Lupus autoimmunity and metabolic parameters are exacerbated upon high fat diet-induced obesity due to TLR7 signalling

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Systemic lupus erythematosus (SLE) patients have increased prevalence of metabolic syndrome but the underlying mechanisms remain unknown. SLE is a chronic systemic autoimmune disease that is characterized by the presence of autoantibodies against self-nucleic acids and associated proteins. Metabolic syndrome is characterized by several risk factors that include central obesity, insulin resistance, dyslipidemia and increased blood pressure. Metabolic syndrome is highly linked to SLE and is associated with cumulative organ damage. Toll-like receptor 7 (TLR7) that detects single stranded-RNA plays a key role in antimicrobial host defence, but also contributes in the initiation and progression of SLE, however, the role of TLR7 in metabolic disease is unknown. Our latest studies revealed the contribution of TLR7 signalling in high fat diet (HFD)-induced metabolic syndrome and exacerbation of lupus autoimmunity. We found that HFD aggravated lupus severity and induced pronounced metabolic abnormalities in TLR8-deficient (TLR8ko) mice, which develop spontaneous lupus-like disease due to increased TLR7 signalling by dendritic cells (DCs). In contrast, upon HFD TLR7/8ko mice did not develop SLE and both TLR7ko and TLR7/8ko mice were fully protected from metabolic abnormalities, including body weight gain, insulin resistance and liver inflammation. Interestingly, HFD led to an increase of TLR7 expression in WT mice, that was coupled with increased TNF production by DCs, and this phenotype was even more profound in TLR8ko mice. Our findings uncovers the implication of TLR7 signalling in the interconnection of SLE and metabolic abnormalities, indicating that TLR7 might be a novel approach as a tailored therapy in SLE and its metabolic implications, as well as in metabolic syndrome.

Keywords : TLR7, dendritic cells, metabolic syndrome, systemic lupus erythematosus, inflammation
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