HYDROXYCHLOROQUINE INHIBITS SOLUBLE CD154 PRODUCTION THROUGH CA2+ AND PKC SIGNALLING PATHWAY

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Background: Over-expression of membranous CD154 and soluble CD154 (sCD154) in T lymphocytes is important in pathogenesis of autoimmune diseases. PKC pathway induces sCD154 production through promoting shedding of membranous CD154.

Objectives: Hydroxychloroquine (HCQ) has been used in the treatment of autoimmune diseases for decades. We sought to identify the effects of HCQ on sCD154 and a possibly regulatory mechanism.

Methods: CD4+ T cells were isolated from the blood of healthy donor. After stimulation with ionomycin +PMA and various concentrations of HCQ, concentration of sCD154 in the medium, expression of membranous CD154, Ca2+ pathway and PKC signalling pathway were assessed.

Results: HCQ attenuated intracellular sustained calcium storage release and membranous CD154 synthesis in activated T cells. Besides, HCQ inhibited PKC activation and subsequently shedding of membranous CD154.

Conclusions: HCQ inhibited production of sCD154 in activated T cells through suppressing Ca2+ and PKC signalling pathway. These findings provide one of the mechanistic insights into HCQ treatment.

REFERENCES:

DECREASED IRISIN LEVEL AS RISK FACTOR OF PATHOLOGICAL FRAC TURES IN RHEUMATOID ARTHRITIS PATIENTS

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Background: Recent studies have been suggested that adipokines and myokines may be implicated in bone metabolism and pathogenesis of osteoporosis (OP). Previous studies have revealed inverse correlation between irisin levels and vertebral fragility fractures, but no significant correlation was found between irisin and bone mineral density (BMD) as well as with lean weight. There is no previously published data about irisin levels in rheumatoid arthritis (RA) patients.

Objectives: To investigate serum irisin levels in patients with RA.

Methods: We studied 170 people: 110 RA patients (mean age 53.58±12.32; hereinafter Ms/SD) and 60 healthy controls. All patients with RA were examined using dual-energy X-ray absorptiometry using LUNAR DPX-Pro densitometer. Osteoporotic fractures were confirmed by X-ray examination and/or by anamnesis data. All patients were passed through extensive clinical and laboratory examination, including N-terminal propeptide of procollagen type I, C-telopeptide of type I collagen, 25(OH)-vitamin D concentration. Serum irisin levels were measured by ELISA (BioVendor test system, Cat N RAG018R).

Results: The mean concentration of irisin in RA group was 14.48±7.07 mg/ml which was significantly lower than of healthy donors – 20.49±4.82 mg/ml (p<0.001). We subsequently divided all of RA patients into two groups: the first one (n=44) included patients with reduced serum irisin levels (below 10.85 mg/ml), and the second one (n=66) with normal irisin levels (above 10.85 mg/ml).

Conclusions: We have therefore revealed relationships between decreased serum irisin levels, 25(OH)-vitamin D concentration and higher incidence of pathological bone fractures in this group (p=0.047). There wasn’t any significant correlation between serum irisin level and BMD at any localization, lean, or fat weight. We did not reveal any difference of bone turnover markers (serum C-terminal telopeptide of type I collagen, serum N-terminal propeptide of type I procollagen (PINP)) between these groups.

REFERENCES:
Mean cytokine levels for the SLE patients and healthy controls are shown in the table 1.

Abstract AB0058 – Table 1

<table>
<thead>
<tr>
<th>Cytokine</th>
<th>SLE patients (pg/mL)</th>
<th>Healthy controls (pg/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>IL2</td>
<td>3.43 (12.2)</td>
<td>3.36±0.2</td>
</tr>
<tr>
<td>IL4</td>
<td>58.65 (64.4)</td>
<td>89.05±51.10</td>
</tr>
<tr>
<td>IL5</td>
<td>18 (5.71)</td>
<td>7.3±5.2</td>
</tr>
<tr>
<td>IL10</td>
<td>12.29 (32.82)</td>
<td>1.92±2.6</td>
</tr>
<tr>
<td>IL13</td>
<td>44.97 (273.78)</td>
<td>42.89±24.06</td>
</tr>
<tr>
<td>IL21</td>
<td>3.18 (5.61)</td>
<td>2.8±0.34</td>
</tr>
<tr>
<td>INF1A</td>
<td>15.69 (24.59)</td>
<td>4.8±1.84</td>
</tr>
<tr>
<td>BlyS</td>
<td>2293.82 (6984.48)</td>
<td>1181.15±220.04</td>
</tr>
</tbody>
</table>

The systemic lupus erythematosus (SLE) is an autoimmune disease characterised by deregulation of cytokine production. INF1A is a proinflammatory cytokine considered as a key molecule in the SLE etiopathogenesis, being responsible indirectly of IL10 upregulation. BlyS is involved in autobody production and clinical activity in SLE, and its expression is regulated by other cytokines as IL10 and INF1A. IL2 is an anti-inflammatory cytokine in SLE, but its loss leads to the production of the pro-inflammatory cytokines as IL4, IL5 and IL13.

Objectives: To analyse the association among inflammatory cytokine levels and clinical activity, as well as to identify a cytokine profile related to disease activity in SLE.

Methods: A cross-sectional, observational study of 142 patients diagnosed of SLE (SLE SLECC 2012 criteria), and 35 healthy controls, was performed. A complete blood-test and an interview were carried out to collect their clinical data. We analysed inflammatory cytokines serum levels by colorimetric methods. Biostatistical analysis with R was performed.

Results: Mean cytokine levels for the SLE patients and healthy controls are shown in the table 1.