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To Study the Function of Heme Molecules in Mycobacterium TB Survival and Pathogenesis

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ABSTRACT:

Background: Mycobacterium tuberculosis is an aerobic gram positive pathogen which causes deadly disease called tuberculosis (TB) which is still a major threat to life. Mycobacterium tuberculosis Pathogen enters in host by inhalation of air because these pathogens are present in air droplets released by other TB infected persons. It ultimately reaches to lung alveoli and gives rise to primary TB. **Aims & objectives:** To study the function of heme molecules in mycobacterium TB survival and pathogenesis. **Methods & Materials:** Asteraceae family member Artemisia afra is a plant that has been identified. A drug called Artemisinin was extracted from the plant Artemisia afra. Because this medication targets the heme molecule, which senses the pathogen's need for less oxygen to survive, replication is fully stopped. **Results**: In order to absorb iron, the heme molecule takes nascent oxygen. If it is possible, we may create a synthetic molecule that alters the heme's oxygen binding site. When this happens, oxygen cannot bind to the heme, and the pathogen dies from a lack of oxygen. **Conclusion:** Macrophages mycobacterium replicates itself and increases its number in host cell. Artemisinin is a drug obtained from the plant Artemisia which target the heme molecule in mycobacterium and stop its replication.

Keywords*:* Mycobacterium Tuberculosis; H37Rv; Rv0203; Hememolecule; Artemisia Afra

INTRODUCTION:

Mycobacterium is an aerobic, bacteria. As these pathogens are present in air droplets released by sneezing or coughing of Mycobacterium tuberculosis infected individuals, Mycobacterium strains are present in the air and enter the host through nasal inhalation. These pathogens ultimately reach the lungs where they cause primary infection of the lungs and secondary infection of lymphoid organs. Air droplets carry the infection into the body's circulatory system where it attacks macrophages to replicate.

Mycobacterium tuberculosis H37Rv is a pathogen that assaults hosts with great success [1]. This pathogen enters the host circulation through Micro fold cells in addition to respiration. Figure 1 illustrates how a microfold cell might help Mycobacterium spread outside of the mucosa and mediate initial infection [2]. In 2015, 6.1 million new cases of tuberculosis were

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reported to national authorities and the WHO, and an increase in the disease was seen between 2013 and 2015, according to a 2016 WHO report [3]. Since iron is a co-factor for at least 40 of the enzymes in Mycobacterium and also helps to keep iron levels in balance, iron is the molecule that is essential for the survival of this pathogen [4]. Mycobacterium produces and uses siderophores (low-molecular-weight iron chelators) to sequester iron since its pathogenicity depends on its capacity to ingest iron [5]. Only when the heme is in ferrous (Fe2+) in the host circulation is oxygen absorption possible. A loss of O2 (CO2 + C2CO), an increase in hydrogen (C + 2H2CH4), or a gain of electrons (O2 +e-O2•-) are all considered reductions. Lung macrophages and neutrophils produce significant amounts of reactive oxygen species (ROS) and reactive nitrogen species during the phagocytosis of Mycobacterium (RNS). Using NADPH as an electron donor, NADPH oxidase catalyses the one-electron reduction of O2, resulting in O2•- 2O2 + NADPH O2• + NADP+ + H+. [6].

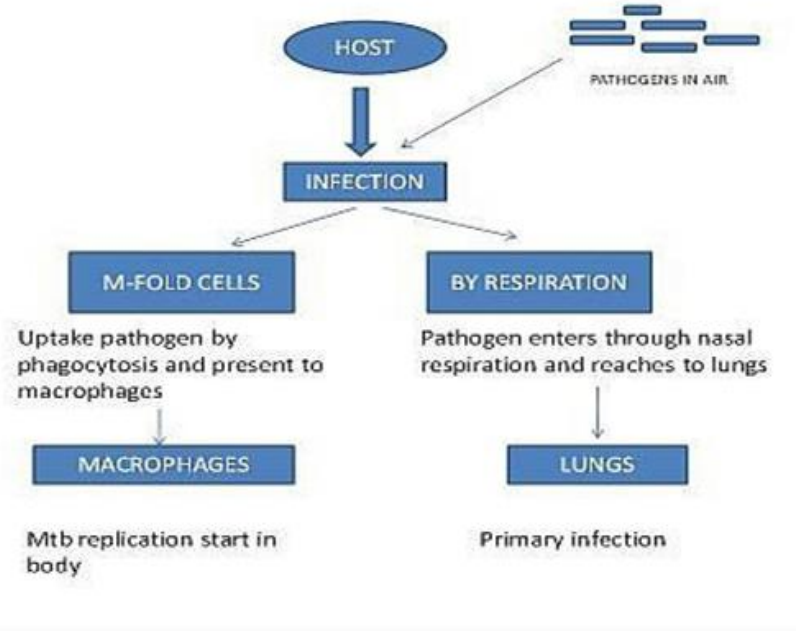

Figure 1: Mycobacterium infection in host

Mycobacterium has evolved a variety of mechanisms to absorb iron, including the use of siderophore molecules to scavenge iron from the host body and the heme molecule method depicted in Figure 2. As was mentioned above, the heme molecule creates an aerobic environment for pathogen survival by only accepting newly formed oxygen. A gene called Rv0203 in pathogens may translate the protein molecule heme. A gene called Rv0203 in pathogens may translate the protein compound heme. Rv0203 is a highly unusual heme transfer protein with a distinctive structure. It features an alpha-helical structure and a dimer of dimmers, each of which is made up of four antiparallel helices and five alpha-1 helices on each monomer. Alpha 5-helices form a weak hydrophobic core in an off-tilt cage-like structure that is created when two dimers link together [7]. Staphylococcus aureus and Escherichia coli are two organisms that have the capacity to absorb heme.

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Double knockout studies were used to examine the function of Rv0203. Mycobacterium protein tags were used to conduct the mutation experiment. Rv0203-His was used to tag histidine, but the natural protein was untagged (Rv0203-notag). By means of a bis-his co-ordination bond, Rv0203-His binds to heme. In a mutagenesis experiment, it was found that the residues His63, His89, and Tyr59 help Rv0203 bind to heme effectively. When using stopped flow techniques, the rate of heme binding to Rv0203- His and Rv0203-notag is equal [8]. Asteraceae family member Artemisia afra has been identified in a recent study as a plant. A drug called Artemisinin was extracted from the plant Artemisia afra. Because this medication targets the heme molecule, which senses the pathogen's need for less oxygen to survive, replication is fully stopped. Artemisinin prevents replication by extracting dichloromethane. Artemisinin was found to have the ability to eradicate Mycobacterium tuberculosis infections to undetectable levels [9]. It grows in loamy sands to sandy or calcareous clay loams of volcanic or granitic origin and is frequently found in Africa and South Africa [10].

Artemisia afra also exhibits powerful pharmacological activities including antimicrobial, antioxidant, CNS-effects (sedative, antidepressant), cardiovascular, and spasmolytic activity which has been well documented and reviewed recently by Liu et al. [11]

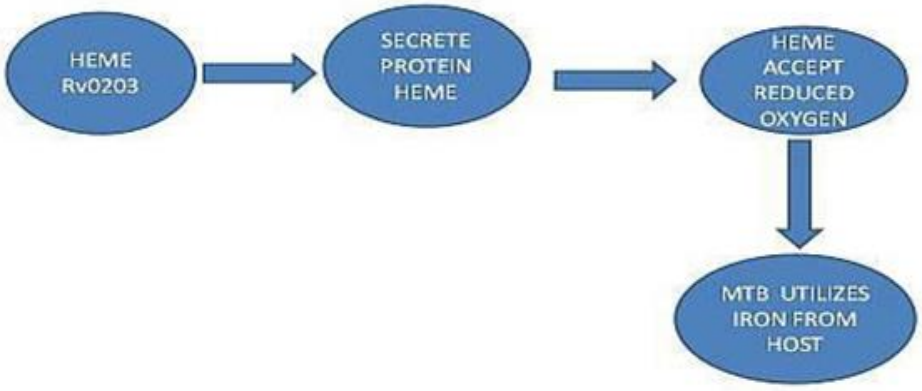

Figure 2: Iron uptake by using heme molecule

CONCLUSION

I would like to summarise my points by saying that Mycobacterium tuberculosis is a fatal illness that is brought on by various Mycobacterium strains in various geographic locations. Airborne pathogens can enter a host through inhalation and microfold cells. This is an aerobic bacteria, and the heme protein that the gene Rv0203 translates into provides a location for binding oxygen. Heme is activated by the binding of oxygen and scavenges iron from host machinery. A recent drug, artemisinin, stops M. tuberculosis replication in the host and almost eradicates TB. a strategy for treating TB.

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