Infection with Mycobacterium tuberculosis


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28/02/2022
**Introduction**

Reactome is open-source, open access, manually curated and peer-reviewed pathway database. Pathway annotations are authored by expert biologists, in collaboration with Reactome editorial staff and cross-referenced to many bioinformatics databases. A system of evidence tracking ensures that all assertions are backed up by the primary literature. Reactome is used by clinicians, geneticists, genomics researchers, and molecular biologists to interpret the results of high-throughput experimental studies, by bioinformaticians seeking to develop novel algorithms for mining knowledge from genomic studies, and by systems biologists building predictive models of normal and disease variant pathways.

The development of Reactome is supported by grants from the US National Institutes of Health (P41 HG003751), University of Toronto (CFREF Medicine by Design), European Union (EU STRP, EMI-CD), and the European Molecular Biology Laboratory (EBI Industry program).

**Literature references**


Reactome database release: 79

This document contains 6 pathways (see Table of Contents)
Infection with Mycobacterium tuberculosis (Mtb) is soon countered by the host's immune system, the organism is however almost never eradicated; ten per cent of infections will develop into "open tuberculosis", while the other ninety per cent become "latent", a state that can persist for decades until loss of immune control. Approximately 25% of the world's population is estimated to harbour latent tuberculosis. Latent infection involves the bacterium being internalized by phagocytes where it stops and counters the innate immune answer (Russell 2011, Russell et al. 2010). When a status-quo is reached, Mtb enters a non-replicating persistent state (Barry et al. 2009, Boshoff & Barry 2005). Weakening of the immune defense sooner or later enables the waking up and multiplication of the bacterium inside the phagocyte, necrosis of the cell, and escape, analogous to the burst of lytic viruses (Repasy 2013).

**Literature references**


**Editions**

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Modulation by Mtb of host immune system

Location: Infection with Mycobacterium tuberculosis

Stable identifier: R-HSA-9637628

Diseases: tuberculosis

Mtb enhances its chances for being taken up by a phagocyte by blocking adaptive immune responses, as well as other innate immune system responses. Components of the bacterial cell wall also specifically promote phagocytosis via both the opsonic pathway and the presentation of adhesins (Esparza et al. 2015).

Literature references


Editions

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Mycobacterium tuberculosis (Mtb) encounters a vastly changed environment shortly after being internalized by macrophages. The compartment it resides in, the phagosome, is acidified and devoid of important metal ions and is flooded with reactive oxygen and nitrogen species. Steps will be soon taken by the macrophage to "mature" the phagosome with all kinds of lysosomal digestive enzymes. However, unlike most other bacteria species, Mtb has evolved solutions to each of these threats. As a last resort to a strong immune response, some bacteria will enter a dormant state (de Chastellier 2009, Flannagan et al. 2009). To what extent this is true is still unclear (McDaniel et al. 2016). Upon weakening of the immune defense, Mtb reawakens from its dormant state and starts to multiply inside the phagocyte (Repasy et al. 2013).

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Latent infection - Other responses of Mtb to phagocytosis

Location: Infection with Mycobacterium tuberculosis

Stable identifier: R-HSA-1222499

Diseases: tuberculosis

*Mtb* encounters a vastly changed environment, soon after it gets internalized by macrophages. The compartment it resides in, the phagosome, is acidified and devoid of important metal ions. It is flooded with reactive oxygen and nitrogen species. And steps will be soon taken by the macrophage to "mature" the phagosome with all kinds of lysosomal digestive enzymes. However, unlike most other bacteria species *Mtb*. has evolved solutions to each of these threats and, after making sure these are installed, it soon will enter a dormant state (de Chastellier, 2009; Flannagan et al, 2009). A combination of the host defense and the response of the infecting bacillus (active and passive) ensure suppression of bacterial metabolic activity and replication, resulting in a non-replicating state (Russell 2011, Russell et al. 2010).

**Literature references**


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The relatively constant numbers of Mycobacterium tuberculosis (Mtb) during the chronic phase of infection are due to a balance between rapid replication and death (McDaniel et al. 2016). The relatively safe environment for Mtb in the phagocyte’s phagosome is overcome when about 20-25 bacterial cells accumulate (Repasy et al. 2013). First, the phagosomal membrane is destroyed. Then, by injuring mitochondria and depleting NAD+, cell necrosis is started, resulting in Mtb escape (Lee et al. 2011).

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Antimicrobial action and antimicrobial resistance in Mtb

Location: Infection with Mycobacterium tuberculosis

Stable identifier: R-HSA-9639775

Diseases: tuberculosis

Antimicrobial compounds kill microorganisms or inhibit their growth, either in the host, outside on the skin (antiseptics), or in the environment (disinfectants). In the host they are named after the target symbiont, for example antibiotics, antifungals, and antiparasitics. It suffices to permanently stop an essential pathway in the symbiont to kill it. Broad spectrum antimicrobials usually target a conserved pathway like protein synthesis or cell wall construction, in order to affect a whole taxonomic group (Arenz & Wilson 2016, Barry et al. 2007, Green 2002).

Resistance of microorganisms (bacteria, viruses, parasites) to antimicrobials is one of the most important public health problems. Many mechanisms exist, and they are either acquired by mutation, by horizontal gene transfer, or are already intrinsic to the organism. The main mechanisms are modification of the antimicrobial, or its removal from the place of action, modification of its binding partner in the affected pathway, or usage of a back-up pathway. Participation of the organism in a consortium (like in biofilms) enables additional resistance mechanisms (Aminov & Mackie 2007, Peterson & Kaur 2018, van Acker et al. 2014, van Acker & Coenye 2016).

The events described here are specific to Mtb infection.

Literature references


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