INFLAMMASOME DRIVES RELEASE OF MITOCHONDRIAL DNA ENCLOSED IN EXTRACELLULAR MEMBRANE VESICLES AND PROPAGATION OF INFLAMMATION IN BEHÇET’S DISEASE

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Background: It has been reported that mitochondrial DNA (mtDNA) is released into the cytosol by mitochondrial stress and induces pro-inflammatory cytokine production via inflammasome and intracellular DNA sensors. Also, mtDNA in the extracellular space is known to result in sterile inflammation. However, the molecular mechanism of mtDNA release and its pathological significance in autoimmune diseases (ADs) has not been elucidated.

Objectives: To clarify the molecular mechanism of mtDNA release and its pathological significance in ADs.

Methods: To achieve the target of our study 20 patients with OA of the knee in flare-up were selected from out-patients clinic. The patients were followed up two weeks after the first setting until they entered into remission. Twenty normal controls age, sex and body mass index (BMI) matched were recruited. In the first setting all patients had their sera, and synovial fluid measured for Visfatin, in the second setting sera and synovial fluid (if any) was drawn for Visfatin measurement. Measurement of Visfatin by (ELISA) for quantitative determination of human visfatin in biological fluids.

Results:

1. serum visfatin of patients and control groups:

<table>
<thead>
<tr>
<th>P value</th>
<th>t</th>
<th>Control ng/ml</th>
<th>Patients ng/ml</th>
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<tbody>
<tr>
<td>0.0001</td>
<td>42.09</td>
<td>216.00±30.25</td>
<td>847.90±59.86</td>
</tr>
<tr>
<td>0.001</td>
<td>23.6</td>
<td>216.00±30.25</td>
<td>542.45±59.60</td>
</tr>
</tbody>
</table>

Flare up ng/ml Patients ng/ml

Remission

Visfatin was elevated both systemically and locally in the patients with knee OA, was elevated during flare-ups and decrease during remission, was higher in serum than in synovial fluid of patients and There was no difference in the level of visfatin in relation to aging or gender difference.

REFERENCES
[3] O. Guisal, J. R. Gonzalez-Juanatey, and F. Lago.(2007) ‘The emerging role of adipokines as mediators of cardiovascular function: physiologic and dependent manner. We then studied the mechanism of secretion of mtDNA in EMVs and found that both human primary monocyte and monocyte-like cell line containing mtDNA-containing EMVs after stimulation with ATP or LPS. Further, BD-derived monocytes secreted more abundant mtDNA in EMVs than monocytes derived from healthy donors. Additionally, the inhibition of caspase-1 activity reduced the secretion of mtDNA in EMVs.

Conclusion: We revealed a novel mechanism of inflammation propagation involving inflammasome and mtDNA; activated inflammasome releases mtDNA-containing EMVs and subsequently leads to mtDNA-induced inflammation via NLRP3 inflammasome. Such inflammatory mechanism may contribute to the exacerbation of inflammation in BD.

Disclosure of Interests: None declared