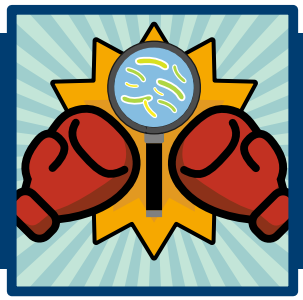
UNIT: TUBERCULOSIS

LESSON 3: ME VS. TB - BOOSTING THE IMMUNE SYSTEM TO DEFEAT AN ANCIENT ADVERSARY

Activity 3D: *DON'T SPILL THE TB: A SCIENCE THEATER*



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General Information

Tuberculosis (TB), ***Mycobacterium tuberculosis***, is a bacterium that is estimated to have existed nearly as long as humans. Historically, TB infection has been known by different names: white plague, phthisis, and consumption. Most people who are exposed to TB generally recover, usually without even knowing they were infected. Tuberculosis is spread as an aerosol and generally affects the lungs. When an infected person exhales, coughs, sneezes, or even sings, the TB bacteria is carried on droplets and stays suspended in the air for hours. When someone inhales these minute droplets, the TB is carried into the lungs where it attaches to cells within the lung.

Host-Directed Therapies & Cell Death Pathways

All cells have a limited life span. At the end of the cell's lifespan, it experiences a cell death pathway. Although there are several cell death pathways, the two primary pathways associated with TB research are apoptosis (A-pop-**toe**-sis) and necrosis (neh-**CROW**-sis). Apoptosis is the "normal" cell death pathway. During apoptosis, the cell membrane stays in tack, keeping all contents inside as the body eliminates the cell.

However, when a cell is infected with TB, the bacteria activate specialized receptors embedded in the cell membrane. When activated, these specialized receptors shut off apoptosis and activate the necrosis cell death pathway. With the necrosis pathway activated, the cell membrane will rupture, releasing bacteria into the body for more TB to infect other cells. As infected cells undergo necrosis chemical signals alert the immune system to send macrophages (**MAC**-row-fayj), the first line of defense. Using affixes, the word macrophage is derived from Greek meaning "big eater". The prefix "macro" meaning big and the suffix "phage" meaning to eat. The word is correctly pronounced in several ways, such as **MAC**-row-fahj or **MAC**-row-fayj.

The macrophages surround cells infected with TB through phagocytosis (fay-go-sigh-**TOE**-sis). Once the cell is surrounded the macrophage destroys the cell and kills the TB bacteria. The macrophage then undergoes necrosis. As it breaks apart, the "dead" TB is released into the body which alerts other immune cells of the invader. These other immune cells migrate to the area to kill the TB. However, if there are too many TB bacteria, the other immune cells surround the infected cells. This forms a ball called a granuloma (gran-you-**LOW**-ma). Tuberculosis bacteria inside the granuloma are still alive but encapsulated and unable to infect more cells.

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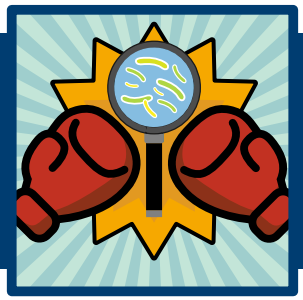

Antibiotics and TB

Antibiotics have been used successfully to treat TB infections, specifically rifampicin (RIF), isoniazid (INH), pyrazinamide (PZA), and ethambutol (EMB). Of these, RIF and INH are most frequently used to treat TB. But these antibiotics have harsh side effects such as chronic fatigue, blurred vision, easy bruising or bleeding. In addition, long-term use of antibiotics can cause tingling, numbness and burning in the hands and feet. Some of these side effects may be permanent.

The formation of granulomas by macrophages and other immune cells (macrophages, T cells, neutrophils, eosinophils, fibroblasts, collogen) present another problem for treatment. Antibiotics have limited success penetrating granulomas to reach the TB bacteria inside.

TB and Apoptosis

Boosting the immune system interferes with TB's ability to shut off apoptosis, meaning cells infected with TB do not break apart preventing TB from spreading. Although dead, the cell stays intact, and the body eliminates the cell, and the TB contained inside. It had been suspected that HDTs could be a mechanism to control TB's ability to shut off apoptosis, but until this study, there was limited research to support this idea. However, the positive results shown by the introduction of HDTs to treat cancer provided the necessary evidence to investigate HDTs effect on TB treatment.

Based on prior research and with information about HDTs from cancer research, Texas Biomed scientists sought to discover the impact of HDTs on TB. Unlike antibiotics which attack the TB bacteria, HDTs boost the immune system by increasing antimicrobial activities of immune cells to destroy TB while still inside infected cells. To treat granulomas the addition of HDTs changes the solubility of granulomas. By increasing the solubility of the surface of granulomas, it increases the ability of antibiotics to enter the granuloma and kill TB bacteria inside the structure.

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