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   2019T002

2. Title

   Role of smoking in intracellular metabolism-regulated chronic inflammatory response

3. Period

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4. Summary

In this study, we aimed to clarify the significance of intracellular metabolism in chronic inflammatory diseases, and to elucidate the effect of α7nAChR activation on cellular metabolism and the mechanism underlying the onset and progression of chronic inflammatory diseases. Here we showed that inflammatory macrophages rely on extracellular serine and depleting serine causes aberrant cytokine production. On the other hand, activation of macrophage α7nAChR exerts and anti-inflammatory effect. As a mechanism, we found that cellular glutathione is decreased and thereby activating transcription factor Nrf2, and that is indispensable for anti-inflammatory effect of α7nAChR activation. We also found that intervention in lipid metabolism modulates the pathogenesis of autoimmune diseases, a typical chronic inflammatory disease, and that oral nicotine intake attenuates autoimmune disease. We identified alteration in the gut microbiota and associated changes in bile acid in autoimmune mice, suggesting that activation of α7nAChR may ameliorate systemic chronic inflammatory diseases not only through its anti-inflammatory effects in macrophages but also through changes in lipid metabolism by get microbiota. Thus, our data reveals an aspect of the molecular mechanism of the anti-inflammation by nicotine from the viewpoint of immunometabolism.