Conclusions Patients with APS develop significant morbidity and mortality despite current treatment. More attention should be devoted to APS patients with thrombocytopenia.

New therapies and therapeutic targets – other autoimmune diseases

5-AMINOLEVULINIC ACID COMBINED WITH FERROUS IRON AMELIORATE GRAFT-VERSUS-HOST-INDUCED SYSTEMIC SCLEROSIS IN THE MOUSE

Background and aims Scleroderma or systemic sclerosis (SSc) is a clinically heterogeneous rheumatologic autoimmune disease characterised by skin, internal organs and blood vessels, and there is no effective therapy. The purposes of current study are to develop a model of GvHD-induced scleroderma that more fully represents human condition, and to investigate the effects of 5-aminolevulinic acid (5-ALA), an intermediate of heme synthesis, enhance HO-1 activity to cleave heme to form biliverdin, CO, and iron on this model.

Methods Scl-GvHD was induced by injection of lymphocytes from B10.D2 mice into BALB/c mice deficient in mature T and B cells (recombination activating gene 2 null mice).

Results We successfully established an scl-GvHD model, which is similar to the human disease particularly in the skin, progressive inflammation and fibrosis of internal organs including lung, kidney, and liver. We found that treatment with 5-ALA and iron (Fe^{2+}) significantly reduced progressive inflammation and fibrosis in the skin and ear. Furthermore, by quantitative real-time PCR analysis, 5-ALA and Fe^{2+} suppressed the inflammatory cytokines and TGF-β, type I collagen mRNAs expression. These results indicate that combination treatment with 5-ALA and Fe^{2+} exhibited a protective effect on tissue fibrosis and inflammation of scl-GvHD model mice.

Conclusions The model of GvHD-induced SSc has shown most of symptoms of human disease and is likely to contribute to better understanding of the disease mechanism. Furthermore, efficacy of the 5-ALA has important implication for clarifying the mechanism of HO-1 activity in autoimmune diseases, and may provide a favourable opportunity for clinical therapy.

ACTIVATION OF MGLUR7 ATTENUATES THE DEVELOPMENT OF ALLERGY-INDUCED ANAPHYLAXIS

Background and aims Scleroderma or systemic sclerosis (SSc) is a clinically heterogeneous rheumatologic autoimmune disease characterised by skin, internal organs and blood vessels, and there is no effective therapy. The purposes of current study are to develop a model of GvHD-induced scleroderma that more fully represents human condition, and to investigate the effects of 5-aminolevulinic acid (5-ALA), an intermediate of heme synthesis, enhance HO-1 activity to cleave heme to form biliverdin, CO, and iron on this model.

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Conclusions The model of GvHD-induced SSc has shown most of symptoms of human disease and is likely to contribute to better understanding of the disease mechanism. Furthermore, efficacy of the 5-ALA has important implication for clarifying the mechanism of HO-1 activity in autoimmune diseases, and may provide a favourable opportunity for clinical therapy.
Background and aims Allergy is a common condition that is caused by an overreaction of the immune system to foreign substances. Severe allergic reactions can result in a systemic life-threatening state referred to as an anaphylactic shock. The progression of the anaphylactic reaction is hard to control after onset, and there is no effective prophylactic treatment available. Recently, mice deficient of the group III metabotropic glutamate receptor mGluR7 were shown to display an anaphylactic-like behaviour when exposed to peripheral histamine, suggesting that mGluR7 works as a neuronal brake on peripheral neurons involved in allergy and anaphylaxis. However, the role of mGluR7 in allergen-induced anaphylaxis is still unknown.

Methods In the PCA model, on the first day, BALB/c mice were lightly anaesthetised with isoflurane and their left ears were intradermally (i.d.) injected with a monoclonal antibody (IgE directed against OVA- trinitrophenol (TNP), 1 μg in 10 μl PBS), whereas the right ears were used as controls (receives an i.d. injection of 10 μl PBS as vehicle). The PCA reaction was induced 24 hours later by an intravenous injection of 50 μg OVA-TNP in 200 μl of 2% Evans blue in PBS.

Results Here, we show that central activation of mGluR7 dampens the development of allergen-induced anaphylaxis as intrathecal, but not intraperitoneal, prophyllactic administration of the mGluR7 allosteric agonist N, N-dibenzylhydroxylamine-1, 2-diamine dihydrochloride [ML1] AMN082 attenuated the development of passive cutaneous anaphylaxis in mice.

Conclusions Activating the mGluR7 system thus represents a potential preventive treatment for anaphylaxis.