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Low-level AFB_1 promotes H1N1 swine influenza virus infection via macrophage polarization to M1/M2

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Swine Influenza Virus (SIV) is a major pathogen of both animals and humans. Aflatoxin B_1 (AFB_1) is one of the most common mycotoxins in feeds and food. However, the central contribution of AFB_1 in SIV infection remains unclear. Here we investigated the involvement of AFB_1 in SIV infection *in vivo* and *in vitro*, as well as its underlying mechanism using mouse and Porcine Alveolar Macrophage (PAM) models. The results of the study *in vivo* showed that low doses of AFB_1 increased SIV infection and its severity as assessed by the increased expression levels of viral Matrix protein (M) mRNA, Nucleo-Protein (NP), matrix protein 1 and ion-channel protein, as well as weight loss, lung index and the lung histologic damage. In addition, increased SIV infection coupled with increases in TNF-α in serum and spleen index but decreases in IL-10 in serum and thymus index were observed after low doses of AFB_1 exposure in SIVinfected mice. The study *in vitro* also demonstrated that low concentrations of AFB_1 promoted SIV replication as demonstrated by the increased viral titers, viral M mRNAand NP expression levels in SIV-infected PAMs, as well as the numbers of positive cells for the NP protein. Furthermore, AFB_1 promoted PAM polarization to M1/M2 in SIV-infected PAMs, as measured by the increased M2 macrophage markers such as IL- 10 and morphological changes under scanning electron microscope. Administration of an immune-stimulant, Lipo-Poly-Saccharide (LPS), reversed PAM polarization to M1/M2, and thereby counteracted the promotion of influenza virus replication induced by AFB_1. Take together, our results first time to confirm that low-level AFB_1 promotes SIV infection via PAM polarization to M1/M2. This work reported here provides important data that point to a role for AFB_1 in SIV infection and opens a new field of study.

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