Innate immunity in rheumatic diseases

AB0051  SERUM AMYLLOYD A AND PENTRAxin 3: IMMUNE RESPONSE AND DISEASE ACTIVITY IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Systemic Lupus Erythematosus (SLE) is an autoimmune disease that involves several molecular patterns with a wide spectrum of clinical manifestations and symptoms. Inflammation and related pathway play a role in SLE pathogenesis. The pentraxin superfamily including long and short pentraxin, CRP, Reactive Protein CRP, Serum amyloid A (SAA), Pentraxin 3 (PTX3) are key components of innate immune system and induce a variety of inflammation associated pathway. However Literature provides several evidences that CRP serum levels not correlated with clinical and immunological manifestations. This situation affected clinical practice and the patient follow up. PTX3 have been identified as a component of inflammatory status in several autoimmune conditions. SAA is an acute phase protein secreted in large quantity during inflammation.

Objectives: We want to evaluated SAA, PTX3 and CRP concentrations, their correlation between SLE Disease Activity Index (SLEDAI), that including complement fractions C3, C4.

Methods: We enrolled fifty patients that fulfilled the SLE American College of Rheumatology criteria and fifty healthy subjects. The SLE disease activity was classified with the SLEDAI (0 to 12). Patients were divided into two groups according to SLEDAI score: inactive group (Group 1, 25 patients, 50%; SLEDAI < 4) and active group (Group 2, 25 patients, 50%; SLEDAI 5 to 12). PTX3 concentration was measured by a sandwich ELISA kit (Hycult) with 2.8 ng/mL cut-off point. SAA concentration was detected by nephelometry performed on a BN ProSpec System (Siemens, Germany), with assay kit based on polyclonal antibodies (Siemens Healthcare Diagnostics Products, Germany, 6.5 mg/L cut-off point). High sensitive CRP concentrations were determined using the c8000 platform (Abbott Laboratories Chicago, Illinois).

Results: Plasma PTX3 and serum SAA levels was significantly higher in SLE patients than in the healthy subjects (PTX3115.7 3.9 ng/mL vs 2.3 ± 1.1; p < 0.001; SAA: 87 ± 77 mg/L vs 2.6 ± 2.5; p < 0.001). These differences were not evident in CRP levels (8.5 ± 7.8 mg/L vs 6.2 ± 2.5). Considering two groups, there were statistical differences in PTX3 level (Group 1: 2.16 ± 0.5 mg/L, p < 0.05) and SAA concentration (Group 2: 114 ± 0.001 mg/L vs Group 1: 3.6 ± 1.7 mg/L, p < 0.05) but not in CRP concentration (Group 2: 11.5 ± 4.8 mg/L vs Group 1: 9.5 ± 3.5). There was a significantly negative correlation between C3, C4 fractions, PTX3 and SAA levels (respectively r = -0.74, p = 0.05, and r = -0.79, p = 0.005). No statistical correlation were appeared between C3, C4 fractions and CRP serum levels (r = -0.12, p = 0.82, and r = -0.18, p = 0.21). We noted a positive significant correlation between SLEDAI, PTX3 and SAA concentration (r = 0.79; p < 0.05, 0.83, p < 0.05, respectively) an increase in PTX3 and SAA levels followed the lupus flare and symptoms. No significant correlation appeared between SLEDAI and CRP (r = 0.15, p = 0.89).

Conclusion: PTX3 and SAA concentration was significantly higher in SLE patients than the healthy control subjects and their levels reflected disease activity. We showed a direct correlation between PTX3 and SAA. In SLE patients PTX3 and SAA concentrations were correlated with SLEDAI. We suggest an integrative viewpoint in which PTX3 and SAA may play a role as a biomarker of disease activity, with synergic work during SLE events. Evidences suggested that PTX3 and SAA could trigger the same molecular pathway, by TLR4, via NF-kB.

Disclosure of Interests: None declared

AB0053  BERGENIN, ACTING AS AN AGONIST OF SIRT1, REDUCE SERUM URATE IN MICE THROUGH THE UPREGULATION OF ABCG2

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Background: About 20% of individuals in the USA have asymptomatic hyperuricemia[1]. However, Urate-lowering therapy in asymptomatic hyperuricemia condition is still controversial considering the benefit and side effects[2]. Therefore, safe and effective anti-hyperuricemia therapies are necessarily.

Objectives: Bergenin, the major bioactive ingredient isolated from Saxifraga stolonifera, could activate SIRT1. In this study, we identify the effect of bergenin on hyperuricemia, and explored the related mechanisms.

Methods: Significant hyperuricemia was established in C57BL/6N mice treated with oxoxate and yeast polysaccharide. Bergenin was administered to the mice at the same time. The serum uric acid and creatinine levels, clearance of uric acid and creatinine, the intestinal uric acid and creatinine, the intestinal acid excretion and renal pathological lesions were determined were used to evaluate the anti-hyperuricemic effects. The location and expression levels of ABCG2 in the kidney and intestine were analyzed. HK-2 and Caco-2 cell lines were exposed to soluble uric acid with or without the treatment of Bergenin. Then the expression of ABCG2 and underlying mechanisms were explored.

Results: The administration of bergenin decreased serum uric acid in hyperuricemic mice by the promotion of uric acid excretion both in kidney and intestine. Bergenin reuced the downregulation of ABCG2 in the kidney of hyperuricemic mice and upregulated the expression of ABCG2 in the jejunum and ileum. In