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Investigating the Toxin Sequences of the Toxin-Antitoxin System between Mycobacterium Tuberculosis and Mycobacterium Bovis

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ABSTRACT

Tuberculosis counts as a significant clinical disease caused by Mycobacterium tuberculosis or, less commonly, Mycobacterium Bovis [1]. Also, Toxin antitoxin is a unique system in bacterias such as Mycobacterium, and different types of protein contribute to this system. In this research amino acid sequences of type 2 toxin protein have been analyzed between Mycobacterium Bovis and Mycobacterium tuberculosis as the principal cause of tuberculosis. Data analyses indicate the presence of different amino acids in MazF7, VapC11, VapC18, vapC24, VapC48, and VapC49 among two variant. understanding of this construction leads to measuring the resistant parameter more clearly against the drugs. Moreover, the presence of many similarities in the toxin sequence confirmed that these two variants more probably come from the same ancestor.

Keywords: Mycobacterium Tuberculosis, Mycobacterium Bovis, Toxin- Antitoxin system, Bioinformatics

Introduction

Tuberculosis counts as a consequential clinical disease caused by Mycobacterium tuberculosis or, less commonly, Mycobacterium Bovis. Many types of research have been done based on bioinformatics analysis which indicates Mycobacterium tuberculosis evolved from Mycobacterium Bovis [2]. There are some hypotheses which said that an ancient ancestor of M. tuberculosis-infected hominids in East Africa 3 million years ago until now [3].

M.tuberculosis is an anaerobic, non–spore-forming, nonmotile bacillus with a specific future. Over a hundred species of Mycobacterium have been recognized yet [4]. M.tuberclusis and M. Bovis are counted as two important types of this family that induce Tuberculosis in humans. therefore in this research, these two types of Mycobacterium were investigated and compared with each other.

The prokaryotic kingdom consists of numerous creatures with specific and unclear cellular mechanisms. Toxin-antitoxin system has been recently discovered by scientists which are distributed among bacteria [5]. This system typically included protein toxin and antitoxin that can be coding RNA or protein. Toxin antitoxin was initially found in the bacteria plasmid [6], and later bioinformatics analysis identified the presence of TA (toxin-antitoxin) loci in several chromosomal genes [7]. Many parameters such as environmental stress, plasmid loss, and bacteriophage infection can infect the bacteria and put it in a dangerous situation, also these parameters activate essential cellular processes which lead to growth inhibition and finally, cell death [8].

According to the antitoxin activities, five types of antitoxin families have been described named: types (I), (II), (III), (IV), and (V) [9]. Some of the antitoxins inhibit toxin synthesis like type one [10]. On the other hand, some of the antitoxins directly connect to the protein and inactive toxin example type (II) [11]. In the following, these proteins contrast between Mycobacterium tuberculosis and Mycobacterium Bovis to see the similarities and differences.

Generally, 79 TA systems have been identified in Mycobacterium tuberculosis which 67 of them belong to the type 2 families. Typically they are separated into six specific systems called: VapBC, MazEF, YefM\YoeB, RelBE, HigBA, and ParDE [12]. In this

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research, the amino acid sequence of these proteins has been analyzed and contrasted with each other.

Materials and Methods

114 protein sequences of the different toxin-antitoxin type 2 families have been collected from the NCBI data bank. Samples consist of two types of the toxin-antitoxin system, including MazF and Vapi. 18 samples are all, related to the MazEF system and, the rest are for VapBC. Table 1 shows data with accession numbers in NCBI. after data collection, protein sequences in FASTA format were imported to the MEGA 11, then sequences were aligned in multiple duel groups to detect the contrasting easier.

Table 1
Protein name and accession number in NCBI

Name	Mycobacterium tuberculosis variant bovis	Mycobacterium tuberculosis
VapB	QPC48540.1	UOP13931.1
MazF1	TXA01530.1	QJF20518.1
MazF2	TWZ99346.1	QJF20718.1
MazF3	QPC51308.1	UOP16756.1
MazF4	QPC51675.1	UOP17125.1
MazF5	TXA04589.1	BCX21894.1
MazF6	QPC48552.1	UOP13943.1
MazF7	QPC48624.1	WP_244703471.1
MazF8	AYP12564.1	QJF22322.1
MazF9	UOP14700.1	QPC49279.1
VapC1	TXA00930.1	UOP15799.1
VapC2	TWZ98959.1	BCX20219.1
VapC4	QPC52106.1	UOP16290.1
VapC6	QPC50909.1	UOP16346.1
VapC7	TKZ14245.1	QJF20720.1
VapC8	TWZ99341.1	BCX20591.1
VapC9	SIT99584.1	QJF21024.1
VapC10	AMC50186.1	QJF21455.1
VapC11	WP_217416959.1	UOP17185.1
VapC12	TXA03923.1	BCX21659.1
VapC13	AMC50729.1	QEX89624.1
VapC14	TXA03708.1	BCX21906.1
VapC16	TXA03457.1	QJF22279.1
VapC17	TXA04515.1	BCX22513.1
VapC18	TKZ12090.1	BCX22533.1
VapC19	TXA03167.1	BCX22535.1
VapC20	QPC49056.1	UOP14463.1
VapC21	QPC49238.1	UOP14658.1
VapC22	TXA02931.1	BCX22816.1
VapC23	TXA02897.1	BCX22852.1
Vapc24	CAB5247952.1	BCX20159.1
VapC26	UOP16277.1	QPC50842.1
VapC29	QPC50873.1	UOP16310.1
VapC30	UOP16315.1	QPC50878.1
VapC31	TWZ99259.1	BCX20673.1
VapC32	TWZ99734.1	QJF21175.1
VapC34	AYP12102.1	BCX21682.1
VapC35	TXA03700.1	BCX21915.1
VapC36	SIU00609.1	BCX21940.1
VapC37	TXA03572.1	BCX22085.1
VapC38	TXA01050.1	BCX22479.1
VapC39	QJF22581.1	TXA03185.1
VapC41	TXA03115.1	BCX22592.1
VapC42	SIU01398.1	GJJ21051.1
VapC43	SIU01518.1	BCX22862.1
VapC44	TXA00356.1	BCX23340.1
VapC45	TXA02606.1	QEX91020.1
VapC46	TXA02422.1	BCX23415.1
VapC47	TXA02399.1	QJF23445.1

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VapC48	AYP13804.1	BCX23736.1
VapC49	TWZ98837.1	BCX23191.1
VapC50	SIU02404.1	BAX42915.1

Two different types of toxin-antitoxin system type (II) were collected from the NCBI data bank for M.bovis and M.tuberculosis.

Results

Investigation through the data indicates most of these proteins have the same and similar sequence compared to each other but some differences were found in 7 types of proteins which will be discussed in the following.

MazF7 is one of the ten proteins in the MazEF system. MazF7 is one of the toxins of this family that contain 136 amino acid [13]. Analysis identified amino acid 5 in these sequences are different between the M.bovis and M. tuberculosis. Amino acid 5 of MazF7 in them. Bovis is Arginine but in the M.tuberculsis is Glutamine.

The VapBC family was first discovered from a virulence plasmid in Salmonella Dublin and has the highest number of loci in Mycobacterium tuberculosis. The activity of VapC toxins is under the expression of cognate antitoxins, therefor when they are complexed with VapB antitoxins, it causes toxin inactivation. Most VapC toxins have ribonuclease activity so the expression of toxins in the cell can cause Potent translation inhibition followed by growth arrest and even cell death. Vapc2 is a protein of the VapBC family. Analyses identified M.bovis VapC2 proteins have two more aminoacids at the second and third amino of the sequences which are called Aspartic Acid and Valine in order.

It has been identified that VapBC49 has an important role in drug-tolerant [15] analysis reveals many contrasts in this samples. also amino acid 52 in VapC11 is different between Bovis and tuberculosis variants. Moreover, VapC18, VapC24, and VapC48 have been counted as differences too. The differences reported in Table 2.

Table 2
Seven types of protein have different amino acid sequences with specific future

Protein name	Variant	Description
MazF7	M.bovis	Amino acid 5 is Arginine
	M.tuberculosis	Amino acid 5 is Glutamine
VapC2	M.tuberculosis	Have two more amino acids in the second and third position including Glutamic acid and Valine.
VapC11	M.bovis	Amino acid 52 is Glycine
	M.tuberculosis	Amino acid 52 is Acpartic acid
VapC18	M.bovis	Contain 17 more Amino acid at the primary part of the sequence
VapC24	M.bovis	Amino acid 31 is Serine
	M.tubeculosis	Amino acid 31 is Alanine
VapC48	M.tuberculosis	Contain 7 more Amino acid at the primary part of the sequence
VapC49	M.bovis, M.tuberculosis	Alignment reveals many dissimilarities in these samples

Conclusion

Investigating the protein sequences of the different toxin-antitoxin system indicate characteristic protein with specific future. Understanding these contrasts leads us to detect the potential region of the protein. These regions must be considered in drug design. M.bovis and M.tuberculosis both can occur tuberculosis in humans. Using a distinct drug to target this protein is important and can boost the treatment. Moreover designing a unique antibiotic or other drug Based on the M.bovis toxin sequences can be useful in veterinary science.

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