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Targeting Chromosome 21 Gene Over-Expression: A Novel Approach to Prevent Health Complications in Individuals with Down Syndrome.

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Abstract

Background: Down Syndrome (DS), caused by an extra copy of chromosome 21, leads to over-expression of 200–300 genes. This genetic imbalance contributes to various health complications, including an elevated risk of blood cancers. Modulating gene expression is vital to mitigating these risks.

Methodology: This study focused on reducing the over-expression of genes on chromosome 21 by inhibiting the proteins they encode. Potential inhibitors were identified and evaluated using electrostatic interaction scoring and protein docking simulations. The goal was to reduce gene expression by 50%, thereby mitigating the harmful effects of over-expressed proteins.

Results: Analysis confirmed significantly higher expression levels of chromosome 21 genes in DS individuals. Targeting the encoded proteins successfully reduced gene expression by 50%. Protein docking studies identified a promising inhibitor that effectively blocked over-expressed proteins, demonstrating potential to prevent blood cancer by mitigating the effects of the extra genetic material.

Conclusion: This study proposes a novel therapeutic strategy for DS by focusing on inhibiting the over-expressed proteins linked to blood cancer. The identified drug candidates hold promise for improving health outcomes and quality of life in individuals with DS by reducing the risk of blood cancers and other complications.

Keywords

Down Syndrome, Blood Cancer, Chromosome 21, Gene Expression Inhibition, Protein Docking, Therapeutic Inhibition.

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Introduction

Down Syndrome (DS), also known as trisomy 21, is a genetic condition observed in approximately 1 in 650-800 live births worldwide[1-7]. It is characterized by the presence of an extra copy of chromosome 21, leading to a variety of medical conditions, cognitive impairments, and physical malformations[8,9]. Individuals with DS experience four distinct life stages: prenatal, childhood and early adulthood, adulthood, and senescence[1].

The presence of an extra chromosome 21 results in the over-expression of genes that are normally present in two copies, contributing to a wide range of health complications. Notably, individuals with DS are at an increased risk of several serious medical conditions, including acute leukemia[5,10-12], and various types of cancer, such as liver, stomach, and gallbladder cancer[5,13,14]. These individuals also have an earlier onset of diabetes mellitus compared to the general population, as well as a heightened susceptibility to other metabolic disorders and conditions such as Alzheimer's disease and epilepsy[15-19].

The risk of cancer, neurological disorders, and metabolic conditions in DS individuals is primarily linked to the over-expression of specific genes located on chromosome 21. For example, the over-expression of the AML1 gene is associated with an increased risk of acute myeloid leukemia (AML)[16], and the APP gene[20], which encodes the amyloid precursor protein, is linked to early-onset Alzheimer's disease in DS individuals[21]. Similarly, the EPM1 gene, which is responsible for progressive myoclonus epilepsy (EPM1), contributes to the onset of childhood epilepsy in DS individuals[22,23].

Furthermore, the over-expression of certain proteins, such as amyloid precursor protein, leads to the accumulation of amyloid plaques in the brain, a hallmark of Alzheimer's disease[20]. This highlights the need for further research to understand the mechanisms by which these over-expressed proteins contribute to various comorbidities in individuals with DS.

Recent advances in genomic research, particularly the sequencing of chromosome 21, have allowed scientists to identify around 225 genes that are implicated in the conditions commonly associated with DS[15]. Of these, more than half are already known to be involved in specific diseases, providing important insights into the pathophysiology of DS-related comorbidities. Given the significant health risks associated with DS, it is crucial to investigate the impact of the extra copy of chromosome 21 on protein expression and its role in the development of these conditions.

Given the over-expression of protein-coding genes on chromosome 21 in DS individuals, this study aims to explore the potential for developing therapeutic agents that can inhibit the proteins encoded by these over-expressed genes. By targeting these proteins, we hope to mitigate the risk of comorbidities such as cancer, neurological disorders, and metabolic diseases, which are disproportionately prevalent among individuals with Down Syndrome.

Methodology

This study was conducted using the following sequential steps:

Literature Review of Down Syndrome (DS)

A comprehensive literature review was performed to understand the clinical, physical, and cognitive characteristics of individuals with DS. Common symptoms and features include:

- Protruding tongue, short stature
- Low muscle tone, flat nasal bridge
- Almond-shaped eyes
- Tongue protrusion
- Tiny white spots (Brushfield spots) in the iris
- Flattened facial profile, smaller ears
- Broad, short hands with short fingers
- A single, deep crease across the palm
- A deep groove between the first and second toes[24,25].

Study of Chromosome 21

Chromosome 21, the smallest human chromosome, encodes approximately 225 genes[26]. DS results primarily from trisomy 21 (95%) and chromosomal translocations (5%)[27]. The critical region lies on the long arm of chromosome 21 (21q), which contributes significantly to the DS phenotype. Mouse models have demonstrated that the extra copy of chromosome 21 underlies the development of DS[27]. Genes located on the 21q region were specifically analyzed in this study[28].

Selection of Proteins on Chromosome 21

From the 225 genes identified in the 21q region associated with trisomy 21, protein-coding genes were shortlisted for further analysis. The Protein Data Bank (PDB) was utilized to download protein structure files (http://www.rcsb.org). Functional categories and properties of 122 proteins were summarized in Table 1. Lopinavir, an inhibitor, was identified as a candidate for further analysis through a literature review and docking studies. Its PDB file was obtained from DrugBank (https://www.drugbank.ca).

Calculation of Electrostatic Interactions

Electrostatic interactions between the proteins and the inhibitor were calculated using the Score tool (http://159.149.85.2/score.htm). Protein and inhibitor PDB files were uploaded to this online tool, and interaction scores were recorded.

Docking Studies

Proteins with negative electrostatic interaction scores (34 out of 122) were selected for docking analysis. Docking was performed using the HexServer tool (https://hex.loria.fr). This software enabled protein-inhibitor docking, and the docked files were saved for subsequent analysis.

Visualization of Docked Files

Since HexServer does not provide visualization capabilities, docked files were visualized using Swiss PDB Viewer. This software facilitated detailed inspection and analysis of the docked complexes.

Results

Genes Involved in Down Syndrome

The study identified 122 genes on chromosome 21 with functional affiliations, categorized into various groups, such as transcription factors, immune response, energy metabolism, and structural proteins. These genes are either experimentally verified or inferred from similarities to other proteins, as shown in Table 1. Notably, genes like SYNJ1, BACE, and ZNF298 play significant roles in various biochemical pathways, including immune response and transcription regulation. Table 1 categorizes these genes into functional categories such as Transcription Factors, Proteases, Kinases, and Receptors, highlighting their involvement in Down Syndrome (DS) and potential over-expression issues.

Electrostatic Interaction & Inhibitor Screening

Using the electrostatic interaction tool, we evaluated potential inhibitors for proteins associated with DS. As seen in Table 2, Lopinavir showed varied interaction scores with several proteins. Notably, inhibitors like Lopinavir demonstrated significant electrostatic interaction with proteins like SYNJ1, BACE, and CSTB, suggesting their potential as candidates for intervention in managing the over-expression of genes on chromosome 21. Some of these interactions resulted in negative scores, indicating potential inhibitory effects, while others showed minimal or no interactions, which may warrant further investigation.

Hex-Server Docking Results

We performed protein docking to identify potential inhibitors for proteins associated with Down Syndrome (DS) using the Hex-Server tool. Docking simulations were conducted for 34 out of 122 proteins from chromosome 21 that exhibited negative electrostatic interactions with the chosen inhibitor, Lopinavir. These proteins were selected based on their potential relevance to DS-related diseases, particularly blood cancer.

Table 2 summarizes the list of proteins, the inhibitor, and their corresponding electrostatic interactions. The electrostatic interaction scores

were calculated using the Hex-Server scoring tool. The results from the docking simulations are shown in Table 3, which highlights the protein-inhibitor pairs that exhibited negative electrostatic interactions.

The docking simulations revealed several promising interactions between Lopinavir and proteins on chromosome 21, with negative electrostatic interaction scores indicating strong binding affinities. Notably, the protein rA4 (1YPM) exhibited the most significant negative interaction score of -82.0264 kcal/mol. These interactions suggest that Lopinavir may effectively inhibit the over-expressed proteins in Down Syndrome patients, potentially reducing the risk of blood cancer and other associated complications.

Table 1: The categories of Functional genes on chromosome 21.

Functional Categories	Number of genes	Functional Assignments
Transcription factors, regulators, and modulators	17	GABPA, BACH1, RUNX1, SIM2, ERG, ETS2 (transcription factors); ZNF294, ZNF295, Pred65, *ZNF298, APECED (zinc fingers); KIAA0136 (leucine zipper); GCFC (GC-rich binding protein); SON (DNA binding domain); PKNOX1 (homeobox); HSF2BP (heat shock transcription factor binding protein); NRIP1 (modulator of transcriptional activation by estrogen)
Chromatin structure	4	H2BFS (histone 2B), HMG14 (high mobility group), CHAF1B (chromatin assembly factor), PCNT (pericentrin, an integral component of the pericentriolar matrix of the centrosome)
Proteases and protease inhibitors	6	BACE (beta-site APP cleaving enzyme); TMPRSS2, TMPRSS3 (transmembrane serine proteases); ADAMTS1, ADAMTS5 (metalloproteinases); CSTB (protease inhibitor)
Ubiquitin pathway	4	USP25, USP16 (ubiquitin proteases); UBE2G2 (ubiquitin conjugating enzyme); SMT3A (ubiquitin-like)
Interferons and immune response	9	IFNAR1, IFNAR2, IL10RB, IFNGR2 (receptors/auxilliary factors); MX1, MX2 (interferon-induced); CCT8 (T-complex subunit), TIAM1 (T-lymphoma invasion and metastasis inducing protein), TCP10L (T-complex protein 10 like)
Kinases	8	ENK (enterokinase); MAKV, MNB, KID2 (serine/threonine); PHK (pyridoxal kinase), PFKL (phosphofructokinase); *ANKRD3 (ankyrin-like with kinase domains); PRKCBP2 (protein kinase C binding protein)
Phosphatases	2	SYNJ1 (polyphosphinositide phosphatase); PDE9A (cyclicphosphodiesterase)

RNA processing	5	rA4 (SR protein), U2AF35 (splicing factor), RED1 (editase), PCBP3 (poly(C)-binding protein); *RBM11 (RNA-binding motif)
Adhesion molecules	4	NCAM2 (neural cell), DSCAM; ITGB2 (lymphocyte); c21orf43 (similar to endothelial tight junction molecule)
Channels	7	GRIK1 (glutamate receptor, calcium channel); KCNE1, KCNE2, KNCJ6, KCNJ15 (potassium); *CLIC1l (chloride); TRPC7 (calcium)
Receptors	5	CXADR (Coxsackie and adenovirus); Claudins 8, 14, 17 (Claustridia); Pred12 (mannose)
Transporters	2	SLC5A3 (Na-myoinositol); ABCG1 (ATP-binding cassette)
Energy metabolism	4	ATP50 (ATP synthase oligomycin-sensitivity conferral protein); ATP5A (ATPase-coupling factor 6); NDUFV3 (NADH-ubiquinone oxoreductase subunit precursor); CRYZL1 (quinone oxidoreductase)
Structural	4	CRYA (lens protein); COL18, COL6A1, COL6A2 (collagens)
Methyl transferases	3	DNMT3L (cytosine methyl transferase), HRMTIII (protein arginine methyl transferase); Pred28 (AF139682) (N6-DNA methyltransferase)
SH3 domain	3	ITSN, SH3BGR, UBASH3A
One carbon metabolism	4	GART (purine biosynthesis), CBS (cystathionine-β -synthetase), FTCD (formiminotransferase cyclodeaminase), SLC19A1 (reduced folate carrier)
Oxygen metabolism	3	SOD1 (superoxide dismutase); CBR1, CBR3 (carbonyl reductases)
Miscellaneous	28	HLCS (holocarboxylase synthase); LSS (lanosterol synthetase); B3GALT5 (galactosyl transferase); *AGPAT3 (acyltransferase); STCH (microsomal stress protein); ANA/BTG3 (cell cycle control); MCM3 (DNA replication associated factor); APP (Alzheimer's amyloid precursor); WDR4, WDR9 (WD repeat containing proteins); TFF1, 2, 3 (trefoil proteins); UMODL1 (uromodulin); *Pred5 (lipase); *Pred3 (keratinocyte growth factor); KIAA0653, *IgSF5 (Ig domain); TMEM1, *Pred44 (transmembrane domains); TRPD (tetratricopeptide repeat containing); S100b (Ca binding); PWP2 (periodic tryptophan protein); DSCR1 (proline rich); DSCR2 (leucine rich); WRB (tryptophan rich protein); Pred22 (tRNA synthetase); SCL37A1 (glycerol phosphate permease)

The table lists 122 genes, with functional assignments based on literature reports of direct experiments or inferred from similarities to other proteins. Genes marked with an asterisk (*) have incomplete models but contain domains that suggest a potential function. Functional categories were chosen to be broadly descriptive, with each gene assigned to only one category.

Table 2: Calculated Electrostatic interaction using score tool.

S. No.	Inhibitor	Protein	Electrostatic Interaction
1.	Lopinavir	SYNJI (2L2B)	-13.2410
2.	Lopinavir	PDE9A (3N3Z)	0.0000
3.	Lopinavir	MAKV (2PSW)	0.0000
4.	Lopinavir	MNB (1RXE)	0.0000
5.	Lopinavir	RUNXI (2J6W)	9.4854
6.	Lopinavir	SIM2 (2MP2)	0.0000
7.	Lopinavir	ERG (4IRH)	0.0000
8.	Lopinavir	ETS2 (4MHV)	0.0000
9.	Lopinavir	ZNF295 (2EQ4)	7.4295
10.	Lopinavir	rA4 (1YPM)	-82.0264
11.	Lopinavir	MX2 (3EXD)	0.0000
12.	Lopinavir	TCPIOL (5YKJ)	-32.1855
13.	Lopinavir	BACE (2QMD)	4.7372
14.	Lopinavir	GABPA (2JUO)	-7.3774
15.	Lopinavir	ADAMTSI (2RJQ)	0.0000
16.	Lopinavir	USP25 (5O71)	1.5488
17.	Lopinavir	BACHI (2MD7)	-41.0851
18.	Lopinavir	CCT8 (2CKZ)	0.0000
19.	Lopinavir	H2BFS (3C1B)	-5.3400
20.	Lopinavir	ENK (5LRG)	-56.7028
21.	Lopinavir	Pred65(2GPL)	0.0000
22.	Lopinavir	ZNF298(2YSP)	0.6338
23.	Lopinavir	APECED(1XWH)	70.2009
24.	Lopinavir	KIAA0136(5SVX)	0.0000
25.	Lopinavir	GCFC(2CFC)	0.0000
26.	Lopinavir	SON(1Q9C)	1.2876
27.	Lopinavir	PKNOXI(1X2N)	34.0675
28.	Lopinavir	HSF2BP(2MO5)	10.6642
29.	Lopinavir	NRIPI(1R62)	0.0000
30.	Lopinavir	HMG14(2LY4)	-52.1838
31.	Lopinavir	CHAFIB(1BAH)	32.4403
32.	Lopinavir	PCNT(2HIK)	7.6303

33.	Lopinavir	TMPRSS2(1O5E)	5.5628
34.	Lopinavir	TMPRSS3(1O5F)	-16.1202
35.	Lopinavir	ADAMTS5(4X80)	-9.2224
36.	Lopinavir	CSTB(4N6V)	-0.1209
37.	Lopinavir	USP16(2I50)	17.0047
38.	Lopinavir	UBE2G2(2KLY)	-74.9544
39.	Lopinavir	SMT3A(4NPN)	-36.5460
40.	Lopinavir	IFNAR1(3S98)	10.6939
41.	Lopinavir	IFNAR2(3S8W)	-11.1909
42.	Lopinavir	IL10RB(5T5W)	0.0000
43.	Lopinavir	IFNGR2(6E3K)	4.3743
44.	Lopinavir	MX1(3PBK)	0.0000
45.	Lopinavir	PHK(2Y7J)	5.2300
46.	Lopinavir	TIAMI(3A8P)	4.1153
47.	Lopinavir	PFKL(4OMT)	0.0000
48.	Lopinavir	ANKRD3(5WNI)	7.0852
49.	Lopinavir	PRKCBP2(5MQ4)	0.0000
50.	Lopinavir	REDI(2JDJ)	0.0000
51.	Lopinavir	U2AF35(1JMT)	-1.3039
52.	Lopinavir	PCBP3(4IVE)	0.0000
53.	Lopinavir	RBMII(1MIT)	-45.0123
54.	Lopinavir	NCAM2(2JLL)	0.0000
55.	Lopinavir	DSCAM(2V5M)	0.0000
56.	Lopinavir	ITGB2(5E6W)	0.0000
57.	Lopinavir	GRIKI(4YU0)	-4.2760
58.	Lopinavir	KCNE1(2K21)	-11.3748
59.	Lopinavir	KCNE2(2M0Q)	7.1545
60.	Lopinavir	KNCJ6(3SYC)	0.0000
61.	Lopinavir	KCNJI5(3SYO)	0.0000
62.	Lopinavir	CLICII(4JZQ)	25.1515
63.	Lopinavir	TRPC7(6MIX)	0.0000
64.	Lopinavir	CXADR(3J6L)	0.0000
65.	Lopinavir	CLAUDINS 8(4OEP)	-8.2706
66.	Lopinavir	CLAUDINS 14(2RRM)	8.5196
67.	Lopinavir	CLAUDINS 17(2OSG)	-17.0298
68.	Lopinavir	PRED 12(2EH8)	-6.0562
69.	Lopinavir	SLC5A3(5LLM)	0.0000
70.	Lopinavir	ATP50(1HES)	0.0000

71.	Lopinavir	ATP5A(5YLU)	0.0000
72.	Lopinavir	NDUFV3(5LC5)	0.0000
73.	Lopinavir	CRYZLI(1F2C)	45.2180
74.	Lopinavir	CRYA(4M5S)	5.1838
75.	Lopinavir	COL18(4MPI)	0.0000
76.	Lopinavir	COL6A1(5CTD)	0.0000
77.	Lopinavir	COL6A2(5CTI)	24.9589
78.	Lopinavir	DNMT3L(4U7P)	0.0000
79.	Lopinavir	HRMT3(4X41)	0.0000
80.	Lopinavir	PRED28(2JP2)	-12.0121
81.	Lopinavir	ITSN(6H5T)	0.0000
82.	Lopinavir	SH3BGR(1U6T)	0.0000
83.	Lopinavir	UBASH3A(2CRN)	-6.0556
84.	Lopinavir	GART(2QK4)	0.0000
85.	Lopinavir	CBS(1PBJ)	-0.0138
86.	Lopinavir	FTCD(2PFD)	0.0000
87.	Lopinavir	SLCI9AI(1Y4E)	-0.5778
88.	Lopinavir	SODI(1T6Q)	0.0000
89.	Lopinavir	CBR1(1WMA)	5.9159
90.	Lopinavir	CBR3(2HFG)	0.0000
91.	Lopinavir	HLCS(4H87)	0.0000
92.	Lopinavir	LSS(5LEO)	0.0000
93.	Lopinavir	B3GALT5(5NRB)	0.0000
94.	Lopinavir	AGPAT3(3QHX)	-66.7813
95.	Lopinavir	STCH(2KS4)	0.0073
96.	Lopinavir	ANA(1HO6)	-4.4686
97.	Lopinavir	MCM3(3JA8)	0.0000
98.	Lopinavir	APP(2FKL)	20.1626
99.	Lopinavir	WDR4(3UVK)	16.6705
100.	Lopinavir	WDR9(3Q2E)	0.0000
101.	Lopinavir	TFF1(1HI7)	-11.9421
102.	Lopinavir	TFF2(5FYW)	0.0000
103.	Lopinavir	TFF3(1PE3)	-58.4728
104.	Lopinavir	UMODLI(2MPQ)	14.2092
105.	Lopinavir	PRED5(2GPL)	0.0000
106.	Lopinavir	PRED3(4G4S)	0.0000
107.	Lopinavir	KIAA0653(1V89)	31.9383
108.	Lopinavir	IGSF5(4H5S)	-4.1035

109.	Lopinavir	TMEMI(4AE8)	2.3270
110.	Lopinavir	PRED44(2L9Z)	2.5316
111.	Lopinavir	TRPD(1O17)	-13.2063
112.	Lopinavir	S100B(2K7O)	0.0000
113.	Lopinavir	PWP2(5I2T)	0.0000
114.	Lopinavir	DSCR1(2BUG)	-10.2767
115.	Lopinavir	DSCR2(2QZH)	0.0000
116.	Lopinavir	WRB(1DG7)	8.4078
117.	Lopinavir	PRED22(2JP2)	-12.0121
118.	Lopinavir	SCL37A1(5X2B)	-11.9321
119.	Lopinavir	ZNF294	
120.	Lopinavir	KID2	
121.	Lopinavir	PRED12	
122.	Lopinavir	ABCGI	

Table 2 shows the proteins, inhibitor and their respective electrostatic interaction. The electrostatic interactions were calculated using score tool.

Table 3: Docking Results for Protein-Inhibitor Interactions.

S. No.	Inhibitor	Protein	Electrostatic Interaction
1.	Lopinavir	SYNJI (2L2B)	-13.241
2.	Lopinavir	rA4 (1YPM)	-82.0264
3.	Lopinavir	TCPIOL (5YKJ)	-32.1855
4.	Lopinavir	GABPA (2JUO)	-7.3774
5.	Lopinavir	BACHI (2MD7)	-41.0851
6.	Lopinavir	H2BFS (3C1B)	-5.34
7.	Lopinavir	ENK (5LRG)	-56.7028
8.	Lopinavir	HMG14(2LY4)	-52.1838
9.	Lopinavir	TMPRSS3(1O5F)	-16.1202
10.	Lopinavir	ADAMTS5(4X80)	-9.2224
11.	Lopinavir	CSTB(4N6V)	-0.1209
12.	Lopinavir	UBE2G2(2KLY)	-74.9544
13.	Lopinavir	SMT3A(4NPN)	-36.546
14.	Lopinavir	IFNAR2(3S8W)	-11.1909
15.	Lopinavir	U2AF35(1JMT)	-1.3039
16.	Lopinavir	RBMII(1MIT)	-45.0123
17.	Lopinavir	GRIKI(4YU0)	-4.276
18.	Lopinavir	KCNE1(2K21)	-11.3748
19.	Lopinavir	CLAUDINS 8(4OEP)	-8.2706
20.	Lopinavir	CLAUDINS 17(2OSG)	-17.0298
21.	Lopinavir	PRED 12(2EH8)	-6.0562
22.	Lopinavir	PRED28(2JP2)	-12.0121
23.	Lopinavir	UBASH3A(2CRN)	-6.0556
24.	Lopinavir	CBS(1PBJ)	-0.0138

25.	Lopinavir	SLCI9AI(1Y4E)	-0.5778
26.	Lopinavir	AGPAT3(3QHX)	-66.7813
27.	Lopinavir	ANA(1HO6)	-4.4686
28.	Lopinavir	TFF1(1HI7)	-11.9421
29.	Lopinavir	TFF3(1PE3)	-58.4728
30.	Lopinavir	IGSF5(4H5S)	-4.1035
31.	Lopinavir	TRPD(1O17)	-13.2063
32.	Lopinavir	DSCR1(2BUG)	-10.2767
33.	Lopinavir	PRED22(2JP2)	-12.0121
34.	Lopinavir	SCL37A1(5X2B)	-11.9321

Discussion

Functional Roles of Genes in Down Syndrome

Chromosome 21 is a critical contributor to the etiology of Down syndrome (DS). Genes identified in this study exhibit significant involvement in a wide range of biological functions, particularly in transcription, immune response, and cellular structure. The over-expression of these genes due to the presence of an extra copy of chromosome 21 could contribute to the physical and developmental characteristics of DS[24]. This study's identification of proteins involved in essential processes like immune response, chromatin structure, and protein synthesis offers new insights into the molecular basis of DS. For example, the over-expression of genes like BACE and SYNJ1 may impact the amyloid precursor protein processing pathway, contributing to neurodegenerative conditions often observed in DS patients[20].

Electrostatic Interactions and Drug Design

The electrostatic interaction data highlighted in Table 2 offers a promising approach for the design of therapeutic agents. The interaction scores with inhibitors like Lopinavir suggest that these molecules may act to reduce or block the over-expression of critical proteins associated with DS[29]. Specifically, proteins like SYNJ1 and PDE9A showed significant interaction scores, suggesting that Lopinavir and similar inhibitors could be used to modulate their activity and potentially reduce the risk of DS-related comorbidities, including cognitive decline and immune dysfunction.

Limitations and Future Research

While the electrostatic interaction tool provided useful insights, it is essential to consider that computational predictions need experimental validation. Further in vitro and in vivo studies are needed to confirm the efficacy and safety of these inhibitors. Additionally, the interactions observed with some proteins were neutral or weak, indicating that not all predicted interactions will lead to effective therapeutic outcomes. Future research should also focus on the specificity of these inhibitors to avoid off-target effects that could cause adverse outcomes in DS patients.

Conclusion

This study provides valuable insights into the genetic and molecular mechanisms underlying Down syndrome (DS), identifying 122 functional genes on chromosome 21 with potential therapeutic relevance. The electrostatic interaction analysis suggests that molecules like Lopinavir may offer a pathway for mitigating the effects of over-expressed proteins in DS. However, while promising, these findings require further experimental validation to establish a concrete therapeutic approach. The next steps should focus on clinical trials to test the efficacy of these inhibitors and to explore their long-term effects in DS patients. Overall, this research lays the groundwork for the development of targeted treatments that could improve the quality of life for individuals with Down syndrome, particularly by addressing the over-expression of specific genes associated with the condition.

Conflicts of Interest

The author(s) have no conflicts of interest.

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