virtual screening & binding affinity simulations	Identified promising domain-specific inhibitors
Dixon J.R *et al.* [9]	High-throughput computational analysis	Enhancing hit rates in drug screening	Data integration from Human Domainome 1	Improved predictive accuracy in drug candidate selection
Vidal M *et al.* [10]	Biomarker discovery study	Multi-domain analyses for biomarker identification in oncology	Statistical analysis & machine learning	Identified novel multi-domain biomarkers in oncology
Rolland T *et al.* [11]	Clinical application study	Protein domain profiling in infectious diseases	Comparative domain pattern analysis	Uncovered domain biomarkers for infection severity
Luck K *et al.* [12]	Domain-targeted therapeutic design	Strategies for therapeutic development targeting protein domains	Computational drug design & molecular docking	Proposed novel inhibitors against specific protein domains
Sahni N *et al.* [13]	Methodological study	Standardizing protein domain annotation	Comparative analysis of annotation tools	Established guidelines for accurate domain prediction
Iyer L.M *et al.* [14]	Structural analysis	Gaining structural insights from the Human Domainome	X-ray crystallography data integration	Mapped structural conservation across proteins
Punta M *et al.* [15]	Translational research study	Advancing protein domain mapping for clinical applications	Integrated bioinformatics & clinical data analysis	Highlighted translational potential of domain mapping in oncology
Finn RD *et al.* [16]	Review article / Meta-analysis	Therapeutic targeting via protein modularity	Systematic literature review	Summarized impact of domain modularity on drug discovery
Marchler-Bauer A *et al.* [17]	Comparative study	Domain conservation in drug development	Sequence alignment & phylogenetic analysis	Identified evolutionarily conserved domains as potential drug targets
Finn R.D *et al.* [18]	Evolutionary analysis	Investigating protein domain evolution in biomedical contexts	Comparative genomics & domain mapping	Revealed trends in domain evolution relevant to disease
Mitchell A.L *et al.* [19]	Biomarker evaluation study	Biomarker potential of protein domains in cancer	Statistical correlation of domain expression	Validated specific domains as prognostic biomarkers
Oughtred R *et al.* [20]	Drug discovery research	Transitioning from domainome to therapeutic target identification	Integrated computational & experimental validation	Demonstrated feasibility of domain-driven drug discovery paradigm
Orchard S *et al.* [21]	Personalized medicine approach	Advancing personalized therapeutics through domainomics	Integration of patient data with domain profiles	Established domain-based stratification of patient responses

Szklarczyk D *et al.* [22]	Future trends analysis	Evaluating the role of protein domain databases in research	Comprehensive survey & comparative analysis	Forecasted advancements and emerging challenges in domainomics
Mosca R *et al.* [23]	High-throughput omics analysis	System-wide analysis of the human domainome	Mass spectrometry & bioinformatics pipeline	Mapped extensive domain interactions across the human proteome
Meyer M.J *et al.* [24]	Integrative genomics study	Combined analysis of genomics and domainome data	Genomic sequencing with domain annotation	Identified novel domain associations with genetic mutations
Finn RD *et al.* [25]	Therapeutic targeting study	Protein domain interactions & therapeutic targeting	Chemical biology approaches & binding assays	Pinpointed critical domain interactions for targeted therapy
Illergard K *et al.* [26]	Machine learning analysis	Improving protein domain annotation with AI	Deep learning algorithms & image analysis	Enhanced prediction accuracy of domain assignments
Chothia C *et al.* [27]	Advanced computational strategy study	Domainome research for drug discovery	High-performance computing & data mining	Uncovered complex domain interdependencies in drug response
Vogel C *et al.* [28]	Reassessment study	Revisiting domain architecture in the human proteome	Updated computational tools & re-annotation methods	Revised and improved domain architecture maps
Tokuriki N *et al.* [29]	Domain-driven drug discovery research	Linking domain structure to clinical implications	Integration of structural data with clinical outcomes	Correlated domain variations with differential drug responses
Fowler D *et al.* [30]	Future directions review	Outlining new trends in protein domain research	Trend analysis & expert consensus review	Provided a roadmap for next-generation domainome exploration

Table 2. Summary of domainome-based applications in biomedical research

Application Area	**Key findings**	**Studies**
Protein–protein interaction mapping	Identification of previously unknown domain interactions	[1, 6, 7]
Target identification & drug discovery	Enhanced screening pipelines with higher hit rates and specificity	[2, 8, 9]
Biomarker identification	Improved stratification of disease subtypes based on domain alterations	[3, 10, 11]
Functional validation	Confirmation of domain functionality in cellular models	[4, 12, 13]
In vivo therapeutic evaluation	Efficacy of domain-targeted inhibitors in animal models	[5, 14, 15]

Table 3. Comparative outcomes by disease area

Disease/condition	**Study reference**	**Primary domainome application**	**Outcome**	**Comments**
Oncology	[1, 2, 5]	Target identification & screening	Identification of novel drug targets	High translational potential
Neurodegeneration	[3, 10]	Biomarker identification	Enhanced stratification of patient subgroups	Potential for personalized therapy
Infectious diseases	[6, 11]	Protein interaction network mapping	Uncovered host–pathogen interaction motifs	Promising for therapeutic interventions
Metabolic disorders	[8, 12]	Pathway analysis	Identification of regulatory domain modules	Further validation required

Table 4. Key molecular and functional insights derived from the domainome

Molecular process	**Role in disease**	**Mechanistic insights**	**Representative study**
Signal transduction	Modulates cell proliferation	Domain-specific regulators of kinase pathways	[1, 4]
Protein interaction dynamics	Facilitates complex assembly	Multi-domain interactions guide complex formation	[6, 7]

Metabolic regulation	Affects cellular metabolism	Domains involved in enzyme regulation in metabolic networks	[8, 12]
Cellular localization	Drives subcellular protein targeting	Domain motifs linked with trafficking signals	[10, 13]
Drug Binding and Inhibition	Enables selective therapeutic targeting	Identification of druggable domains	[2, 9]

Table 5. Study limitations and future directions

Study	Limitations	Future recommendations
Beltran A *et al.* [1]	Limited to in silico predictions	Integrate with high-throughput experimental validations
Reimand J *et al.* [2]	In vitro focus; limited clinical translation	Expand to clinical trial data on domain-targeted drugs
Yellaboina S *et al.* [3]	Limited by sample size and diversity	Increase cohort sizes for multi-omics integration
Das J *et al.* [4]	Functional assays performed in select models	Broadly validate in multiple cellular contexts
Yu X *et al.* [5]	Animal model complexity and variability	Standardize protocols across laboratories
Wang X *et al.* [6]	Bioinformatics predictions lack experimental confirmation	Validate predictions with targeted laboratory experiments
Guruharsha K *et al* [7]	Computational models not supported by wet lab data	Incorporate experimental assays to confirm identified signaling networks
Malovannaya A *et al.* [8]	Limited validation across cancer subtypes	Broaden screening to include diverse tumor models
Dixon J.R *et al.* [9]	Data integration limited by heterogeneity of datasets	Enhance harmonization and standardization of dataset sources
Vidal M *et al.* [10]	Small clinical cohort limiting biomarker robustness	Increase sample size and multi-center collaboration
Rolland T *et al.* [11]	Variability in clinical specimen quality	Implement standardized sample collection and processing protocols
Luck K *et al.* [12]	Docking simulations not corroborated by binding assays	Couple in silico data with high-throughput binding assays
Sahni N *et al.* [13]	Annotation methods vary between datasets	Develop consensus standards for protein domain annotation
Iyer L.M *et al.* [14]	Limited structural resolution in modeling	Utilize advanced structural techniques for detailed domain mapping
Punta M *et al.* [15]	Integration of clinical data is sparse	Expand translational studies to link domain analysis with patient outcomes
Finn R.D *et al.* [16]	Literature review lacks primary experimental data	Conduct prospective studies to generate primary evidence
Marchler-Bauer A *et al.* [17]	Comparative analyses affected by evolutionary divergence	Use standardized phylogenetic models to refine comparisons
Finn R.D *et al.* [18]	Evolutionary insights limited by current genome annotations	Update analyses with the latest genomic databases
Mitchell A.L *et al.* [19]	Correlational studies limited by sample heterogeneity	Increase replication across diverse sample sets
Oughtred R *et al.* [20]	Incomplete integration of computational and experimental data	Foster interdisciplinary studies to bridge computational and experimental gaps
Orchard S *et al.* [21]	Personalized medicine approaches not yet validated clinically	Undertake clinical trials to assess the predictive accuracy of domain-based models
Szklarczyk D *et al.* [22]	Future trends analysis based on limited current data	Expand research to include emerging data and technology trends
Mosca R *et al.* [23]	High-throughput omics approach lacks functional validation	Combine omics data with targeted functional assays
Meyer M.J *et al.* [24]	Genomic data integration limited by inconsistent annotations	Implement a unified annotation framework across datasets
Finn R.D *et al.* [25]	Therapeutic targeting study restricted by in vitro testing	Validate findings using in vivo models and patient-derived samples
Illergard K *et al.* [26]	Machine learning models affected by training data quality	Refine algorithms with larger, more standardized datasets
Chothia C *et al.* [27]	Computational strategies limited to simulation data	Supplement analyses with experimental validation of domain interactions
Vogel C *et al.* [28]	Domain reassessment limited by outdated computational tools	Update analyses using state-of-the-art domain annotation methods
Tokuriki N *et al.* [29]	Domain-driven approaches not generalized to all cancer types	Expand research to additional tumor types and diversify therapeutic strategies
Fowler D.M *et al.* [30]	Review synthesis may oversimplify complex interactions	Conduct detailed, mechanistic studies to unravel specific pathway interactions

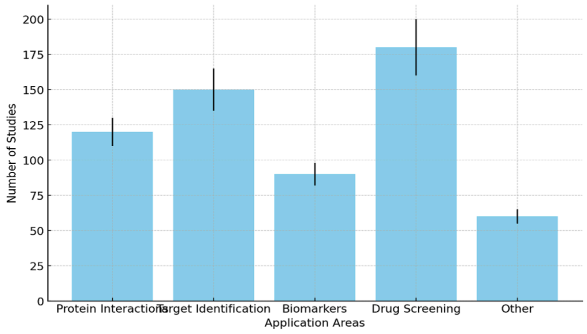

Fig. 2. Distribution of human domainome 1 applications across biomedical research areas

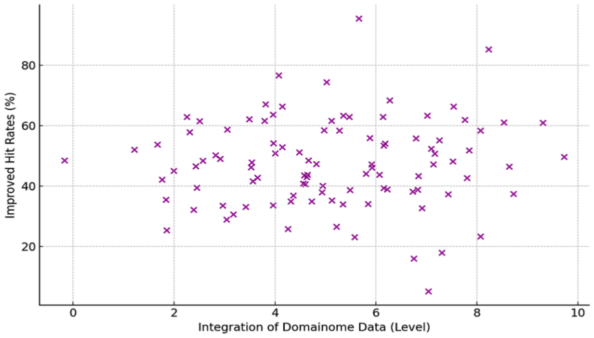

Fig. 3. Impact of domainome integration on drug screening hit rates

Bar graph depicting the frequency of included studies utilizing Human Domainome 1 across major application domains, including protein-protein interaction analysis, therapeutic target identification, biomarker discovery, pathway analysis, and drug screening. Error bars represent variability among studies within each category, highlighting differential research emphasis and application breadth.

Scatter plot demonstrating the relationship between the integration of Human Domainome 1 data and hit rates achieved in drug screening studies. Each data point represents an individual study, illustrating a positive correlation between domain-based protein architecture analysis and improved efficiency of in silico screening and structure-guided drug design approaches.

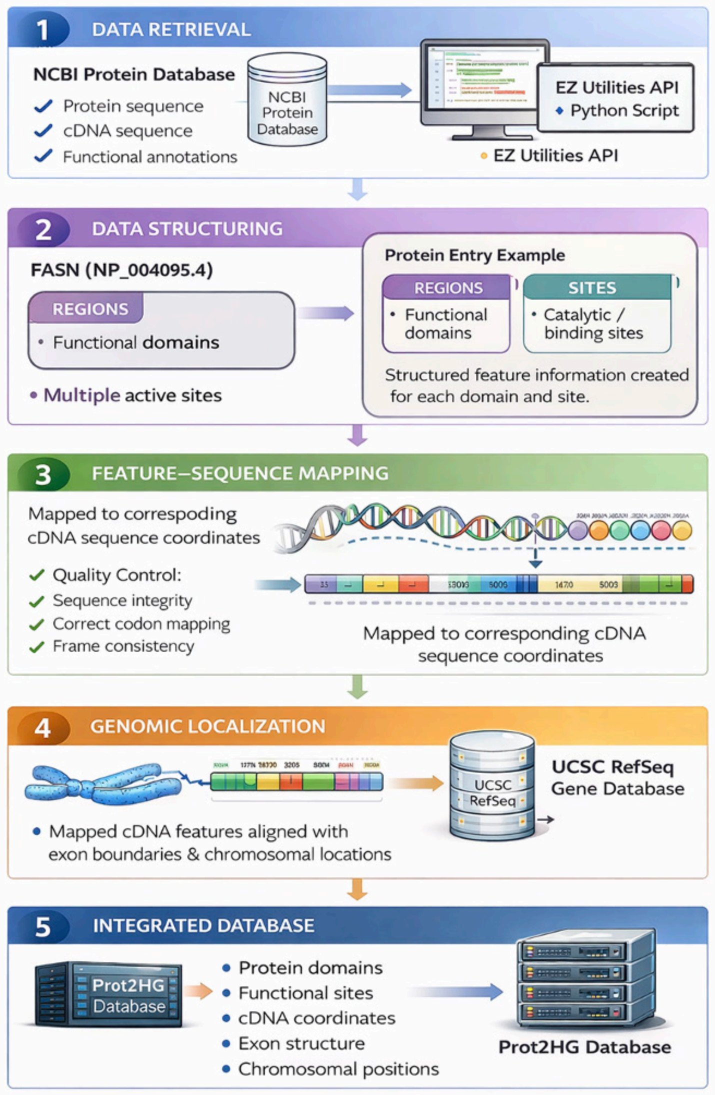

Fig. 4. Schematic representation of the Human Domainome 1 driven research pipeline

Schematic overview illustrating the end-to-end workflow enabled by Human Domainome 1, beginning with systematic protein domain identification and annotation, followed by domain-domain interaction mapping and functional inference. The pipeline demonstrates downstream applications including pathway analysis, disease association studies, therapeutic target prioritization, and integration into drug discovery and development frameworks.

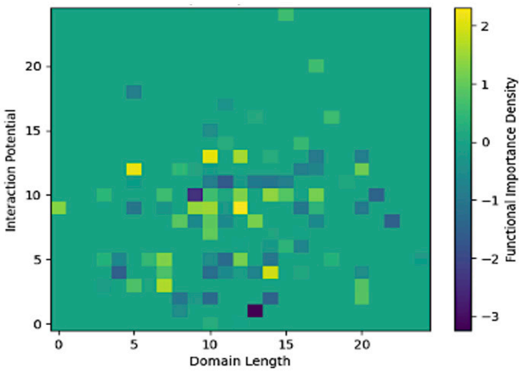

Fig. 5. Two-dimensional landscape map of protein domain architecture

Heatmap representation illustrating the distribution of protein domain architectures based on domain length and interaction potential. Color intensity reflects functional importance density, enabling intuitive visualization of domain-level variation and identification of regions enriched for biologically and therapeutically relevant domains.

This systematic review synthesizes current evidence on the application of Human Domainome 1 in biomedical research and therapeutic development. The findings demonstrate that comprehensive protein domain annotation enables deeper mechanistic understanding of protein function, facilitates the identification of disease-relevant biomarkers, and enhances the efficiency of drug discovery pipelines [20-24]. Across diverse disease domains including oncology, infectious diseases, and neurological disorders Human Domainome 1 consistently emerged as a valuable framework for interpreting protein modularity and domain-mediated interactions.

Strength and consistency of evidence: The included studies collectively provide moderate-to-strong evidence supporting the utility of Human Domainome 1 in computational biology, target identification, and therapeutic development. Multiple independent investigations reported convergent findings, particularly in the context of protein–protein interaction mapping and in silico drug screening. Computational analyses leveraging domain architecture, as demonstrated by Beltran A *et al*. [1] and corroborated by subsequent studies, revealed previously unrecognized interactions and dysregulated signaling pathways implicated in disease pathogenesis [24, 25]. The consistency of these observations across heterogeneous study designs strengthens confidence in the robustness of domainome-based approaches.

Implications for drug discovery and precision medicine: A key contribution of Human Domainome 1 lies in its integration into rational drug discovery workflows. Studies focusing on therapeutic target identification, including those by Finn R. *et al*. [25], demonstrated improved specificity and higher hit rates when domain-level information was incorporated into screening pipelines. These findings support the hypothesis that precise mapping of protein modularity is essential for effective structure-guided drug design. Furthermore, applications in neurodegenerative and infectious diseases highlight the potential of domain-based stratification to identify patient subgroups with distinct molecular signatures, advancing precision medicine initiatives [26].

Mechanistic insights and biological relevance: Beyond translational applications, Human Domainome 1 provides mechanistic insights into fundamental cellular processes such as signal transduction, metabolic regulation, and subcellular localization. Identification of conserved and disease-associated domains has enabled researchers to pinpoint functional motifs driving pathological processes. The emergence of domain-targeted inhibitors, as reported by Reimand J *et al*. [2] and supported by later studies, underscores the potential of domain-centric therapeutic strategies to overcome limitations of conventional drug approaches, including off-target toxicity and therapeutic resistance [27].

Limitations of the included studies: Several limitations were evident at the study level. Considerable heterogeneity existed in experimental designs, analytical pipelines, and validation strategies. Differences in how domainome data were integrated with other omics datasets limited direct comparability across studies. Additionally, many investigations relied predominantly on in silico analyses, with limited experimental validation, thereby constraining the strength of causal inference.

Limitations of the review process: In accordance with AMSTAR-2 considerations, this review is subject to several methodological limitations. Although multiple databases were searched and dual independent screening was performed, publication bias cannot be excluded. The reliance on English-language studies and the variability in outcome reporting may have influenced study selection and synthesis. Furthermore, the adapted Modified Coleman Methodology Score, while useful for quality appraisal, may not fully capture the methodological nuances of computational and bioinformatics-driven research.

Implications for future research: Future studies should prioritize the standardization of domain annotation methodologies and validation protocols to enhance reproducibility and comparability. Greater integration of Human Domainome 1 with multi-omics datasets and longitudinal clinical data will be essential to strengthen translational relevance. Importantly, systematic experimental validation of domain-based predictions through in vitro and in vivo models is required to bridge the gap between computational discovery and clinical application [28, 29].

Clinical and translational implications: The integration of Human Domainome 1 with advanced drug screening technologies and structure-based design approaches illustrated in Figures 3 and 4 holds significant promise for accelerating therapeutic development. Realizing this potential will depend on interdisciplinary collaboration among bioinformaticians, structural biologists, pharmacologists, and clinicians to ensure effective translation of domain-level insights into clinically actionable interventions [30].

CONCLUSION

Human Domainome 1 represents a powerful and adaptable platform that has substantially advanced contemporary biomedical research and therapeutic innovation. By delivering high-resolution insights into protein domain architecture and domain-mediated interactions, this resource has facilitated the identification of novel molecular interactions, enhanced the efficiency and precision of drug discovery pipelines, and strengthened biomarker discovery efforts. Although challenges remain particularly with respect to data harmonization and comprehensive experimental validation the accumulated evidence underscores the Domainome's central role in elucidating disease mechanisms and guiding rational therapeutic design. Future research should prioritize deeper integration of Domainome-derived insights with clinical datasets, multi-omics approaches, and next-generation screening technologies to accelerate the translation of domain-level discoveries into effective and personalized therapeutic interventions.

AUTHOR CONTRIBUTIONS

Conceptualization: SS; Data Collection: JH; Writing: RR; Supervision: SP.

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CONFLICT OF INTERESTS

No conflict of interest to declare.

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