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 SIV-infected 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 mRNA and 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.