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Loss of TLR4 prevents tumor progression through metabolic reprogramming of tumor-associated macrophages

Liyun Shi[1,2], **Yina Ding**[1], **Zhe Lu**[1], **Bing Wang**[1] and **Songxue Wang**[1]
[1]Hangzhou Normal University, China
[2]Nanjing University of Chinese Medicine, China

The differentiation of macrophages with diverse effector functions is accompanied by changes in metabolism. Till now we know little about how macrophages sense and translate the environment cues into the metabolic signaling to reprogram their functional phenotypes. Here, we show that toll-like receptor 4 (TLR4) expressions in tumor associated macrophages (TAMs) was up-regulated during cancer development and inversely with tumor progression. Genetic abrogation of TLR4 in mice inhibited lung cancer development and the *in vivo* depletion of macrophages showed that these cells were essential for the anti-tumoral responses. We show that the activation of TLR4 in macrophages resulted in Akt/MTOR activation, Bcl6-mediated inhibition of glycolysis and therefore tumor-promoting M2-state. In contrast, deletion of TLR4 enabled macrophages to transform to Hif-1α driven glycolysis and the resultant tumor inhibiting M1 state. Moreover, our study demonstrates that TLR4 mediated macrophage polarization significantly impacted tumor progression and stemness like traits. This study reveals that the TLR signaling in TAMs may constitute a metabolic barrier for immunological elimination of tumors and hence a potential target for immunotherapy for cancers.

The anti-allergic and immunomodulatory effects of *Lactobacillus murinus* in a murine model of food allergy

Tong-Rong Jan[1], **Hong-Jen Liang**[2] and **Chung-Hsiung Huang**[1,3]
[1]National Taiwan University, Taiwan
[2]Yuanpei University, Taiwan
[3]National Institute of Infectious Diseases and Vaccinology, Taiwan

Previous results showed that *Lactobacillus murinus* was capable of colonizing in the porcine gastrointestinal tract, suggesting its potential as a probiotic *in vivo*. The present study aimed to investigate the anti-allergic and immunomodulatory effects of *L. murinus* using a murine model of food allergy. BALB/c mice were sensitized with ovalbumin (OVA) by intraperitoneal injection and then repeatedly challenged with OVA by gavage to induce allergic responses. Allergic diarrhea and immune parameters associated with food allergy were monitored. The density of enteric flora, including lactic acid bacteria (LAB) and non-specific bacteria was also measured. Daily oral administration with *L. murinus* restored the diminished density of fecal LAB and markedly attenuated the occurrence of allergic diarrhea, mast cell infiltration and degranulation in the intestine and serum IgE production in allergic mice. The expression of IL-4 by splenocytes was down-regulated, whereas the level of IFN-γ was up-regulated by *L. murinus*. Concordantly, a decreased expression of IL-4 and GATA3 and an increased expression of IFN-γ and T-bet were observed in the duodenum of allergic mice-administered with *L. murinus*. Moreover, *L. murinus* enhanced IL-12 production and suppressed OX40 ligand expression by intestinal $CD11c^+$ cells. Taken together, these results demonstrated that oral administration with *L. murinus* modulated intestinal $CD11c^+$ cell functionality, promoted T-helper 1 polarization, suppressed IgE production and attenuated allergic responses which were closely associated with the maintenance of enteric LAB density. These findings suggest that *L. murinus* may be exploited as an immunoactive probiotics against food allergy.