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Foamy Macrophages in *Mycobacterium tuberculosis* Pathogenesis

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Abstract

Tuberculosis is becoming an emergency in modern era with its effective sustainability in human host. Pathogenicity of its causing factor *Mycobacterium tuberculosis* is very effective and variable. Alveolar macrophages which provide innate immunity to host, are the target cells of bacilli. As TB infection is categorised in two phases: early and latent phase, granuloma is the major characteristic feature of latent phase and maintenance of latency is dependent on foamy macrophages (FMs). Foamy macrophages are providing the environment which is essential for bacilli to survive and escape from host immune system for longer time. FMs are the source of fatty acids in the form of triacylglycerol (TAG) as bacilli enzyme tgs1 is used in converting host fatty acids into TAG. FMs require more attention to gain knowledge regarding dormancy of Mtb and survivality.

Keywords: Foamy macrophages; TAG; Granulomas; Mycobacterium; dormancy

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Summary

The pathogen *Mycobacterium tuberculosis* (Mtb) is an infectious agent of tuberculosis. According to WHO report it is estimated that in 22 high burden of countries, there are 88% of TB cases and it is also estimated that 1/3 population of the planet is anchor with this bacterium [1]. Mtb modify immune system of host so that it can survive and maintain its growth in long term. Mtb can persist inside host for decades undetected encased within an organized immune cells leading to formation of inflammatory structure called granuloma. There is no biomarker for this disease progression because yet the systemic immune response is comparable in those individual developing disease versus those with effective containment [2]. *M. tuberculosis* is an intracellular, pathogenic causative agent of TB that infects macrophages primarily and survives in infected host macrophage cells for long time. The host-pathogen interaction is the initial step to the disease progression that facilitates the binding of host cell and Mycobacterium. When the *M.tuberculosisis* inhaled and reaches to the lung, it is internalized by the lung macrophages. At infection site there is accumulation of macrophages, lymphocytes and dendrite cells, to form the granulomas, which is a pathological feature of TB [3]. Macrophages play an important role in the immune response to infection with *Mycobacterium tuberculosis*. Tuberculosis (TB) is characterized by the interaction in between the bacilli and granulomas in alveolar macrophage within the host. The macrophage with the large number of lipid-free vacuoles and filled with the lipid-containing bodies is known as foamy macrophages (FMs), which found in the granulomatous structure during latent stage of disease [4]. The basic roles of these foamy macrophages are to serve as a rich nutrient reservoir. In foamy macrophages the cell is surrounded by the rim of lymphocytes, and later the coat of fibroblasts encloses it [5]. Within the human granulomas structures, *M. tuberculosis* has the long chain of fatty acid and the mycolic acid (MA) which differentiates the human monocyte-derived macrophages into FMs. In a recent study it has been shown that FMs plays a vital role in survival strategies in human granulomas during Mtb infection and also it displays that only highly virulent mycobacterium like *M. tuberculosis* and *M. Avium*, can induce the formation of FMs in mature granulomas not in saprophytic type like *M. smegmatis* [6]. The Oxygenated mycolic acid, produced by these pathogenic species, which is responsible for the formation of the FMs. The direct role of the oxygenated mycolic acid is independently formed the appearance and the stage of the disease [7]. In FMs the ingested Mtb was not killed but instead exists in the non-replicating state and also over-expressed dormancy gene. In foamy macrophages, the engulfed Mtb-containing phagosome migrates towards the lipid bodies, so in lipid bodies bacteria are free and favoring bacilli's access for nutrient. From these facts it is estimated that the FMs

could form the secure source of nutrition for tubercle bacilli [8]. Previously it was suggested that post primary tuberculosis start as the lipid pneumonia as it was observed that lipid droplets are aggregate in alveolar macrophages in TB patients [9,10]. Based on observations it is proposed that in adipose tissue of mammals, seed oils of plant and the lipid insulin bodies in prokaryotes, the fatty acid are generally stored in the form of triacylglycerol (TAG) as it is recommended that it serves as storage form of energy. In the same manner it assumed that probably TAG behaves as the energy source for the latent Mtb. TAG accumulation is the critical event for the Mtb dormancy which depicts the importance of enzyme triacylglycerol synthase 1 (tgs1). Tgs1 serve as the primary contributor in TAG synthesis within the pathogen, as it shows in a study that deletion of tgs1 led to the complete loss of the TAG accumulation by Mtb [11-13].

It has been also reported that in hypoxic condition in lipid anchored FMs in granuloma contain large amount of TAG which provide lipid rich environment to Mtb for survival and proper growth. The oxygen concentration is much lower in phagosome of activated macrophage in comparison of extracellular oxygen concentration [14]. In granuloma, TAG enriched environment promote Mtb to switch into latent state [15]. It is also demonstrated that Mtb accumulate TAG by the import of host derived fatty acids and the composition of Mtb TAG is much similar to host TAG. Mtb resides in lipid loaded macrophage gather neutral lipid by which it loses its acid fastness [16-18].

From the above discussion it is concluded that foamy macrophages which is made up of fatty acid, involve in the pathogenesis of Mtb. FMs have a major role in maintaining latent phase of Mtb as it serves as a reservoir of energy source. Role of oxygenated mycolic acid is significant in the formation of FMs. FMs are characterized by the accumulation of TAG, hypoxic conditions, and activity of tgs1. All the above conditions are requiring for the transition of Mtb into latent phage. How the Bacilli of Mtb survives in various stressful conditions is still a mysterious question. There are several signaling aspects are involve in the phase conversion of Mtb which needed more profound research to elaborate various new facet of Mtb pathogenesis.

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References

1 http://www.who.int/tb/publications/global_report/gtbr15_main_text.pdf

2 Cardona PJ, Kim MJ, Allain S, Altare F (2009) Foamy macrophages and the progression of the human TB granuloma. Nat Immunology. 10: 943-948.

3 Cardona PJ, Llatjos R, Gordillo S, Diaz J, Ojanguren I (2000) Evolution of granulomas in lungs of mice infected aerogenially with Mycobacterium tuberculosis. Scand J Immunol 52: 156-163.

4 Ridley DS, Ridley MJ (1987) Rationale for the histological spectrum of tuberculosis: a basis for classification. Pathology 19: 186-192.

5 Saunders BM, Cooper AM (2000) Restraining mycobacteria role of granulomas in mycobacterial infections. Immunol Cell Biol 78: 334-341.

6 Peyron, P, Vaubourgeix J, Poquet, Y, Levillain F, Botanch C et al. (2008) Foamy Macrophages from Tuberculous Patients'Granulomas Constitute a Nutrient-Rich Reservoir for M.tuberculosis Persistence. PLOS Pathogens doi:10.1371/journal.ppat.1000204.

7 Boissier F, Bardou F, Guillet V, Joseph S U, Daffe M (2006) Further insight into S-adenosylmethionine-dependent methyltransferases: structural characterization of Hma, an enzyme essential for the biosynthesis of oxygenated mycolic acids in Mycobacterium tuberculosis. J Biol Chem 281: 4434-4445.

8 Virchow R (1860) Cellular pathology as based on physiological and pathological histology. John Churchil, London, UK.

9 Florey H (1958). Tuberculosis. General pathology based on lectures delivered at the sir William dunn school of pathology. Saunders WB (ed.) Philadelphia and London, pp: 29-870.

10 Pagel W (1925) Zur Histochemie der Lungentuberkulose, mitbesonderer Berrucksichtung der Fettsubstanzen und Lipoide. (Fat and lipoid content to Tuberculous tissue. Histochemical investigation). Virchows Arch Path Anat 256: 629-640.

11 Daniel J, Deb C, Dubey VS, Sirakova TD, Abomoelak B (2004) Induction of a novel class of diacylglycerol acyltransferases and triacylglycerolaccumulation in Mycobacterium tuberculosis as it goes into a dormancy-like state inculture. J Bacteriol 186: 5017-5030.

12 Sirakova TD, Dubey VS, Deb C, Daniel J, Korotkova TA (2006) Identification of a diacylglycerol acyltransferase gene involved in accumulation of triacylglycerol in Mycobacterium tuberculosis under stress. Microbiology 152: 2717-2725.

13 Deb C, Lee CM, Dubey VS, Daniel J, Abomoelak B (2009) A novel in vitro multiple-stress dormancy model for Mycobacterium tuberculosis generates a lipid loaded, drug-tolerant, dormant pathogen. PLOS One doi:6010.13 journal.pone.0006077.

14 James PE, Grinberg OY, Michaels G, Swartz HM (1995) Intraphagosomal oxygen in stimulated macrophages. J Cell Physiol 163: 241-247.

15 Neyrolles O, Herna´ndez-Pando R, Pietri-Rouxel F, Forne`s P, Tailleux L (2006) Is adipose tissue a place for Mycobacterium tuberculosis persistence? PLOS. doi:10.1371/journal.pone.0000043.

16 Garton NJ, Waddell SJ, Sherratt AL, Lee SM, Smith RJ et al. (2008) Cytological and transcript analyses reveal fat and lazy persister-like bacilli intuberculous sputum. PLOS Med 5: e75 0001-0012.

17 Reed MB, Gagneux S, Deriemer K, Small PM, CEB (2007) The W-Beijing lineage of Mycobacterium tuberculosis overproduces triglycerides and has the DosR dormancy regulon constitutively upregulated. J Bacteriol 189: 2583-2589.

18 Seiler P, Ulrichs T, Bandermann S, Pradl L, Jorg S et al. (2003) Cell-wall lterations as an attribute of Mycobacterium tuberculosis in latent infection. J Infect Dis 188: 1326-1331.