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

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Abstract

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, nucleoprotein (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, lipopolysaccharide (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.

Recent Publications

1. **Sun Y**, Xu C, Li C, et al. Characterization of the serum metabolic profile of dairy cows with milk fever using ^{1}H-NMR spectroscopy[J]. Veterinary Quarterly, 2014, 34(3): 159-163.
2. **Sun Y**, Wang B, Shu S, et al. Critical thresholds of liver function parameters for ketosis prediction in dairy cows using receiver operating characteristic (ROC) analysis[J]. Veterinary Quarterly, 2015, 35(3): 159-164.
3. Xu C, **Sun Y H**, Yang W, et al. Urine Proteomics Analysis of Dairy Cows with Fatty Liver[J]. Pakistan Veterinary Journal, 2016, 36(1). **Co-first author**.
4. Xu C, Xia C, **Sun Y**, Xiao X, Wang G, Fan Z*, et al.* Metabolic profiles using (1)H-nuclear magnetic resonance spectroscopy in postpartum dairy cows with ovarian inactivity. *Theriogenology* 2016, 86(6)**:** 1475-1481.
5. Xu C, Shu S, Xia C, Wang P, **Sun Y**, Xu C*, et al.* Mass spectral analysis of urine proteomic profiles of dairy cows suffering from clinical ketosis. *The Veterinary quarterly* 2015, 35(3): 133-141.



I am Yuhang Sun, a PhD student, and I will graduate next June from Nanjing Agricultural University. My supervisor is Prof. Kehe Huang, and my research topic was animal nutrition and immunity. My master's degree was obtained from Heilongjiang Bayi Agricultural University, and my graduate thesis topic is ^{1}H-NMR based plasma metabolic profiling of dairy cows suffered from ovary standstill. Besides the above SCI papers, another two manuscripts about veterinary toxicology were under review. Our results first time to confirm that low-level AFB_1 promotes SIV infection providing important data that point to a role for AFB_1 in SIV infection and may open a new field of study.

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