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Computational analysis of missense mutations in squalene epoxidase associated with terbinafine resistance in clinically reported dermatophytes

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Dermatophyte infections, as a significant public health threats, are increasingly associated with antifungal drug resistance, particularly to terbinafine. Mutations in the squalene epoxidase (*SQLE*) gene have been linked to resistance by altering amino acid residues and interfering with drug-protein interactions. This study applied computational tools including I-Mutant, ConSurf, HOPE, DynaMut2, STRING, and molecular docking to assess the structural and functional impact of clinically reported SQLE missense mutations in terbinafine-resistant dermatophyte isolates. Twelve out of fourteen mutations significantly reduced SQLE stability, with L393F, L393S, and F397L identified as the most destabilizing. ConSurf analysis revealed that residues F311, L393S, L393F, F397I, L437P, H440Y, and H440T were highly conserved, structurally buried, and essential for SQLE integrity, while V237I, F397L, and F415S were conserved but less critical. Notably, Q408L was identified as functionally significant and surface-exposed, underscoring its potential as a key contributor to resistance. Conserved regions were found to be more susceptible to functional disruption than non-conserved ones. HOPE analysis highlighted changes in size, charge, and hydrophobicity in the mutant residues, suggesting potential disruption of SQLE's functional architecture. Also, DynaMut2 analysis predicted decreased flexibility and stability in most mutants. Molecular docking identified altered binding pockets in four variants F397L, L437P, F415V, and Y394N compared to the wild-type, potentially compromising terbinafine binding. STRING network analysis revealed functional interactions between SQLE and ten proteins involved in ergosterol biosynthesis. These findings offer valuable molecular insights into terbinafine resistance mechanisms and identify conserved, mutation-sensitive sites that may guide antifungal drug development and resistance management strategies.

Keywords Dermatophytes, Terbinafine resistance, *SQLE* mutation, Computational tools

Superficial mycoses are the most common fungal infections in humans, affecting approximately 20–25% of the global population. Additionally, up to 70% of individuals may serve as asymptomatic carriers of these pathogens[1,2]. Dermatophytes, a group of keratinophilic fungi, are responsible for infections of the skin, hair, and nails as known as dermatophytosis. These infections impact millions worldwide and are becoming increasingly difficult to manage due to rising antifungal resistance. Antifungal resistance poses a significant barrier to the effective treatment of dermatophytosis. A major contributor to this resistance is the accumulation of genetic mutations in antifungal drug targets, which can prevent effective drug–protein interactions[3,4]. Terbinafine, an allylamine antifungal agent, is widely used as a first-line therapy against dermatophytes. Its mode of action involves the inhibition of squalene epoxidase (*SQLE*), a critical enzyme in the ergosterol biosynthesis pathway. Inhibiting *SQLE* leads to intracellular accumulation of squalene, depletion of ergosterol, and ultimately, fungal cell death[5]. However, clinical reports from regions such as India and the Middle East have identified an increasing number of terbinafine-resistant strains. These cases are frequently associated with missense mutations in the *SQLE* gene,

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which may reduce terbinafine's binding affinity and compromise its antifungal efficacy[5–14]. Despite these findings, the molecular mechanisms underlying how these mutations affect SQLE's structure, stability, and interaction with terbinafine remain unclear. Understanding how these mutations influence protein–ligand interactions is essential for developing new therapeutic strategies[15]. Computational methods provide a cost-effective and rapid alternative to experimental approaches for assessing the structural and functional consequences of mutations, particularly when structural data are limited. While many studies have focused on detecting genetic markers of resistance, few have performed an in-depth structural and bioinformatics analysis of *SQLE* mutations.

To address this gap, the present study investigates the effects of clinically reported *SQLE* missense mutations using a comprehensive computational approach. Tools such as I-Mutant, DynaMut2, ConSurf, HOPE, AlphaFold, STRING, and molecular docking were employed to predict the impact of mutations on protein stability, structural integrity, evolutionary conservation, and protein–protein interactions. These insights aim to inform experimental research and guide antifungal drug development strategies.

Results

Visualization of SQLE amino acid substitutions and drug susceptibility

SQLE mutations previously reported in terbinafine-resistant *Trichophyton* isolates were visualized using the MUTe_DRUG_spot tool. The lollipop plot (Fig. 1) illustrates the distribution and frequency of these mutations along the SQLE sequence, highlighting their potential correlation with terbinafine resistance phenotypes.

SQLE stability analysis

To evaluate the impact of missense mutations on SQLE stability, I-Mutant 3.0 was used to predict changes in Gibbs free energy ($\Delta\Delta G$). Out of 14 analyzed mutations, 12 were predicted to decrease protein stability ($\Delta\Delta G < -0.5$), indicating a destabilizing effect. Only two mutations—H440Y and S443P—were associated with increased protein stability (Table 1). Among the most destabilizing mutations were L393S, F415S, and F397L, suggesting that these substitutions may compromise protein integrity and function.

Structural and functional impact of mutations

Structural analysis using the HOPE server revealed that seven mutant residues (F397L, F397I, L393S, Q408L, F311L, F415S, and H440T) were smaller than the corresponding wild-type residues. These changes are likely to disrupt hydrophobic core interactions, creating cavities and weakening intramolecular stability. Conversely, larger mutations on the protein surface may interfere with intermolecular interactions, potentially impacting SQLE's ability to bind terbinafine effectively (Fig. 2).

Evolutionary conservation analysis

ConSurf analysis assessed the evolutionary conservation of each mutated residue to determine its potential functional importance. Residues F311L, L393S, L393F, F397I, L437P, H440Y, and H440T were identified as highly conserved and structurally buried, suggesting a critical role in SQLE function. Notably, Q408L was both highly conserved and surface-exposed, indicating potential involvement in substrate or inhibitor interactions. Other conserved residues included V237I, F397L, and F415S (Table 2, Fig. 3).
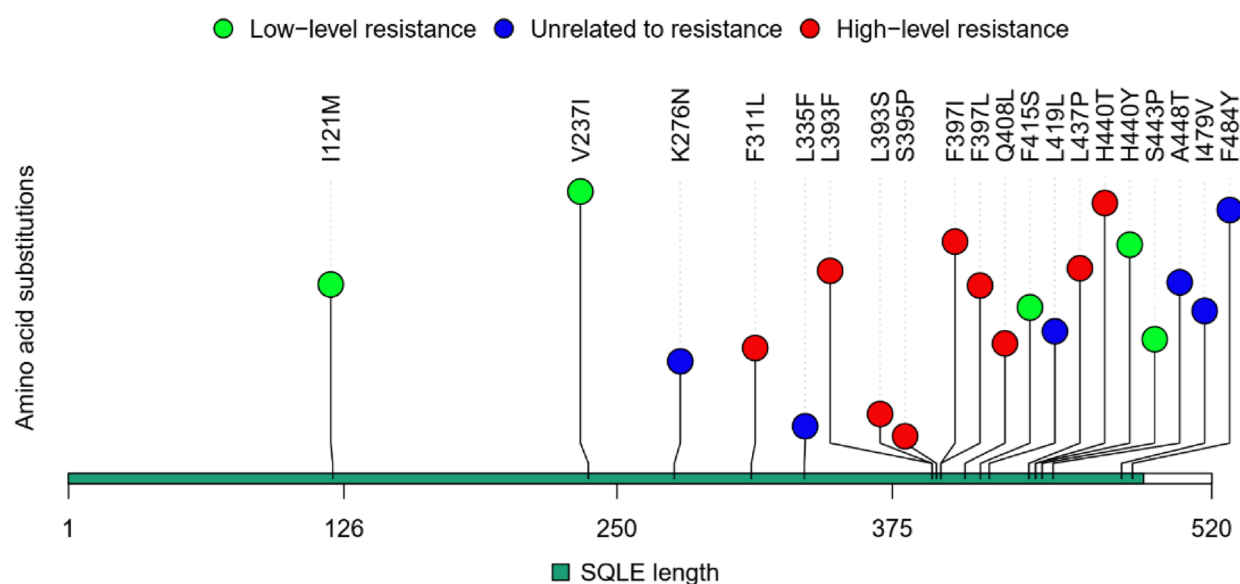

Fig. 1. Lollipop plot explains the number of SQLE amino acid substitutions in terbinafine susceptibility of *Trichophyton* sp.

SL	Variant	Stability	DDG
1	I121M	Decrease	− 1.55
2	V237I	Decrease	− 1.58
3	F311L	Decrease	− 1.82
4	L393F	Decrease	− 1.42
5	L393S	Decrease	− 2.99
6	S395P	Decrease	− 1.10
7	F397L	Decrease	− 1.94
8	F397I	Decrease	− 0.57
9	Q408L	Decrease	− 0.27
10	F415S	Decrease	− 2.45
11	L437P	Decrease	− 0.76
12	**H440Y**	**Increase**	**1.11**
13	H440T	Decrease	− 0.68
14	**S443P**	**Increase**	**0.12**

Table 1. Predicted effects of SQLE mutations on protein stability using I-Mutant 3.0 (ΔΔG values < 0 indicate decreased stability). Significant values are in bold.

3D structure prediction and molecular docking

The 3D structure of wild-type SQLE was modeled using AlphaFold with high confidence (pLDDT > 90 for most α-helical regions) (Fig. 4). Point mutations were introduced into the wild-type structure, and molecular docking with terbinafine was performed using CB-Dock2. Four mutant variants—F397L, L437P, F415V, and Y394N—showed altered binding pockets compared to the wild-type protein, suggesting impaired terbinafine interaction (Fig. 5). The remaining mutations did not significantly affect the binding site.

Protein dynamics and flexibility analysis

DynaMut2 analysis was conducted to predict changes in protein flexibility and stability due to mutations. Ten out of the fourteen mutations were classified as destabilizing, with negative ΔΔG values and altered vibrational entropy. Four mutations (S395P, Q408L, H440Y, and S443P) were found to increase protein stability, but the majority of substitutions led to disruption of inter-residue bonds essential for maintaining SQLE structure (Table 3).

Protein–protein interaction network analysis

STRING analysis identified interactions between SQLE and ten other proteins involved in the ergosterol biosynthesis pathway. High-confidence associations (score ≥ 0.7) were observed with squalene synthase (TERG_05883), lanosterol synthase (TERG_08595), and C-8 sterol isomerase (TERG_06755), among others. (Bifunctional lycopene cyclase/phytoene; TERG_03917), (Fatty acid hydroxylase domain-containing protein; TERG_08545), (Tryptophan synthase; TERG_03555) with a score ≥ 0.7, (Δ (24(24(1)))-sterol reductase; TERG_02979), (Cytochrome P450 51; TERG_01703), (sterol 22-desaturase; TERG_04906), and (Sucrase/ferredoxin; TERG_02609) with a score ≥ 0.6. These interactions suggest that SQLE mutations may influence the stability and activity of the broader ergosterol synthesis network (Fig. 6).

Discussion

The increasing emergence of terbinafine-resistant dermatophytes poses a serious challenge to the effective treatment of dermatophytosis[2]. Patients infected with resistant strains often experience prolonged infections, require more intensive treatment regimens, and face elevated healthcare costs. Several studies have highlighted the growing prevalence of terbinafine resistance among *Trichophyton* species, largely attributed to missense mutations in the squalene epoxidase (SQLE) gene[5–14]. SQLE is a key enzyme in the ergosterol biosynthesis pathway, and terbinafine functions by inhibiting its activity, thereby depleting ergosterol and causing toxic accumulation of squalene. Mutations in SQLE can induce conformational or physicochemical changes that reduce terbinafine binding efficiency while preserving enzymatic function, leading to therapeutic failure[16–27]. In this study, a computational approach was used to examine the effects of clinically reported SQLE mutations on protein stability, structure, and interactions. The results show that most mutations lead to reduced protein stability, with notable destabilizing mutations including L393F, L393S, and F397L. These mutations occur in highly conserved residues, indicating their likely structural or functional importance. Importantly, moderate destabilization may reduce drug binding without fully impairing SQLE activity, allowing fungal survival despite antifungal treatment. The mutations can have a significant impact on protein stability by quantifying the Gibbs free energy associated with folding/unfolding in mutant proteins in comparison to wild-type proteins[28]. In protein science, the effects of single amino acid substitutions on protein stability are one of the most promising setbacks. A structural stability prediction is crucial for protein engineering and design, as well as for understanding drug resistance. DynaMut implements two distinct, well established normal mode approaches that allow you to analyze protein dynamics and visualize them by sampling conformations to assess how mutations change protein dynamics and stability via vibrational entropy[29]. Based on the results of the current study, the structural
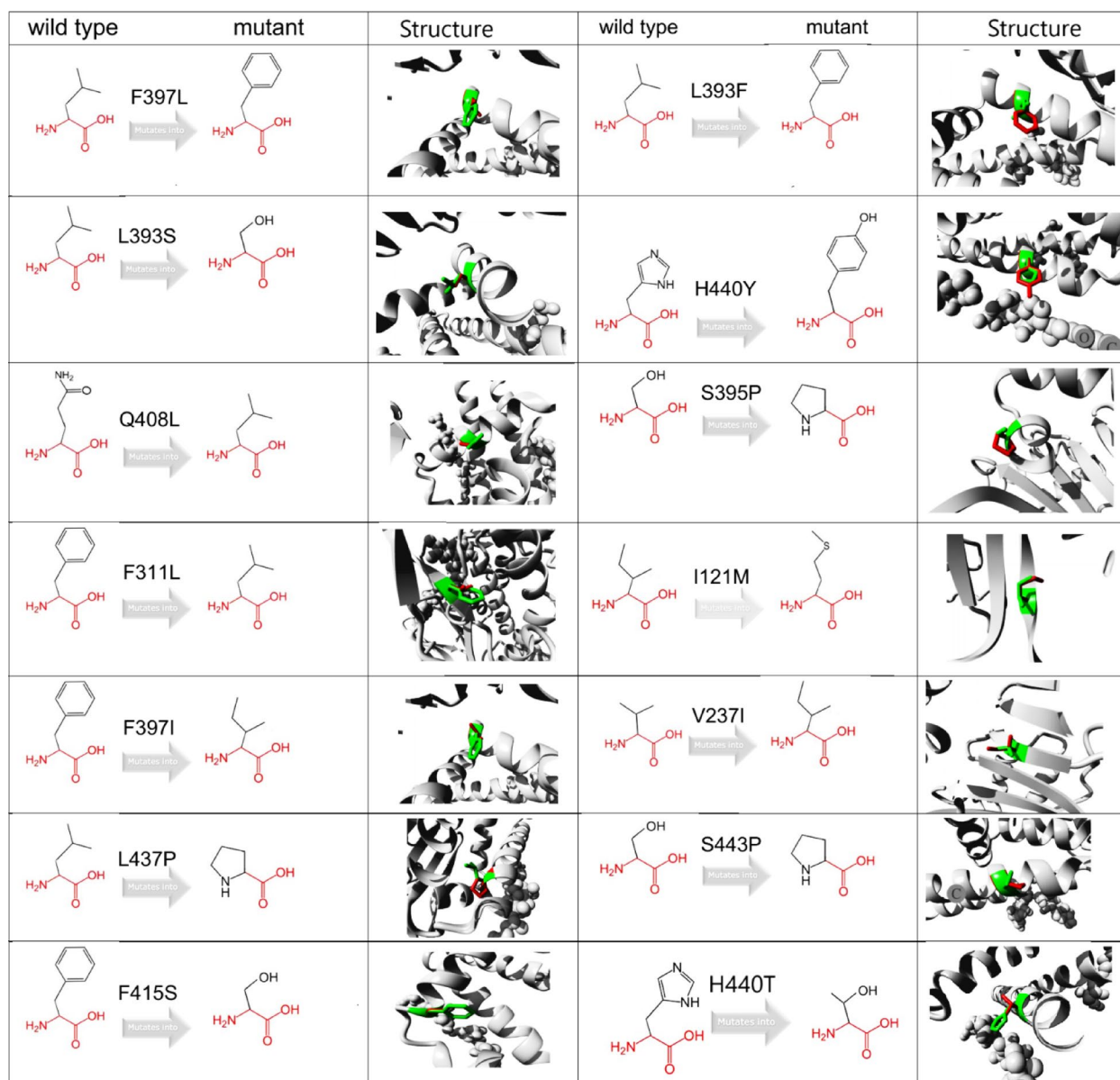
Fig. 2. SQLE structural models created by HOPE web server (https://www3.cmbi.umcn.nl/hope) showing wild-type and mutant residue locations. red: mutant residues, green: wild-type residues, grey: protein backbone.

conformation of SQLE was altered by 10 high risk destabilizing mutations and four mutations found to increase its molecular flexibility which results in bonds disruption and then SQLE-terbinafine interaction failure. While moderate destabilization may alter terbinafine binding and confer resistance, extreme instability could impair SQLE function and compromise fungal viability.

Protein stability changes were quantified through ΔΔG calculations using I-Mutant and DynaMut2. Twelve of the fourteen analyzed mutations such as Leu393Phe and Phe397Leu had negative ΔΔG values, indicating a destabilizing effect. Furthermore, DynaMut2 analysis revealed alterations in vibrational entropy and flexibility, suggesting that these mutations may disrupt local folding and molecular interactions. Evidence from the literature indicates that mutations and harmful SNPs are typically found in the coil and helix regions rather than in turns[30,31]. However, these methods are optimized for soluble proteins, which may impact predictions for membrane-associated proteins like SQLE.

By understanding how mutations affect the protein's 3D structure, further research can be designed, and ultimately new drugs and diagnostic tools can be developed. Using AlphaFold, 3D protein structures are predicted with high accuracy and a predicted local distance difference test (pLDDT) measures confidence for every residue PLDDT calculates the degree of prediction and experimental structure based on the local distance difference test C (lDDT-C)[32]. The wild-type SQLE protein structure was successfully predicted using AlphaFold, yielding a high-confidence model with a pLDDT score above 90 for most regions. Mutations were introduced

Amino acid change	Prediction score	ConSurf prediction	Functional/structural
I121M	5	Average	–
V237I	8	Conserved	
F311L	9	Highly conserved	S
L393S	9	Highly conserved	S
L393F	9	Highly conserved	S
S395P	5	Average	–
F397L	8	Conserved	
F397I	9	Highly conserved	S
Q408L	8	Conserved	F
F415S	8	Conserved	
L437P	9	Highly conserved	S
H440Y	9	Highly conserved	S
H440T	9	Highly conserved	S
S443P	5	Average	–

Table 2. ConSurf prediction of evolutionary conservation and structural/functional categorization of SQLE mutations.

into the model, and structural overlays showed localized changes around the mutation sites. Molecular docking showed that four mutations (F397L, L437P, F415V, and Y394N) significantly altered the terbinafine–SQLE binding pocket, indicating potential loss of binding efficiency. This finding supports the hypothesis that drug resistance may arise from specific conformational shifts in the drug-binding domain, driven by these mutations.

The mutation's charge difference might cause mutant residues and adjacent residues to reject one another[33,34]. Findings from the Hope server gave important details on the potential impacts of missense mutations of SQLE. Structural insights provided by HOPE showed that many mutations altered the physicochemical characteristics of the residues, such as size, hydrophobicity, and charge. These changes can disrupt the local protein environment and potentially affect terbinafine binding. F397L, F397I, L393S, Q408L, F311L, F415S, and H440T mutant residues are smaller than wild-type residues, which might interfere with the interactions of other domains essential to the protein's functioning. For instance, Leu393Phe introduced a bulkier hydrophobic residue, possibly distorting the binding pocket, while Phe397Leu reduced local aromaticity, weakening interactions with terbinafine. L393S, S395, Q408L, H440Y, H44OT, S443P, and F415S mutant residues were more hydrophobic than wild-type residues, which could lead to the loss of hydrogen bonds with other molecules. Additionally, Q408L, identified as a highly conserved and surface-exposed functional residue, may contribute to terbinafine resistance by directly affecting drug accessibility.

The ConSurf web server examines the evolutionary pattern of the macromolecule's amino/nucleic acids to identify the positions that are significant for structure or function[35]. ConSurf analysis identified seven mutated residues as highly conserved, including F311, L393S, L393F, F397I, L437P, H440Y, and H440T. One mutation (Gln408Leu) was highly evolutionarily conserved and functional, suggesting their importance in protein functional stability. It confirmed that most of the critical mutations occurred at conserved sites, reinforcing their potential role in maintaining protein integrity or facilitating drug interactions. Mutations in highly conserved residues are generally more likely to disrupt function compared to mutations in variable regions. High conservation amino acids (i.e., those whose positions evolve slower than other positions) are particularly likely to have biological importance, such as ligand binding[36]. Compared to non-conserved areas, mutations in highly conserved regions are more destructive[37]. The conserved regions that are not mutated may serve as targets for antifungal drugs. ConSurf and HOPE analyses further support the hypothesis that these mutations disrupt critical structural regions. In particular, substitutions such as Leu393Phe and Phe397Leu occur in or near domains essential for drug interaction. Although direct binding affinity was not measured, the observed physicochemical shifts are consistent with resistance phenotypes.

The functional and regulatory interactions among proteins are responsible for much of the complexity within cells. While these interactions are increasingly understood, new interactions continue to be discovered across different databases, experimental modalities, and levels of mechanistic detail as well as protein–protein interactions-both physical and functional-are systematically collected and integrated in the STRING database[38]. STRING network analysis highlighted interactions between SQLE and several key proteins in the ergosterol biosynthesis pathway, including C-8 sterol isomerase (ERG2), sterol C-24 reductase (ERG4), and lanosterol 14α-demethylase (ERG11). This suggests that SQLE mutations could have downstream effects on the pathway, potentially triggering compensatory mechanisms or altering the regulation of ergosterol biosynthesis genes[27,39]. The similar findings were reported by Zhang et al., who used a cDNA microarray approach to assess the transcriptional profile of *T. rubrum* response to terbinafine[40]. In that instance, nevertheless, the authors did not notice any ERG1 gene modification as an early step in the late pathway of ergosterol biosynthesis. Due to its essential significance for membrane permeability, lanosterol 14α-demethylase is mostly researched in fungi[41]. SQLE interacted with TERG_03917 contributes to the pathway of carotenoids, which serve as antioxidants that protect fungal membranes[42]. In silico functional, structural and pathogenicity analysis of missense single nucleotide polymorphisms in human MCM6 gene using GeneMANIA and STRING indicate both the structural
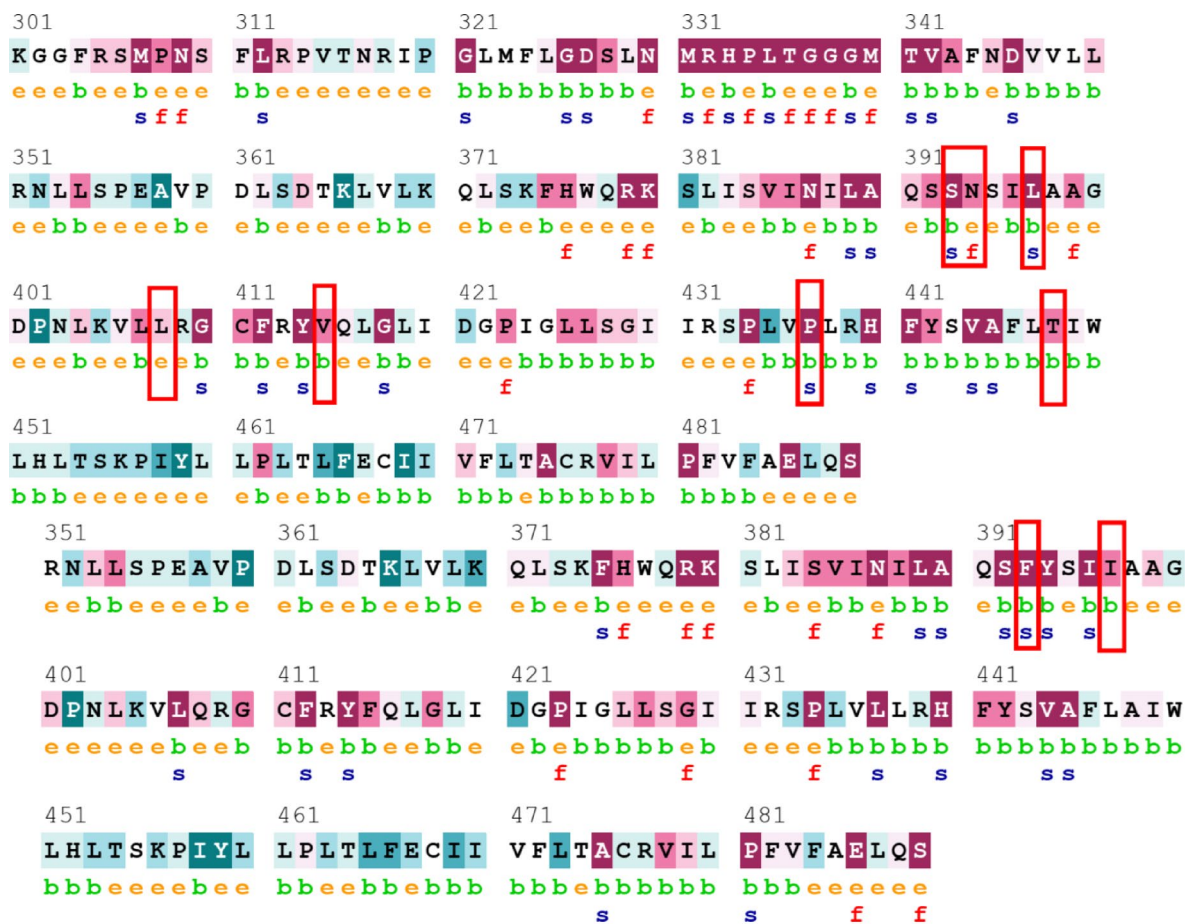
Fig. 3. Color-coded ConSurf conservation plot of SQLE residues; A bar with color coding displays the conservation score. e—An exposed residue according to the neural network algorithm. b—A buried residue according to the neural network algorithm—A predicted functional residue (highly conserved and exposed). s—A predicted structural residue (highly conserved and buried).

and functional integrity of the gene, along with other major genes involved in DNA replication and cell proliferation[43]. Our findings showed six genes (TERG_05883, TERG_03917, TERG_08595, TERG_06755, and TERG_08545) that are important in the synthesis of ergosterol interacted with SQLE. Both SQLE -interacted genes and conserved regions that are not mutated could serve as alternative targets for antifungals.

In summary, terbinafine resistance in dermatophytes is strongly linked to specific missense mutations in SQLE. These mutations destabilize protein structure, alter critical residues, and reduce terbinafine binding, collectively contributing to resistance. Understanding these molecular mechanisms is essential for developing novel antifungal strategies and refining diagnostic tools. While computational tools such as I-Mutant, DynaMut2, and HOPE offer valuable insights into mutation impacts, it is important to note that these models were originally developed for soluble proteins. SQLE, being membrane-associated, may have structural features that limit prediction accuracy. Thus, caution should be exercised when interpreting absolute stability and flexibility scores. Resistance may not arise solely from impaired drug binding but could also involve broader regulatory responses and compensatory network changes. Future studies, including transcriptomic and proteomic profiling, are needed to better understand how mutations in SQLE influence the fungal cell as a whole.

Conclusion

This study provides a comprehensive computational analysis of clinically reported missense mutations in the squalene epoxidase (SQLE) gene associated with terbinafine resistance in dermatophytes. By employing a combination of bioinformatics tools, we assessed how these mutations affect protein stability, structure,
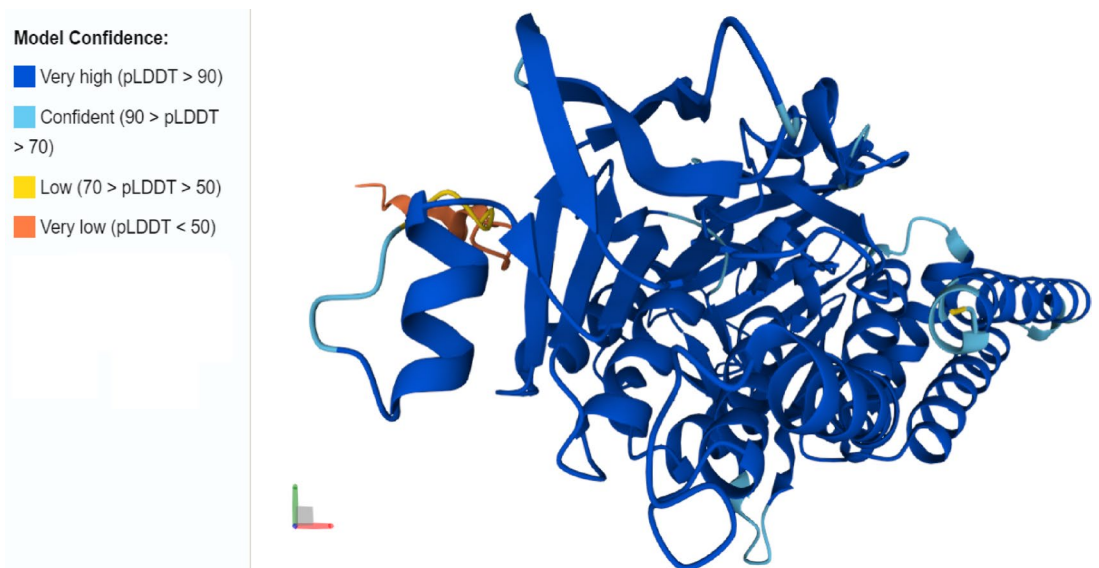
Fig. 4. The predicted structure of *T. rubrum* SQLE (UniProt ID: A0A289ZNH1) obtained from AlphaFold server (https://alphafold.ebi.ac.uk/).

evolutionary conservation, and interactions with terbinafine. Our findings reveal that the majority of SQLE mutations lead to decreased protein stability and alterations in structural flexibility, particularly at highly conserved residues. These mutations were shown to impact key physicochemical properties such as residue size, hydrophobicity, and charge—factors essential for maintaining SQLE function and facilitating terbinafine binding. Molecular docking confirmed that several of these mutations disrupt the binding pocket and interfere with drug interaction, suggesting a mechanistic basis for resistance. Furthermore, protein–protein interaction analysis demonstrated that SQLE operates within a network of enzymes involved in ergosterol biosynthesis. Mutations in SQLE may thus influence broader metabolic pathways, either directly through structural disruption or indirectly via compensatory regulatory mechanisms. Importantly, conserved regions unaffected by mutations may serve as alternative targets for future antifungal development.

Altogether, this study advances our understanding of the molecular mechanisms underlying terbinafine resistance and underscores the value of computational approaches in prioritizing mutations for experimental validation. These insights can guide the design of new therapeutic strategies and support the development of more accurate diagnostic tools for resistant dermatophyte infections. While in silico predictions offer valuable early-stage insights, experimental confirmation, such as site-directed mutagenesis, enzyme activity assays, and antifungal susceptibility testing is necessary to validate these findings and explore their clinical relevance.

Methods
Visualization of SQLE missense mutations
The amino acid sequence of *Trichophyton rubrum* squalene epoxidase (*SQLE*) was retrieved in FASTA format from UniProt (https://www.uniprot.org/) (Accession Number: A0A289ZNH1), which is identical to the SQLE sequence of *T. mentagrophytes* and *T. interdigitale* (A0A059JE48 and A0A1U9IDN6, respectively). Missense mutations associated with terbinafine resistance were collected from published clinical studies, and only mutations confirmed to be linked with resistance phenotypes were included (Table 4).

Mutation mapping and visualization were performed using the MUTe_DRUG_spot tool (https://github.com/mkubiophysics/MUTe_DRUG_spot). This tool generates lollipop plots to indicate the positions of amino acid substitutions in the protein sequence and their association with resistance to specific antifungal agents. Each lollipop denotes a specific mutation, with colors representing the corresponding antifungal drug resistance[45].

Assessment of SQLE protein stability based on sequence
The I-Mutant Suite 3.0 server (https://bio.tools/i-mutant_suite)[46] was used to predict the effect of each SQLE missense mutation on protein stability. This tool applies a support vector machine (SVM) algorithm to predict changes in Gibbs free energy ($\Delta\Delta G$) resulting from single amino acid substitutions. Input data included the SQLE FASTA sequence, the mutation position, and the amino acid change. Predicted $\Delta\Delta G$ values below 0 were considered destabilizing, while values above 0 indicated increased stability.

Evolutionary conservation of missense mutations analysis
To evaluate the functional importance of each mutated residue, evolutionary conservation was analyzed using the ConSurf web server (http://consurf.tau.ac.il). ConSurf employs a Bayesian algorithm to assess the evolutionary conservation of amino acids based on multiple sequence alignments[35]. Scores range from 1 to 9, with residues classified as variable (1–3), intermediate (4–6), or conserved (7–9). Residues predicted to be highly conserved
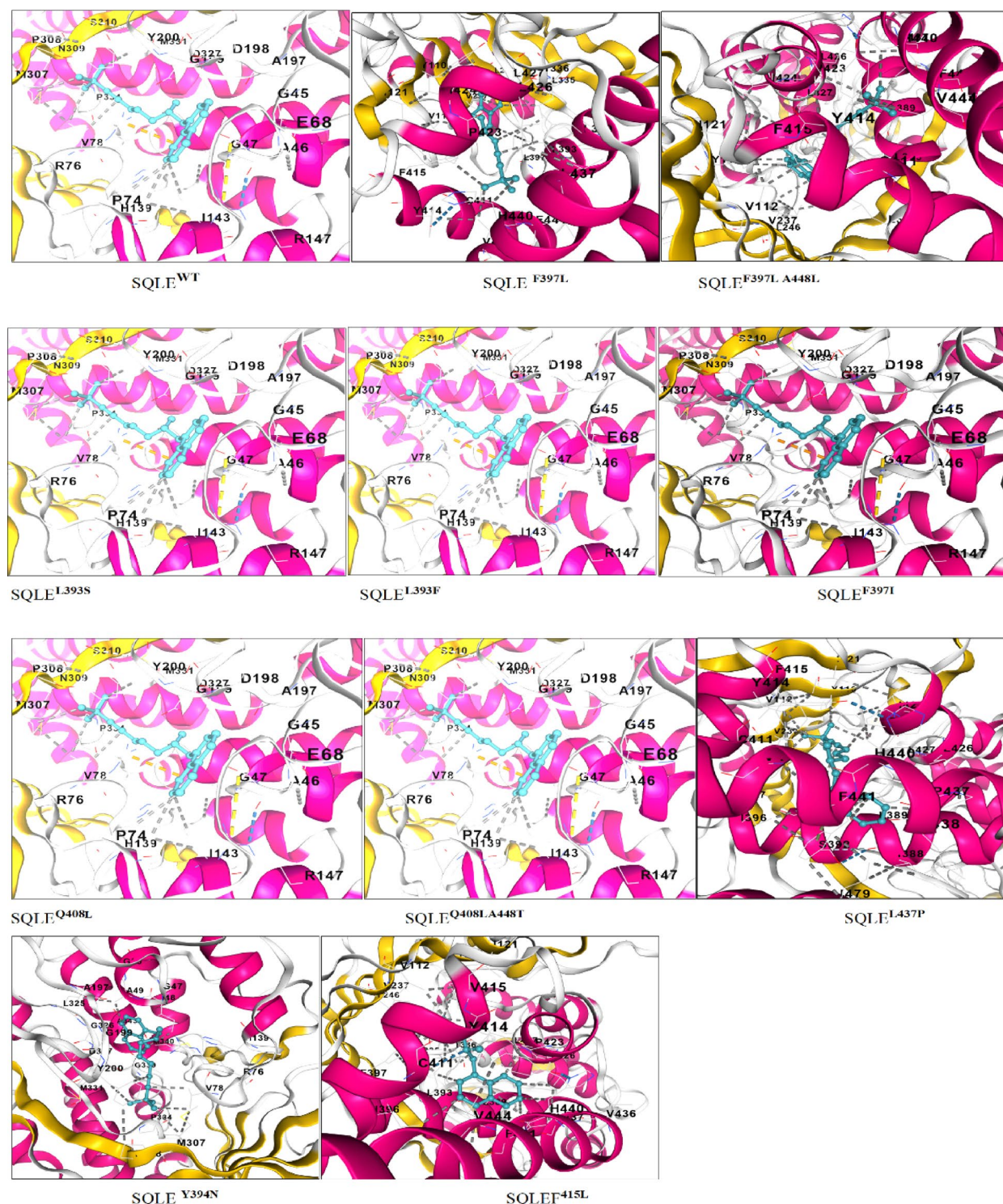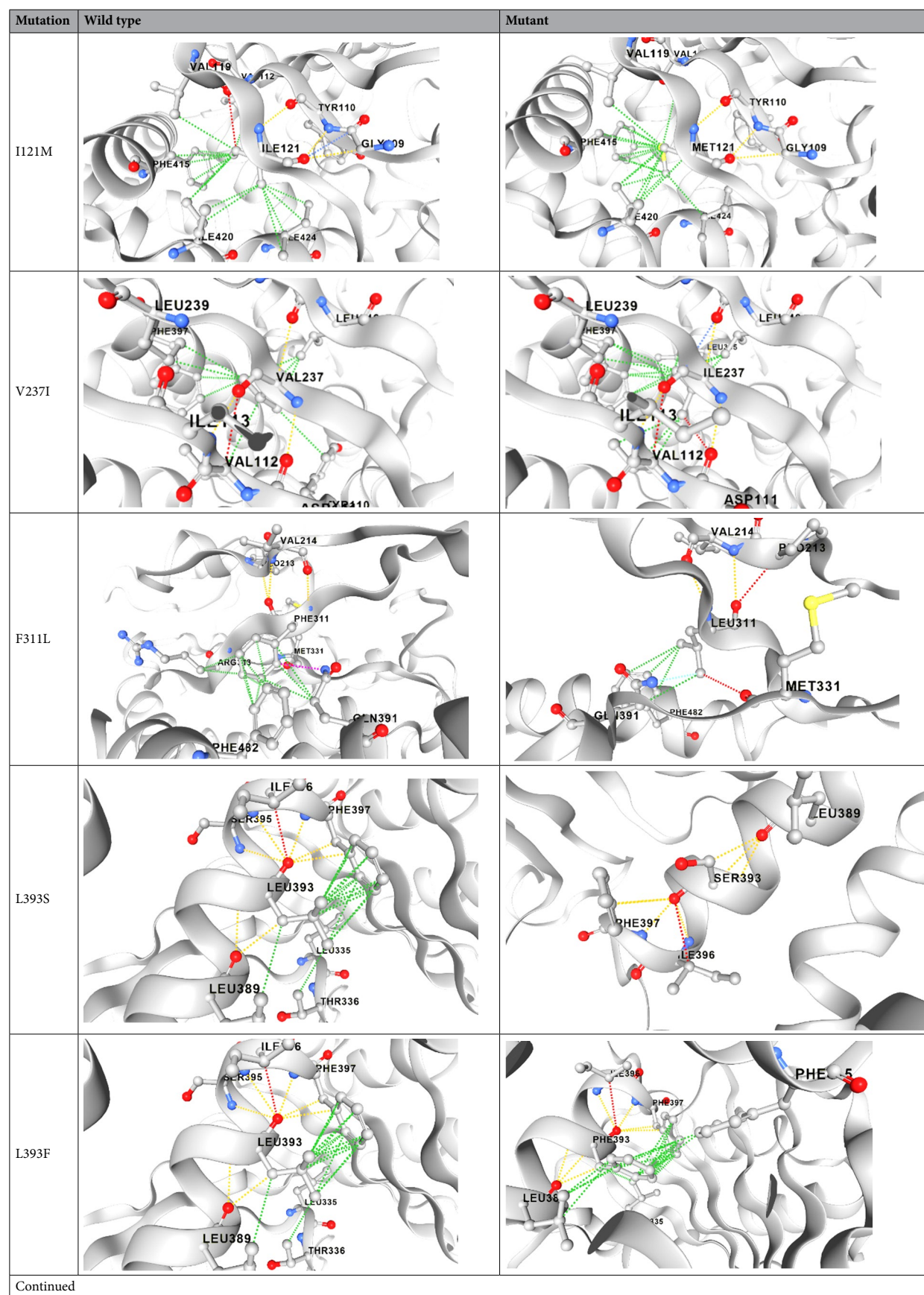
Fig. 5. Comparison of terbinafine-binding site in wild-type and mutated SQLE variants obtained from UniProt (https://www.uniprot.org/) analysis. The protein backbones are depicted as secondary structure, whereas terbinafine is shown in a gray stick representation.

and exposed were considered functionally important, while conserved and buried residues were considered structurally important.

Structural and functional effects of missense mutations

The structural and physicochemical consequences of each mutation was analyzed using HOPE web service (https://www3.cmbi.umcn.nl/hope)[33]. The server generates 3D visualizations and textual explanations based on

Mutation	Wild type	Mutant
I121M		
V237I		
F311L		
L393S		
L393F		
Continued		

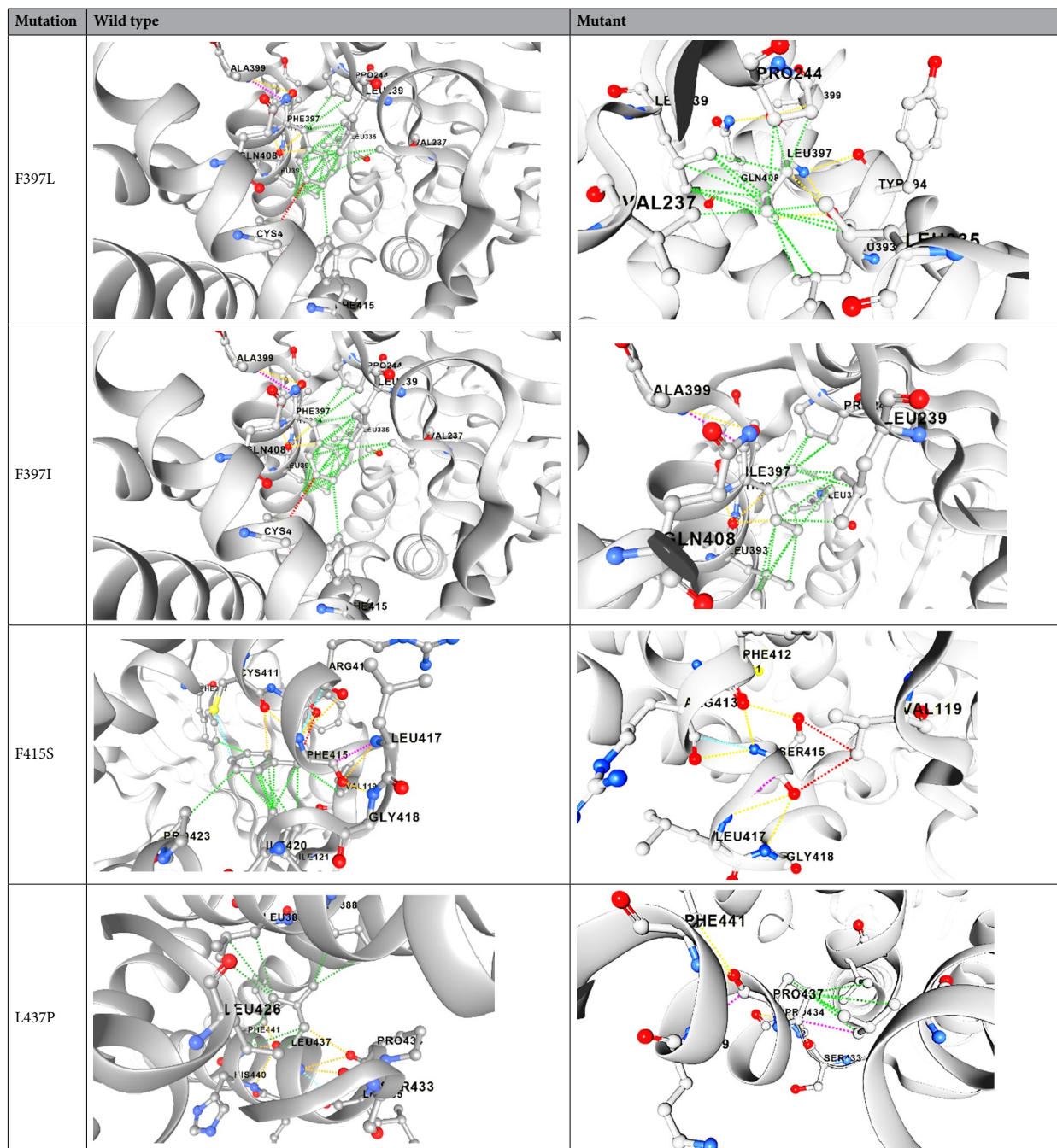| Mutation	Wild type	Mutant
F397L		
F397I		
F415S		
L437P		

Table 3. DynaMut2 predictions of ΔΔG and bond network changes associated with SQLE mutations. ΔΔG (kcal/mol) values were negative for all mutations which indicates the disability of SQLE. Green bonds refer to hydrophobic, red to hydrogen, yellow to ionic, blue to carbonyl and pink to clashes.

UniProt annotations and structure predictions. Inputs included the wild-type sequence, residue position, and mutant amino acid. HOPE identifies changes in size, charge, polarity, and hydrophobicity that may affect protein function or stability.

SQLE 3D structure prediction and molecular docking

The wild-type 3D structure of *T. rubrum* SQLE was predicted using AlphaFold (https://alphafold.ebi.ac.uk/)[47] based on UniProt ID A0A289ZNH1. Structural models of mutant SQLE proteins were generated by introducing point mutations using PyMOL 3.1 software (https://pymol.org/). The structure of terbinafine (PubChem CID: 1,549,008) (https://pubchem.ncbi.nlm.nih.gov/) was downloaded and used for docking analysis.

Protein–ligand interactions were assessed using CB-Dock2 (https://cadd.labshare.cn/cb-dock2/), which integrates cavity detection, homologous template fitting, and molecular docking using AutoDock Vina 1.1.2
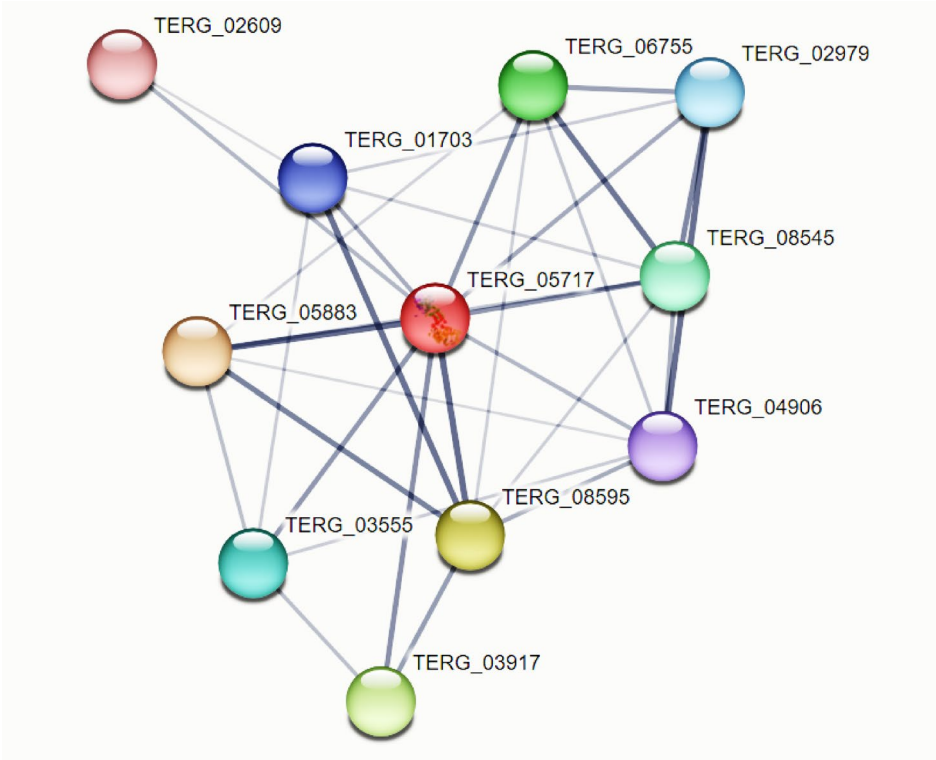
Fig. 6. STRING-based protein–protein interaction network centered on SQLE (TERG_05717), showing its connections with key enzymes involved in ergosterol biosynthesis.

SQLE mutations	MIC (μg/ml)	References
L393S	2, > 8	10,19,23
L393F	2, > 4, > 8, 8	4,19,23,26
Y394N	8	44
F397L	8, > 8, 16	8,9,12,19,26
F397L/A448T	4, > 32	14,23
F397I	1	23
Q408L/A448T	1, > 8, 16	21,24
Q408L	1, 8	8,25
L437P	1	23
F415V	16	22
F311L	4	9
I121M	4 to > 8	19
V237I	4 to > 8	19
S395P	4	20

Table 4. Mutaions of *SQLE* reported in highly terbinafine resistant dermatophytes.

(https://vina.scripps.edu/downloads/)[48]. The binding affinity and interaction profiles of wild-type and mutant SQLE–terbinafine complexes were compared.

Prediction of mutation effects on protein dynamics

To assess changes in protein flexibility and dynamics due to mutations, the DynaMut2 server (https://biosig.lab.uq.edu.au/dynamut2/) was used[29]. This tool integrates normal mode analysis and machine learning to estimate the change in Gibbs free energy ($\Delta\Delta G$) and vibrational entropy between wild-type and mutant proteins. Mutations with $\Delta\Delta G < 0$ were considered destabilizing; those with $\Delta\Delta G > 0$ were considered stabilizing.

Protein–protein interaction network analysis

To evaluate the broader biological impact of SQLE mutations, protein–protein interaction (PPI) analysis was conducted using the STRING database (https://string-db.org/)[38]. The SQLE protein network was analyzed to

identify functionally related proteins, especially those involved in the ergosterol biosynthesis pathway. High-confidence interactions (score ≥ 0.7) were visualized and interpreted to assess the potential consequences of altered SQLE function on related metabolic processes.

Data availability
All data generated or analyzed during this study are included in this published article.

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Author contributions

M. S-G supervised and designed the study. H. RM investigated and carried out the study. M. S-G, H. RM and M. R-A carried out the data analysis. All the authors approved the final version of the manuscript.

Declarations

Competing interest

The authors declare no competing interests.

Additional information

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