News Release

Title

Dietary supplementation with eicosapentaenoic acid inhibits plasma cell differentiation and attenuates lupus autoimmunity

Key Points

- Dietary EPA supplementation ameliorated representative lupus manifestations, including autoantibody production and immunocomplex deposition in the kidneys.
- Dietary EPA supplementation specifically reduced the number of autoantibody-producing plasma cells.
- A combination of lipidomic and membrane dynamics analyses revealed that EPA remodels the lipid composition and fluidity of B cell membranes, thereby preventing B cell differentiation into plama cells.

Summary

Accumulating evidence suggests that cholesterol accumulation in leukocytes is causally associated with the development of autoimmune diseases. However, the mechanism by which fatty acid composition influences autoimmune responses remains unclear. To determine whether the fatty acid composition of diet modulates leukocyte function and the development of systemic lupus erythematosus, we examined the effect of eicosapentaenoic acid (EPA) on the pathology of lupus in drug-induced and spontaneous mouse models. We found that dietary EPA supplementation ameliorated representative lupus manifestations, including autoantibody production and immunocomplex deposition in the kidneys. A combination of lipidomic and membrane dynamics analyses revealed that EPA remodels the lipid composition and fluidity of B cell membranes, thereby preventing B cell differentiation into autoantibody-producing plasma cells. These results highlight a previously unrecognized mechanism by which fatty acid composition affects B cell differentiation into autoantibody-producing plasma cells during autoimmunity, and imply that EPA supplementation may be beneficial for therapy of lupus.

Research Background

Systemic lupus erythematosus (SLE) is a chronic systemic autoimmune disease that affects multiple organs, and it is characterized by autoantibody production. As the concordance rate for SLE in identical twins is only 25-60%, this complex disease is caused by both genetic and environmental factors. Patients with SLE have increased risk of atherosclerosis, and cardiovascular disease is one of the major causes of morbidity and mortality in these patients, suggesting a relationship between the dysregulation of lipid metabolism and autoimmune responses. However, the molecular mechanism by which lipid metabolism influences the pathology of SLE is unclear.

Research Results

In this study, we demonstrated that dietary EPA supplementation in two lupus mouse models, namely imiquimod (IMQ)-induced and spontaneous C57BL/6$^{lpr/lpr}$ models, attenuates autoantibody production and immunocomplex deposition in kidney glomeruli. In addition to the anti-inflammatory effect of EPA in APCs, we discovered that EPA suppresses the differentiation of naïve B cells into autoantibody-producing plasma cells. Dietary EPA supplementation increased its abundance in B cell membrane, thereby increasing their fluidity and attenuating the signal for plasma cell differentiation. These results highlight a mechanism by which cellular fatty acids regulate the function of B lymphocytes in the context of systemic autoimmunity.

Research Summary and Future Perspective

Our findings that EPA directly regulates plasma cell differentiation, which is attributed in part to the altered abundance of cellular fatty acids and increased membrane fluidity, highlight a previously unrecognized role of EPA in autoimmunity. In this study, we employed two different lupus models: (1) IMQ-induced lupus, which is mediated in part by IFN-I production, to mimic patients with SLE and IFN-I signature and (2) spontaneous C57BL/6J$^{lpr/lpr}$ mice that exhibit BAFF, but not IFN-I production to mimic patients with SLE and BAFF signature. We demonstrated that EPA had beneficial effect in both models. Because EPA is approved for the treatment of hypertriglyceridemia and is also available as a dietary supplement, our results identify EPA as a potential universal agent with less toxicity for the treatment of SLE.

Publication

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