OPEN ACCESS Freely available online

Mycobacterial Diseases

Perspective

Role of Lipid Metabolism to Drug Resistance in *Mycobacterium tuberculosis*

Feng Tohkin*

Department of Bacteriology, Niigata University, Niigata, Japan

DESCRIPTION

Mycobacterium tuberculosis (*M. tb*), exacerbated by the rise of drug-resistant strains. Multi Drug-Resistant (MDR) and Extensively Drug-Resistant (XDR) strains of *M. tb* are particularly difficult to treat, posing a challenge to global TB control efforts. Among various adaptations observed in drug-resistant strains, the accumulation of Triacylglycerols (TAGs) has garnered attention due to its potential role in the survival and persistence of these resistant bacteria. Triacylglycerols are non-polar lipids composed of three fatty acids esterified to a glycerol backbone. In bacteria, including *M. tb*, TAGs primarily serve as energy reserves. They are stored in cytoplasmic lipid droplets, which can be utilized when the bacterium faces stress or limited nutrient availability. Although TAG accumulation is common in many organisms under stress conditions, its specific role in drug-resistant *M. tb* presents intriguing possibilities for understanding bacterial survival and persistence.

Mechanisms of TAG accumulation in drug-resistant strains

Research indicates that TAG levels are elevated in drug-resistant *M. tb* isolates compared to drug-sensitive strains. Studies have shown a 1.2-fold increase in TAG accumulation in Streptomycin (SE) and Rifampicin (R)-resistant isolates. This increased lipid storage is not merely incidental but is believed to contribute to the bacteria's ability to resist antibiotics and survive in hostile environments. Antibiotics exert significant stress on *M. tb*, pushing the bacteria to adapt metabolically. One such adaptation is the accumulation of TAGs as an energy reservoir. During antibiotic exposure or nutrient deprivation, the bacteria can rely on these stored lipids to sustain essential processes and remain viable. TAG accumulation provides a buffer against metabolic challenges, allowing drug-resistant strains to persist during extended periods of antibiotic treatment. TAG accumulation is closely linked to the ability of *M. tb* to enter a dormant or latent state. Dormancy is a survival strategy used by the bacterium to evade host immune responses and resist drug treatment. In this state, the bacteria significantly reduce their metabolic activity, making it harder for antibiotics to be effective, as most TB drugs target actively replicating cells. Lipid droplets rich in TAGs accumulate during dormancy, providing an energy source that the bacterium can tap into during its reactivation from latency. The cell envelope of *M. tb* is a complex structure composed of a thick, waxy layer of lipids, making it intrinsically resistant to many antibiotics. TAGs, along with other lipids, are important components of this envelope. Changes in lipid composition, particularly the increased accumulation of TAGs, could reinforce the bacterial cell wall, making it less permeable to drugs. This could explain why drug-resistant strains accumulate more TAGs, as they may rely on a more robust cell envelope to survive antibiotic assault. Drug-resistant *M. tb* strains may undergo metabolic reprogramming that favours lipid biosynthesis over carbohydrate metabolism.

Clinical relevance of TAG accumulation in drug resistance

The accumulation of TAGs in drug-resistant *M. tb* has significant clinical implications. It suggests that lipid metabolism plays an important role in the survival and persistence of drug-resistant strains, particularly during prolonged antibiotic treatment. Targeting lipid metabolism pathways could represent a novel therapeutic approach for treating drug-resistant TB. Disrupting TAG biosynthesis or promoting its degradation could weaken drug-resistant *M. tb* and make it more susceptible to existing antibiotics. Inhibitors that block enzymes involved in TAG formation, such as diacylglycerol acyltransferase, could reduce the bacteria's ability to accumulate lipids, potentially reducing their ability to enter dormancy and resist drugs. TAG accumulation may also contribute to the persistence of drug-resistant *M. tb* in the host, even after the completion of antibiotic therapy. This could explain why patients treated for drug-resistant TB sometimes experience relapse. Lipid storage mechanisms enable the bacteria to survive in a dormant state, ready to reactivate once antibiotic pressure is reduced.

CONCLUSION

The accumulation of TAGs in drug-resistant *M. tb* represents a

Correspondence to: Feng Tohkin, Department of Bacteriology, Niigata University, Niigata, Japan, Email: fengtoh@126.com

Received: 03-Jul-2024, Manuscript No. MDTL-24-33689; **Editor assigned:** 05-Jul-2024, PreQC No. MDTL-24-33689 (PQ); **Reviewed:** 19-Jul-2024, QC No. MDTL-24-33689; **Revised:** 26-Jul-2024, Manuscript No. MDTL-24-33689 (R); **Published:** 02-Aug-2024, DOI: 10.35248/2161-1068.24.14.488.

Citation: Tohkin F (2024). Role of Lipid Metabolism to Drug Resistance in *Mycobacterium tuberculosis*. Mycobact Dis.14:488.

key adaptation that allows the bacteria to survive under antibiotic pressure and evade the immune system. By accumulating TAGs, drug-resistant strains can maintain energy reserves, reinforce their cell envelope, and enter a dormant state, making them more difficult to eliminate. Understanding the role of TAGs in bacterial persistence offers new avenues for therapeutic intervention, particularly in the fight against drug-resistant TB. Targeting lipid metabolism could enhance the efficacy of existing treatments and help overcome one of the major barriers to controlling this global health threat. This shift could be part of a broader strategy to survive under antibiotic pressure. Increased lipid metabolism has been observed in resistant strains, contributing to the accumulation of TAGs. This metabolic flexibility allows the bacteria to adapt to changing environmental conditions, including the presence of antibiotics.