[THU0097] NEUROGENIC INFLAMMATION IN RHEUMATOID ARTHRITIS: POSSIBLE ROLE OF NEUROPEPTIDES ON SYNOVIAL VANILLOID RECEPTORS

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Background: Neurogenic inflammation is caused by neuropeptides, like substance P (SP) and calcitonin gene related peptide (CGRP), which are released by peripheral neurons and induce inflammatory signals. SP and CGRP act through several molecular mechanisms including activation of transient receptor potential vanilloid (TRPV) cation channels, particularly TRPV1. SP and CGRP have been found increased in synovial fluid from rheumatoid arthritis (RA) patients and may induce the production of interleukin in RA synoviocytes [1]. TRPV cation channels are expressed in various non-neuronal cell types including human synoviocytes [2].

Objectives: To investigate whether neuropeptides can increase IL-8 production of synoviocytes as pivotal cytokine involved in joint inflammation. To investigate whether SP and CGRP are able to modulate expression of TRPV1 in RA and healthy synoviocytes.

Methods: RA and healthy synoviocytes were cultured and incubated at 6 hours (SP 10-7M, CGRP10-8M, baseline) and 24 hours (SP 10-7M, CGRP10-8M, SP 10-7M+CAP 10-6M, CGRP 10-8M+CAP 10-6M, baseline). Supernatant of cells incubated 24 hours were assayed by specific ELISA IL-8 Kit. Cells incubated for 6 hours were collected and levels of mRNA of TRPV1 were assayed by Real-Time PCR. Supernatant IL-8 and TRPV1 mRNA are expressed as mean ± standard deviations (SD) and compared by Mann-Whitney Test and t-Student test. The differences are considered significant for $p < 0,05$.

Results: At baseline IL-8 production of RA synoviocytes was significantly higher than healthy cells ($p < 0,05$)(RA: 2,20±0,17 ng/ml; healthy: 1,89±0,08 ng/ml). After 24 hours of incubation with neuropeptides RA and healthy synoviocytes did not shown increased IL-8 production. After 24 hours of co-incubation with SP, CGRP and CAP 10-6 IL-8 production of RA synoviocytes was significantly higher than healthy cells and neuropeptides alone ($p<0,05$) (RA SP10-7M+CAP10-6M=3,07±0,11; healthy SP10-7M+CAP10-6M=1,28±0,12) (RA CGRP 10-8M+CAP10-6M=2,98±0,10; healthy CGRP10-8M+CAP10-6M=1,54±0,46). After 6 hours of incubation with SP and CGRP expression of mRNA TRPV1 was significantly increased ($p<0,05$) in RA synoviocytes than in healthy cells (healthy SP10-7=0,87 ± 0,27; RA SP10-7=4,00 ± 0,45) (healthy CGRP 10-8= 0,65 ± 0,05; RA CGRP 10-8=2,61 ± 0,56).

Conclusions: After co-incubation with SP, CGRP and CAP RA synoviocytes have increased the production of IL-8 suggesting that TRPV1 activation in RA cells may lead to induction of inflammatory stimuli. Levels of TRPV1 mRNA increase in RA synoviocytes after incubation with neuropetides suggesting that SP and CGRP may induce TRPV1 production during disease. In RA neuropeptides may cooperate and activate TRPV1 thus fostering synovial inflammation.

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