Dissemination Patterns of Tetracycline Resistance Genes.

Rita Abi Rizk.

Master's thesis presented at the Ilia State University of School of Natural Sciences and Medicine for Applied Genetics Master's Degree.

According to the requirements Master's

Program of Applied Genetics

Supervisor Cort Anderson, Full Professor

Ilia State University

Tbilisi, 2021

Contents

Acknowledgments: 3
Statement 4
List of abbreviations: 5
Abstract: 6
A. Antibiotic resistance: 7
B. Uses of tetracycline: 8
C. Mechanism of tetracycline antibiotic effect, and mechanisms of Tet resistance 9
1- Efflux of tetracycline: 9
2- Ribosomal protection protein: 10
3- Enzymatic inactivation of tetracycline: 11
D-Antibiotic resistance dissemination: 12
Aim of the study: 17
Materials and Methods 19
1- Selection of sequences for analysis 19
2- Alignment and phylogenetic analysis 20
3- Statistical analysis: 22
Results: 23
Discussion: 29
Conclusion 31
Bibiography 32
Website bibliography: 42
Figure bibliography: 43
Appendix: 44

Acknowledgments:

I would like to express my deepest appreciation to Professor Tarkhnishvili, for his invaluable contribution and suggestions during the entire period of my thesis.

I cannot begin to express my thanks without mentioning Professor Anderson for his guidance and constructive criticism.

My deepest thank you is for Ilia State university family, administration, students and teachers who without their support the completion of this thesis would have not been possible.

I am deeply indebted for the faculty of Engineering and Sciences ,for their chance to allow me to follow the applied genetics program.

Last but not least i would like to extend my sincere thanks to my mother who without her support, sacrifices, and encouragement I could not have completed my thesis.

Statement

As the author of the presented Master's Thesis, I declare that the work is my original work and does not contain materials submitted for publication, published or protected by other authors, which are not mentioned in the work or quoted in accordance with the relevant rules.

R. Abi Rizk

List of abbreviations:

ABC- ATP-binding cassette.

ARB-antibiotic resistant bacteria.

ARG - antibiotic resistance gene.

BLAST-basic logic alignment search tool.

HGT - horizontal gene transfer.

MATE- multidrug and toxin extrusion.

MDR- multidrug resistance.

MIC-minimum inhibitory concentration.

MF - major facilitator.

MEGA-molecular evolutionary genetics analysis software.

NCBI-national center for bioinformatics.

RND-resistance nodulation division.

SMR-small multidrug resistance.

STD- sexually transmitted diseases.

tet – tetracycline resistance gene.

t RNA- transfer ribonucleic acid.

Tuf – gene that codes for elongation factor.

WHO-World Health Organization.

16S r RNA-gene codes for the small ribosomal subunit.

Abstract:

Tetracycline resistance genes confer resistance to tetracycline and its derivatives. This resistance has 3 different mechanisms and is encoded by multiple genes, divided into categories based on the mechanism of resistance. Tetracycline and its derivatives are widely used in different fields: agriculture, medicine, and in the food industry. This extensive use of tetracycline has led to widespread tetracycline resistance in bacteria for the tetracycline antibiotic family.

Maximum parsimony and maximum likelihood phylogenetic analysis of the *tuf* locus and *16S rDNA* provide independent phylogenies of the bacterial taxa carrying the *tet (W)* gene, which confers one variety of tetracycline resistance. The topologies of these loci are generally congruent, while the phylogeny based upon *tet (W)* sequences is radically different from *tuf*- and *16S rDNA*-derived phylogenies. Pearson's test for correlation and Partial Mantel tests on the respective trees indicate significant congruence of *tuf* and *16S rDNA*-based phylogenies, but no congruence with *tet (W)*-derived trees. This indicates that *tet (W)* has experienced an evolutionary history completely different from and independent of the evolution of the host taxa. The strong implication is that *tet (W)* and its consequent tetracycline resistance is present in extant bacterial taxa due to horizontal gene transfer, rather than evolving in and with the bacterial taxa where the gene is currently found. Assuming this pattern is general for other tetracycline resistance genes, which seems likely, this suggests that control and management of resistant bacteria needs to focus on limiting opportunities for conjugation, transduction, and transformation, in order to prevent proliferation of antibiotic resistance in bacterial populations that currently lack the trait3 different mechanisms and is encoded by multiple genes, divided into categories