Titan Cells: Barriers to Phagocytosis

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Cryptococcus neoformans is an opportunistic fungal pathogen, mainly associated with immune-compromised individuals having diseases like HIV/AIDS, lymphoid disorders, transplant recipients as well as patients undergoing chemotherapy. Clinical manifestation of the disease includes skin lesions, pulmonary infections and meningitis [3]. This pandemic infection is at alarming levels in sub-Saharan Africa and third most leading cause of fatalities having one million infections worldwide with 6,50,000 deaths each year. Typically, Cryptococcal spores are inhaled into the lung, where they lodge in alveoli and establish pulmonary infections. Engulfment of normal cryptococcal cells by alveolar macrophages leads to formation of Titan cells via cell enlargement (up to 10 times) which includes cell cycle arrest or increase in DNA content (tetraploidy or octaploidy) [1, 2]. Titan cell formation is induced by cAMP/PKA pathway, which helps in maintaining their virulence through thick anti-phagocytic polysaccharide capsule and melanin pigment [1]. Ste3a pheromone receptor and Gpr5 protein through cAMP/PKA pathway controls the Titan cell formation mediated by activation of Rim101 transcription factor [2].

Okagaki et al. [3] were the first to acknowledge the role of Titan cell production from *C. Neoformans*, involved in preventing the normal cells from phagocytosis during early stage of pulmonary infection. It has been proven, that they are also capable of decreasing the overall rate of phagocytosis [1]. Recently, it has been shown that the large particles such as asbestos, inert beads etc cannot be phagocytised; this phenomenon is known as *frustrated phagocytosis* [1]. Thus,

it suggests that the Titan cells play pivotal role in establishment of cryptococcal infection and its survival.

Efforts had been made to design a vaccine against an epitope of polysaccharide capsule, glucuronoxylomannan (GXM), of cryptococcal cells [4]. Vaccine composed of GXM linked tetanus toxoid had shown to elicit an effective immune response in mice and humans [4]. Discovery of Titan cell and further targeted research can help to highlight their specific epitopes and deciphering their signal transduction pathway, which can be targeted in order to implement an effective strategy against cryptococcal infections.

Story Source

The above story is from Science Daily (May 28, 2012).

References

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