The involvement of mitochondrial activation via glutaminolysis in human B cell differentiation and its relevance to the pathogenesis of SLE

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Background: B cells play a crucial role in Systemic Lupus Erythematosus (SLE). Recently, "Immunometabolism" attract much attention. Glucose and glutamine are important nutrition for energy production such as ATP in various cells. It has been reported that aerobic glycolysis, glutaminolysis and mitochondrial functions enhanced in cancer cells. However, the involvement of metabolic reprogramming in plasmablast differentiation and its relevance to the pathogenesis of SLE remained elusive.

Objectives: We first investigated the abnormality of mitochondria in B cells from patients with SLE by flow cytometry. Next, B cells were isolated from healthy donors (HDs) and metabolic reprogramming were assessed in vitro.

Methods: First, peripheral blood mononuclear cells (PBMCs) were obtained from age-matched 31 HDs and 29 patients with SLE. The mitochondrial membrane potential was measured with DiOc6 by flow cytometry. In addition, CD19+ cells were isolated from HDs and stimulated with CpG (TLR9 ligand) and IFN-α. Change of aerobic glycolysis, glutaminolysis and mitochondrial functions were assessed in the absence of glucose or glutamine and in the addition of metformin, which is known as AMPK activator, in vitro.

Results: We first examined the abnormality of mitochondria in B cells from patients with SLE by flow cytometry. Next, B cells were isolated from healthy donors (HDs) and metabolic reprogramming were assessed in vitro.

Conclusion: These results suggest that mitochondrial activation via glutaminolysis may play an important role in the differentiation from IgD-DCD7 double negative B cells to plasmablasts and production of immunoglobulins in patients with SLE.

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