



Latex beads coated with mammalian cell entry (mce)3a and mce3e proteins of *mycobacterium tuberculosis* are internalized by hela cells

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Received: Nov 07, 2018

Accepted: Jan 16, 2019

Published Online: Jan 21, 2019

Journal: Journal of Case Reports and Medical Images

Publisher: MedDocs Publishers LLC

Online edition: <http://meddocsonline.org/>

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Description

Tuberculosis (TB) is a highly prevalent human infection and a formidable public health challenge. According to the annual surveys conducted by World Health Organization (WHO), there were an estimated 10 million active TB disease cases which resulted in 1.6 million deaths in 2017, the highest from a single infectious agent [1]. The WHO has also estimated that ~25% of the world population is latently infected with *M. tuberculosis* and 5%-10% of the infected individuals will eventually develop active TB during their life time. The lifetime risk of active disease in HIV coinfecting individuals is ~50% [1]. Also, most of the active disease cases in low TB incidence countries occur in latently infected individuals as a result of reactivation of latent infection [2]. The establishment of infection first requires adherence to and internalization by alveolar macrophages. Although

the effector molecules exploited by *M. tuberculosis* for entry into macrophages are not fully defined, invasin-like membrane-associated Mammalian Cell Entry (Mce) proteins play an important role in facilitating the internalization of mycobacteria into mammalian cells [3]. There are four homologous mce operons (mce1-4) on the *M. tuberculosis* genome, each encoding six (A-F) Mce proteins. Previous studies carried out on Mce1A have shown that recombinant *Escherichia coli* cells expressing Mce1A invade and survive inside macrophages and latex beads coated with Mce1A are internalized by non-phagocytic HeLa cells [4]. We have previously shown that latex beads coated with Mce3A and Mce3E are also internalized by mammalian (HeLa) cells [5]. Here we show further evidence that latex beads coated with Mce3A (Figure 1a) and Mce3E (Figure 1b) induce membrane



Cite this article: El-Shazly S, Ahmad S, Mustafa AS, Al-Attiyah R, Krajci D. Latex beads coated with mammalian cell entry (mce)3A and mce3E proteins of *mycobacterium tuberculosis* are internalized by hela cells. *J Case Rep Clin Images*. 2019; 1: 1013.

invagination and formation of pedestal-like structures due to elongation of microvilli surrounding the bead. The beads are subsequently phagocytosed by HeLa cells and appear in the cytoplasm either alone or in clusters without being compartmentalized within vacuoles of the HeLa cells.

Figures

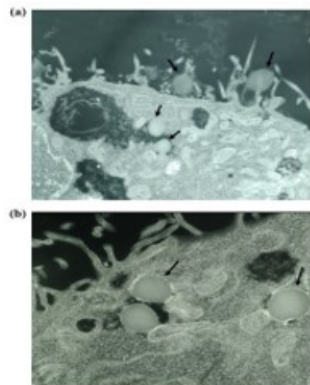


Figure 1: Transmission electron micrographs showing HeLa cell plasma membrane perturbations and formation of pedestal-like structures due to elongation of microvilli surrounding the latex bead coated with pure Mce3A protein (panel a) and completely internalized latex beads coated with Mce3E by HeLa cells (panel b). The protein-coated latex beads in contact with HeLa cells as well as those internalized by HeLa cells are marked by arrows. The results shown here are representative of two separate experiments.

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