Exosomes released from macrophages infected with Talaromyces marneffei activate the innate immune responses and reduce intracellular multiplication

Guangquan Ji<sup>1</sup>, Shan Feng<sup>1</sup>, Wenhao Cheng<sup>1</sup>, Hong Ren<sup>1</sup>, and Renqiong Chen<sup>1</sup> <sup>1</sup>Xuzhou Medical University Affiliated Hospital of Lianyungang

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#### Abstract

Recent studies have shown that exosomes are involved in pathogenesis and in the treatment of various tumors and inflammatory diseases. We examined the impacts of exosomes released from Talaromyces marneffei (T. marneffei)-infected macrophages on human macrophages to determine whether they play a role in the pathogenesis of T. marneffei infection. Exosomes derived from macrophages were extracted using commercial kits and characterized by transmission electron microscopy and western blot. Further, we examine exosomes that regulate IL-10 and TNF- $\alpha$  production and activation of p42 and p44 extracellular signal-regulated kinase 1 and 2 (ERK1/2) and activation of autophagy. We found that exosomes induced activation of ERK1/2 and autophagy, IL-10 and TNF- $\alpha$  production in human macrophages. Furthermore, exosomes decreased the replication of T. marneffei in T. marneffei-infected human macrophages. Interestingly, exosomes isolated from T. marneffei-infected but not from uninfected macrophages can stimulate a proinflammatory response in resting macrophages. Our studies are the first to demonstrate that exosomes isolated from T. marneffei-infected macrophages can induce a proinflammatory response, and we hypothesize that exosomes play significant roles in activation of ERK1/2 and autophagy, the replication of T. marneffei and cytokine release during T. marneffei infection.

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