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Research Article

Drug Targets Prediction for MDR Mycobacterium Tuberculosis Using Insilico Genome Analysis

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Abstract

Mycobacterium tuberculosis is the causative agent of the disease, tuberculosis. The most researched clinical strain of Mycobacterium tuberculosis is H37Rv. To identify possible therapeutic targets, *in-silico* analyses of the *Mycobacterium tuberculosis* H37Rv genome were carried out. The genome sequence was downloaded from the website of NCBI (National Center for Biotechnology Information). The DEG (Database of Essential Genes) was consulted to identify essential genes. Additionally, homology searches with the human genome were conducted using BLASTX. Out of a total of 3924 genes, 594 were determined to be essential for *Mycobacterium tuberculosis*, of which 366 had no sequence similarity to the human genome. Out of 366 genes, 242 potential drug targets have been found after being screened for fictitious and unidentified genes. After functional analysis of these 242 possible targets using Uniprot, 181 of them were identified as potential drug targets. Among the 181 target genes, 42 were related to amino acid biosynthesis, 22 were related to cell wall biosynthesis, 19 to translation, 12 to transcription, 7 to lipid metabolism, 7 to carbohydrate metabolism, etc.

Keywords: - *Mycobacterium tuberculosis H37Rv*, DEG, BLASTX, Drug target, *in silico*, NCBI.

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INTRODUCTION

The primary cause of tuberculosis (TB), Mycobacterium tuberculosis (Mtb), continues to be a serious global health risk. Eight million new cases of tuberculosis (TB) and two million deaths from TB occur annually [1]. Furthermore, it's estimated that a third of people have latent Mtb infection, of which less than 10% will go on to develop active disease in their lifetime. When the balance between natural immunity and the pathogen shifts, as it does in HIV patients and adolescents who are losing their protective immune response during adolescence, active tuberculosis develops [2]. Furthermore, it's estimated that 500,000 new cases of multi-drug-resistant tuberculosis happen annually [3].

The most significant of these is the development of drug resistance, which renders even the front-line medications ineffective, despite the fact that the current medications are incredibly valuable in controlling the disease to the extent that it is being done today [18]. The need for novel therapeutic approaches is highlighted by the rise of drug-resistant strains and the scarcity of potent anti-TB medications [4].

The complexity of managing tuberculosis has increased due to multidrug-resistant tuberculosis (MDR-TB), which is characterized by resistance to at least isoniazid and rifampicin, the two most effective first-line anti-TB drugs. Inadequate medication regimens and patient non-adherence are two of the worst treatment practices that lead to the development of this resistance [5]. MDR-TB entails a higher risk of treatment failure and mortality in addition to necessitating lengthier and more toxic treatment regimens. The situation is further made worse by the emergence of extensively drug-resistant tuberculosis (XDR-TB), which is resistant to additional classes of second-line drugs [18]. A multimodal strategy that includes

enhanced diagnostics, novel treatment approaches, fortified health systems, and effective infection control measures is required to tackle the problem of MDR-TB [6]. To slow the growth of multidrug-resistant tuberculosis (MDR-TB), maintain the effectiveness of current anti-TB medications, and progress the creation of new therapeutic approaches, there must be coordinated international efforts [7].

The biology of MTB can be understood through genome analysis, which also suggests possible therapeutic targets. To predict potential drug targets, this article explores the genome analysis of Mycobacterium tuberculosis. The homology between the target and host which needs to be minimal or nonexistent to prevent host toxicity - the target's activity while it is ill [4], and the target's importance to the pathogen's growth and survival are all significant considerations in this situation. Both the drug resistance issue and the drug discovery process can be improved by identifying new drug targets. These insilico techniques offer the advantages of speed, affordability, and above all a systems view of the entire microbe at one time, allowing for the investigation of issues that are frequently challenging to resolve through experimentation [8]. Drug discovery has seen a paradigm shift from the conventional medicinal chemistry-based ligand-oriented drug development methodologies to target-driven lead discovery and rational drug target identification, which target the molecular causes underlying disease [9-18].

Methodology:

Searching for the *M. tuberculosis H37Rv complete* genes

Using the National Center for Biotechnology Information FTP server (www.ncbi.nlm.nih.gov/FTP), the genome sequence of M. tuberculosis H37Rv was downloaded and saved on the computer.

Screening for Essential genes

Utilizing BLASTN on the Database of Essential Genes server (http://tubic.tju.edu.cn/deg), the gene sequences were screened to determine the essential genes for M. tuberculosis H37Rv survival.

Comparative analysis with human

BLASTX (https://blast.ncbi.nlm.nih.gov/Blast.cgi) was used to compare the essential genes discovered through DEG search with human genes to determine any homology. Genes lacking human homology were subsequently screened for potential hypothetical or putative proteins.

Functional analysis using Uniprot

The UNIPROT (www.uniprot.org) database was used to further investigate the selected target genes to determine their functions.

Results:

The NCBI was used to search the complete genome of M. tuberculosis H37Rv. Following a database search, the genome (Acc. No. AL123456.3) containing 3924 genes were downloaded in FASTA format. 594 genes out of 3924 were determined to be essential when these genes were scanned through BLASTN on the DEG server to identify the essential genes for M. tuberculosis H37Rv. Comparative analyses against the human genome were also conducted to identify genes that are homologous or not.

Since they function similarly to human genes and could cause unintended toxicity when taken as a potential drug target. Genes homologous to human genes were excluded from the list. 366 of the 594 essential genes showed no BLASTX homology search similarity to the human genome. To improve the results, we removed all hypothetical and uncharacterized genes and annotated all the genes that did not have a human homolog. 242 genes were found to be viable candidates for additional target-based medication development after the screening process (Table 1). UNIPROT was utilized to further categorize these putative genes based on their functions. Among the 181 target genes, 42 were related to amino acid biosynthesis, 22 were related to cell wall biosynthesis, 19 to translation, 12 to transcription, 7 to lipid metabolism, 7 to carbohydrate metabolism, and so on (Table 2).

Table 1: Potential drug target genes along with their locus, location, and CDS

S. No	Locus tag	Gene	Location (Base Pair)	CDS
1	Rv0001	dnaA	1..1524	CCP42723.1
2	Rv0058	dnaB	60396..63020	CCP42780.1
3	Rv0086	hycQ	93951..95417	CCP42811.1
4	Rv0112	gca	136289..137245	CCP42837.1
5	Rv0118c	oxcA	142128..143876	CCP42843.1
6	Rv0127	mak	154232..155599	CCP42852.1
7	Rv0189c	ilvD	219996..221723	CCP42916.1
8	Rv0236c	aftD	282649..286851	CCP42964.1
9	Rv0280	PPE3	339364..340974	CCP43010.1
10	Rv0283	eccB3	344022..345638	CCP43013.1
11	Rv0285	PE5	349624..349932	CCP43015.1
12	Rv0286	PPE4	349935..351476	CCP43016.1

13	Rv0289	espG3	352149..353036	CCP43019.1
14	Rv0290	eccD3	353083..354501	CCP43020.1
15	Rv0292	eccE3	355880..356875	CCP43022.1
16	Rv0304c	PPE5	366150..372764	CCP43034.1
17	Rv0305c	PPE6	372820..375711	CCP43035.1
18	Rv0335c	PE6	399535..400050	CCP43065.1
19	Rv0351	grpE	421709..422416	CCP43081.1
20	Rv0399c	lpqK	477327..478556	CCP43130.1
21	Rv0411c	glnH	497314..498300	CCP43142.1
22	Rv0415	thiO	501148..502170	CCP43146.1
23	Rv0416	thiS	502167..502373	CCP43147.1
24	Rv0417	thiG	502366..503124	CCP43148.1
25	Rv0423c	thiC	508582..510225	CCP43154.1
26	Rv0450c	mmpL4	538588..541491	CCP43181.1
27	Rv0453	PPE11	543174..544730	CCP43184.1
28	Rv0509	hemA	600441..601847	CCP43246.1
29	Rv0511	hemD	602819..604516	CCP43248.1
30	Rv0527	ccdA	617493..618272	CCP43264.1
31	Rv0529	ccsA	619891..620865	CCP43266.1
32	Rv0553	menC	644490..645470	CCP43291.1
33	Rv0555	menD	646298..647962	CCP43293.1
34	Rv0557	mgtA	648536..649672	CCP43295.1
35	Rv0588	yrbE2B	685928..686815	CCP43326.1
36	Rv0627	vapC5	718282..718689	CCP43368.1
37	Rv0635	hadA	731930..732406	CCP43378.1
38	Rv0638	secE1	733737..734222	CCP43381.1
39	Rv0651	rplJ	748276..748812	CCP43394.1
40	Rv0703	rplW	802133..802435	CCP43447.1
41	Rv0706	rplV	803689..804282	CCP43450.1
42	Rv0707	rpsC	804282..805106	CCP43451.1
43	Rv0709	rpmC	805526..805759	CCP43453.1
44	Rv0715	rplX	811742..812059	CCP43459.1
45	Rv0716	rplE	812059..812622	CCP43460.1
46	Rv0718	rpsH	812976..813374	CCP43462.1
47	Rv0719	rplF	813398..813937	CCP43463.1
48	Rv0720	rplR	813940..814308	CCP43464.1
49	Rv0721	rpsE	814328..814990	CCP43465.1
50	Rv0736	rslA	828140..828892	CCP43481.1
51	Rv0755c	PPE12	848103..850040	CCP43501.1
52	Rv0788	purQ	882760..883434	CCP43536.1
53	Rv0798c	cfp29	891472..892269	CCP43546.1
54	Rv0824	desA1	917734..918750	CCP43572.1

55	Rv0949	uvrD1	1058260..1060575	CCP43697.1
56	Rv0982	mprB	1097508..1099022	CCP43732.1
57	Rv0993	galU	1109272..1110192	CCP43743.1
58	Rv1005	pabB	1122222..1123598	CCP43755.1
59	Rv1011	ispE	1130191..1131111	CCP43761.1
60	Rv1018c	glmU	1136573..1138060	CCP43768.1
61	Rv1027c	kdpE	1148427..1149107	CCP43777.1
62	Rv1094	desA2	1221959..1222786	CCP43847.1
63	Rv1133c	metE	1259067..1261346	CCP43887.1
64	Rv1177	fdxC	1309005..1309331	CCP43933.1
65	Rv1182	papA3	1320035..1321453	CCP43938.1
66	Rv1201c	dapD	1344216..1345169	CCP43957.1
67	Rv1202	dapE	1345260..1346324	CCP43958.1
68	Rv1208	gpgS	1352144..1353118	CCP43964.1
69	Rv1274	lprB	1424197..1424754	CCP44030.1
70	Rv1284	canA	1437324..1437815	CCP44040.1
71	Rv1285	cysD	1437909..1438907	CCP44041.1
72	Rv1293	lysA	1448028..1449371	CCP44050.1
73	Rv1294	thrA	1449375..1450700	CCP44051.1
74	Rv1295	thrC	1450697..1451779	CCP44052.1
75	Rv1296	thrB	1451997..1452947	CCP44053.1
76	Rv1297	rho	1453204..1455012	CCP44054.1
77	Rv1298	rpmE	1455163..1455405	CCP44055.1
78	Rv1305	atpE	1461045..1461290	CCP44062.1
79	Rv1306	atpF	1461321..1461836	CCP44063.1
80	Rv1307	atpH	1461843..1463183	CCP44064.1
81	Rv1311	atpC	1467315..1467680	CCP44068.1
82	Rv1315	murA	1470321..1471577	CCP44072.1
83	Rv1327	glgE	1492320..1494425	CCP44085.1
84	Rv1347c	mbtK	1511973..1512605	CCP44105.1
85	Rv1388	mihF	1563694..1564266	CCP44147.1
86	Rv1390	rpoZ	1565093..1565425	CCP44149.1
87	Rv1409	ribG	1585194..1586213	CCP44168.1
88	Rv1415	ribA2	1590397..1591674	CCP44174.1
89	Rv1416	ribH	1591671..1592153	CCP44175.1
90	Rv1420	uvrC	1594042..159598	CCP44179.1
91	Rv1446c	opcA	1624454..1625365	CCP44205.1
92	Rv1448c	tal	1626959..1628080	CCP44207.1
93	Rv1477	ripA	1666990..1668408	CCP44237.1
94	Rv1539	lspA	1742244..1742852	CCP44303.1
95	Rv1547	dnaE1	1747694..1751248	CCP44311.1
96	Rv1594	nadA	1794756..1795805	CCP44358.1

97	Rv1599	hisD	1799583..1800899	CCP44363.1
98	Rv1600	hisC1	1800896..1802038	CCP44364.1
99	Rv1602	hisH	1802664..1803284	CCP44366.1
100	Rv1603	hisA	1803294..1804031	CCP44367.1
101	Rv1605	hisF	1804853..1805656	CCP44369.1
102	Rv1606	hisI	1805653..1806000	CCP44370.1
103	Rv1609	trpE	1807903..1809453	CCP44373.1
104	Rv1611	trpC	1810240..1811058	CCP44375.1
105	Rv1612	trpB	1811127..1812359	CCP44376.1
106	Rv1613	trpA	1812359..1813171	CCP44377.1
107	Rv1614	lgt	1813171..1814577	CCP44378.1
108	Rv1622c	cydB	1823360..1824400	CCP44386.1
109	Rv1630	rpsA	1833542..1834987	CCP44394.1
110	Rv1641	infC	1852273..1852878	CCP44406.1
111	Rv1652	argC	1865576..1866634	CCP44417.1
112	Rv1653	argJ	1866631..1867845	CCP44418.1
113	Rv1654	argB	1867842..1868726	CCP44419.1
114	Rv1657	argR	1870842..1871354	CCP44422.1
115	Rv1663	pks17	1886512..1888020	CCP44428.1
116	Rv1712	cmk	1939599..1940291	CCP44478.1
117	Rv1850	ureC	2097961..2099694	CCP44616.1
118	Rv1918c	PPE35	2167649..2170612	CCP44685.1
119	Rv1963c	mce3R	2205582..2206802	CCP44732.1
120	Rv2093c	tatC	2352103..2353029	CCP44868.1
121	Rv2121c	hisG	2379806..2380660	CCP44896.1
122	Rv2122c	hisE	2380663..2380944	CCP44897.1
123	Rv2138	lppL	2397330..2398406	CCP44913.1
124	Rv2145c	wag31	2404616..2405398	CCP44921.1
125	Rv2151c	ftsQ	2409697..2410641	CCP44927.1
126	Rv2152c	murC	2410638..2412122	CCP44928.1
127	Rv2153c	murG	2412119..2413351	CCP44929.1
128	Rv2154c	ftsW	2413348..2414922	CCP44930.1
129	Rv2155c	murD	2414934..2416394	CCP44931.1
130	Rv2156c	murX	2416396..2417475	CCP44932.1
131	Rv2157c	murF	2417472..2419004	CCP44933.1
132	Rv2163c	pbpB	2425048..2427087	CCP44940.1
133	Rv2174	mptA	2435909..2437459	CCP44951.1
134	Rv2178c	aroG	2440332..2441720	CCP44955.1
135	Rv2192c	trpD	2455631..2456743	CCP44969.1
136	Rv2194	qcrC	2457553..2458395	CCP44971.1
137	Rv2195	qcrA	2458392..2459681	CCP44972.1
138	Rv2196	qcrB	2459678..2461327	CCP44973.1

139	Rv2221c	glnE	2489369..2492353	CCP44999.1
140	Rv2225	panB	2497742..2498587	CCP45003.1
141	Rv2231c	cobC	2504605..2505699	CCP45009.1
142	Rv2338c	moeW	2613107..2614063	CCP45126.1
143	Rv2343c	dnaG	2620533..2622452	CCP45131.1
144	Rv2378c	mbtG	2656408..2657703	CCP45166.1
145	Rv2391	sirA	2684679..2686370	CCP45179.1
146	Rv2392	cysH	2686367..2687131	CCP45180.1
147	Rv2398c	cysW	2694981..2695799	CCP45188.1
148	Rv2399c	cysT	2695796..2696647	CCP45189.1
149	Rv2400c	subI	2696644..2697714	CCP45190.1
150	Rv2412	rpsT	2710075..2710335	CCP45203.1
151	Rv2421	nadD	2718173..2718808	CCP45212.1
152	Rv2438c	nadE	2734792..2736831	CCP45230.1
153	Rv2441c	rpmA	2739772..2740032	CCP45234.1
154	Rv2442c	rplU	2740047..2740361	CCP45235.1
155	Rv2444c	rne	2742123..2744984	CCP45237.1
156	Rv2524c	fas	2840123..2849332	CCP45318.1
157	Rv2533c	nusB	2858254..2858724	CCP45328.1
158	Rv2534c	efp	2858727..2859290	CCP45329.1
159	Rv2537c	aroD	2861148..2861591	CCP45332.1
160	Rv2538c	aroB	2861588..2862676	CCP45333.1
161	Rv2540c	aroF	2863207..2864412	CCP45335.1
162	Rv2552c	aroE	2871206..2872015	CCP45348.1
163	Rv2580c	hisS	2904821..2906092	CCP45376.1
164	Rv2608c	PPE42	2935046..2936788	CCP45405.1
165	Rv2612c	pgsA1	2939959..2940612	CCP45409.1
166	Rv2623	TB31.7	2949593..2950486	CCP45421.1
167	Rv2673	aftC	2989291..2990592	CCP45471.1
168	Rv2682c	dxs1	2998052..2999968	CCP45480.1
169	Rv2702	ppgK	3016858..3017655	CCP45500.1
170	Rv2703	sigA	3017835..3019421	CCP45501.1
171	Rv2710	sigB	3022461..3023432	CCP45508.1
172	Rv2726c	dapF	3039825..3040769	CCP45524.1
173	Rv2727c	miaA	3040766..3041461	CCP45525.1
174	Rv2746c	pgsA3	3058602..3059231	CCP45545.1
175	Rv2747	argA	3059262..3059786	CCP45546.1
176	Rv2748c	ftsK	3059855..3062506	CCP45547.1
177	Rv2754c	thyX	3067193..3067945	CCP45553.1
178	Rv2786c	ribF	3093905..3094900	CCP45585.1
179	Rv2830c	vapB22	3137009..3137224	CCP45631.1
180	Rv2833c	ugpB	3139174..3140484	CCP45634.1

181	Rv2841c	nusA	3148385..3149428	CCP45642.1
182	Rv2846c	efpA	3153039..3154631	CCP45647.1
183	Rv2853	PE_PGRS48	3162268..3164115	CCP45654.1
184	Rv2856	nicT	3166684..3167802	CCP45657.1
185	Rv2869c	rip	3180548..3181762	CCP45671.1
186	Rv2882c	frr	3191644..3192201	CCP45684.1
187	Rv2883c	pyrH	3192373..3193158	CCP45685.1
188	Rv2904c	rplS	3213912..3214253	CCP45706.1
189	Rv2906c	trmD	3215665..3216357	CCP45708.1
190	Rv2977c	thiL	3332787..3333788	CCP45782.1
191	Rv2981c	ddlA	3336796..3337917	CCP45786.1
192	Rv2986c	hupB	3343176..3343820	CCP45791.1
193	Rv2987c	leuD	3344033..3344629	CCP45792.1
194	Rv2999	lppY	3357602..335856	CCP45805.1
195	Rv3001c	ilvC	3359585..3360586	CCP45807.1
196	Rv3002c	ilvN	3360624..3361130	CCP45808.1
197	Rv3021c	PPE47	3379376..3380452	Rv3021c_3106
198	Rv3022c	PPE48	3380440..3380682	Rv3022c_3107
199	Rv3101c	ftsX	3469786..3470679	CCP45911.1
200	Rv3112	moaD1	3479700..3479951	CCP45922.1
201	Rv3132c	devS	3497529..3499265	CCP45942.1
202	Rv3136	PPE51	3501794..3502936	CCP45946.1
203	Rv3198c	uvrD2	3569109..3571211	CCP46012.1
204	Rv3240c	secA1	3617682..3620531	CCP46059.1
205	Rv3244c	lpqB	3623159..3624910	CCP46063.1
206	Rv3245c	mtrB	3624910..3626613	CCP46064.1
207	Rv3265c	wbbL1	3645979..3646884	CCP46084.1
208	Rv3275c	purE	3658114..3658638	CCP46094.1
209	Rv3281	accE5	3663689..3664222	CCP46100.1
210	Rv3341	metA	3727488..3728627	CCP46162.1
211	Rv3343c	PPE54	3729364..3736935	CCP46164.1
212	Rv3347c	PPE55	3743711..3753184	CCP46168.1
213	Rv3350c	PPE56	3755952..3767102	CCP46171.1
214	Rv3372	otsB2	3786314..378748	CCP46193.1
215	Rv3423c	alr	3840194..3841420	CCP46245.1
216	Rv3457c	rpoA	3877464..3878507	CCP46279.1
217	Rv3458c	rpsD	3878659..3879264	CCP46280.1
218	Rv3462	infA	3880432..3880653	CCP46284.1
219	Rv3465	rmlC	3882834..3883442	CCP46287.1
220	Rv3490	otsA	3908236..3909738	CCP46312.1
221	Rv3581c	ispF	4023868..4024347	CCP46404.1
222	Rv3593	lpq	4034352..4035710	CCP46416.1

223	Rv3597c	lsr2	4040981..4041319	CCP46420.1
224	Rv3602c	panC	4044281..4045210	CCP46425.1
225	Rv3607c	folB	4048744..4049145	CCP46430.1
226	Rv3608c	folP1	4049138..4049980	CCP46431.1
227	Rv3625c	mesJ	4063901..4064872	CCP46448.1
228	Rv3666c	dppA	4105459..4107084	CCP46489.1
229	Rv3708c	asd	4151180..4152217	CCP46534.1
230	Rv3709c	ask	4152218..4153483	CCP46535.1
231	Rv3710	leuA	4153740..4155674	CCP46536.1
232	Rv3713	cobQ2	4158227..4158922	CCP46539.1
233	Rv3782	glfT1	4228347..4229261	CCP46611.1
234	Rv3792	aftA	4237932..4239863	CCP46621.1
235	Rv3793	embC	4239863..4243147	CCP46622.1
236	Rv3795	embB	4246514..4249810	CCP46624.1
237	Rv3805c	aftB	4266953..4268836	CCP46634.1
238	Rv3806c	ubiA	4268925..4269833	CCP46635.1
239	Rv3808c	glfT2	4270366..4272279	CCP46637.1
240	Rv3858c	gltD	4330039..4331505	CCP46687.1
241	Rv3859c	gltB	4331498..4336081	CCP46688.1
242	Rv3923c	rnpA	4410412..4410789	CCP46752.1

Table 2: Screened drug target genes along with their functions

S. No.	Function	No. of targets
1.	Amino acid Biosynthesis	42
2.	Antibiotic resistance	1
3.	ATP Synthesis	4
4.	Carbohydrate metabolism	7
5.	Carbon fixation	1
6.	Cell division	3
7.	Cell wall biogenesis/degradation	22
8.	Cofactor biosynthesis	4
9.	Cytochrome complex assembly	1
10.	DNA repair	3
11.	DNA Replication	4
12.	Electron transport	5
13.	Lipid metabolism	7
14.	Folate biosynthesis	2
15.	Glycolipid biosynthesis	1
16.	Isoprene biosynthesis	2
17.	Lipoprotein biosynthesis	1
18.	Menaquinone biosynthesis	2
19.	Nitrogen metabolism	1
20.	Nucleotide biosynthesis	2
21.	Pantothenate biosynthesis	2
22.	Pentose phosphate pathway	1
23.	Phospholipid metabolism	2
24.	Porphyrin biosynthesis	1
25.	Protein biosynthesis	4
26.	Protein lipidation	1
27.	Purine metabolism	2

28.	Pyrimidine biosynthesis	4
29.	Riboflavin biosynthesis	4
30.	Siderophore biosynthesis	3
31.	Stress response	1
32.	Sulfur metabolism	2
33.	Thiamine biosynthesis	1
34.	Toxin-antitoxin system	1
35.	Transcription	12
36.	Translation	19
37.	Translocation	3
38.	Two-component regulatory system	3

Table 3: Screened amino acid biosynthesis drug target genes

S. No.	Locus	Gene name	Function
1.	Rv1005	pabB	Amino acid Biosynthesis
2.	Rv0189c	ilvD	
3.	Rv1133c	metE	
4.	Rv1201c	dapD	
5.	Rv1202	dapE	
6.	Rv1293	lysA	
7.	Rv1294	thrA	
8.	Rv1296	thrB	
9.	Rv1599	hisD	
10.	Rv1600	hisC1	
11.	Rv1602	hisH	
12.	Rv1603	hisA	
13.	Rv1605	hisF	
14.	Rv1606	hisI	
15.	Rv1609	trpE	
16.	Rv1611	trpC	
17.	Rv1612	trpB	
18.	Rv1613	trpA	
19.	Rv1652	argC	
20.	Rv1653	argJ	
21.	Rv1654	argB	
22.	Rv2121c	hisG	
23.	Rv2122c	hisE	
24.	Rv2178c	aroG	
25.	Rv2192c	trpD	
26.	Rv2392	cysH	
27.	Rv2537c	aroD	
28.	Rv2538c	aroB	
29.	Rv2540c	aroF	
30.	Rv2726c	dapF	
31.	Rv2747	argA	
32.	Rv2987c	leuD	

33.	Rv3001c	ilvC	
34.	Rv3341	metA	
35.	Rv3423c	alr	
36.	Rv3708c	asd	
37.	Rv3709c	ask	
38.	Rv3710	leuA	
39.	Rv3858c	gltD	
40.	Rv3859c	gltB	
41.	Rv1295	thrC	

Table 4: Screened cell wall biogenesis/degradation genes

S. No.	Locus	Gene Name	Function
1.	Rv0236c	aftD	Cell wall biogenesis/degradation
2.	Rv2145c	wag31	
3.	Rv2152c	murC	
4.	Rv2153c	murG	
5.	Rv2154c	ftsW	
6.	Rv2155c	murD	
7.	Rv2156c	murX	
8.	Rv2157c	murF	
9.	Rv2163c	pbpB	
10.	Rv1018c	glmU	
11.	Rv1477	ripA	
12.	Rv2673	aftC	
13.	Rv2981c	ddlA	
14.	Rv2986c	hupB	
15.	Rv3265c	wbbL1	
16.	Rv3713	cobQ2	
17.	Rv3782	glfT1	
18.	Rv3792	aftA	
19.	Rv3793	embC	
20.	Rv3805c	aftB	
21.	Rv3806c	ubiA	
22.	Rv3808c	glfT2	

Discussion:

Especially in Asia and Africa, tuberculosis (TB) is a major cause of disease and death. Every year, about 8 million people get tuberculosis, and every 15 seconds, someone passes away from the illness (2 million deaths) [3]. 9.2 million new cases of tuberculosis and 1.7 million deaths from the disease were reported globally in 2006; of these, 0.7 million cases and 0.2 million deaths occurred in HIV-positive people [10]. The biggest disadvantage of the current medication regimen is the development of drug resistance. [5]. By changing the target enzymes, Mtb can avoid the effects of antibiotics [11–12].

More than two decades have passed since the last anti-Mtb medication was created. To prevent the "global catastrophe" that the WHO has predicted, new approaches are vitally needed given the growing resistance to the most effective anti-Mtb medications now on the market [13]. Stewart Cole and colleagues' timely discovery of the Mtb H37Rv genome sequence in 1998 gave TB research a much-needed boost by clarifying the pathogen's genetic makeup and identifying numerous novel gene products for mechanistic and structural characterization as well as possible new therapeutic targets [14-15]. Thus, a list of trustworthy targets for Mtb can be quickly generated using a computational approach to drug target discovery. These techniques are quick, inexpensive, and above all offer a comprehensive systemic view of the entire microorganism at one point in time [16].

Considering that it is well accepted that bacteria have both genes that have human host homologues and genes that do not, it takes extremely little time to generate a desirable list when target identification is done using a computational approach. In this case, a database search yielded 3924 total genes in the M. tuberculosis H37Rv genome. To improve the results, we annotated every gene and eliminated any hypothetical genes. 242 genes have been identified as viable targets for medication

after all speculative genes have been eliminated. After functional analysis using Uniprot 181 genes were identified as potential targets. Future drug research may target these genes and their products, and tuberculosis screening may be conducted using currently existing medications.

Conclusion:

Genome analysis of Mycobacterium tuberculosis has provided valuable insights into its biology and identified potential drug targets. By targeting essential pathways and virulence factors, novel therapeutic strategies can be developed to combat drug-resistant TB and enhance treatment outcomes [17-18]. Our findings offer a straightforward framework for combining the enormous amounts of genetic data that are useful for therapeutic target discovery. To avoid unintended toxicity, therapies that selectively target genes with high homology to the host should be developed based on genome homology when searching for novel antituberculosis medications. Using the BLASTX homology searching tool, 242 of the 3924 protein-coding genes of the M. tuberculosis H37Rv genome were revealed to have no human homology. These genes may be useful in the future drug-discovery process or even in screening tuberculosis medications to determine their efficacy (Table. 1).

Continued research and collaboration among scientists, clinicians, and pharmaceutical companies are essential to translate these genomic insights into effective anti-TB therapies.

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