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**Immunomodulatory properties of rumalon, a glycosaminoglycan peptide complex, in patients with osteoarthritis: activation of T helper cell type 2 cytokines and antigen-specific IgG4 antigen-specific IgG4 antibodies.**Klein R<sup>1</sup>, Becker EW, Berg PA, Bernau A.**Author information****Abstract**

**OBJECTIVE:** To assess the immunogenic properties of the glycosaminoglycan peptide complex **Rumalon**, an aqueous extract of bovine cartilage and bone marrow frequently used in patients with osteoarthritis (OA).

**METHODS:** Sera from 31 patients with OA who had received several series of **Rumalon** injections (Group 1, n = 17: before therapy and after one injection series; Group 2, n = 6: after 2-3 injection series; Group 3, n = 4: after 4-8 injection series; Group 4, n = 4: after 9-18 injection series) were tested by ELISA for antibodies against **Rumalon** and its components as well as by a double sandwich ELISA for type 1 [interferon-gamma, interleukin 2 (IL-2)] and type 2 cytokines (IL-4, IL-5, IL-10, IL-13).

**RESULTS:** After the first injection series antibodies to **Rumalon** were induced in 7 of the 17 patients that were all negative before therapy. The antibodies were preferentially of the IgG4 type. IgG4 levels were increased during therapy (ELISA optical density x 1000 in Group 1: 73.9 +/- 209.5; Group 4: 1354.5 +/- 307.6), and in Group 4 all patients had developed these antibodies. Upon analysis of cytokine levels, there was a significant increase in IL-5 (Group 1 before therapy 407.4 +/- 257.1 pg/ml, Groups 3 and 4: 1409.4 +/- 963.1 pg/ml; p < 0.001) and to a lesser extent of IL-10 during therapy (Group 1 before therapy 950.2 +/- 867.8 pg/ml, Groups 3 and 4: 2817.8 +/- 3127.3 pg/ml; p < 0.05), while type 1 cytokines were not affected.

**CONCLUSION:** **Rumalon** appears to have immunomodulatory properties and preferentially stimulates IgG4 antibodies via the activation of type 2 cytokines in vivo. Whether these phenomena can be correlated with the postulated therapeutic effect of **Rumalon** in patients with OA remains to be seen, but pain relief via release of endorphins by Th2 cells could be one explanation.

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