The immunomodulatory role of the extracellular vesicles in experimental models of autoimmune arthritis

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Background: The recent discovery of extracellular vesicles is one of the most significant findings in cell biology of the past decades. The universally and evolutionarily conserved secretion of extracellular vesicles plays an important role in intercellular communication. Nowadays extracellular vesicles attract substantial attention because of their potential use as diagnostic and/or therapeutic tools.

Goals: To investigate the immunomodulatory effect of murine thymus and spleen extracellular vesicles in experimental models of autoimmune arthritis.

Methods:
Extracellular vesicles were isolated by differential centrifugation and gravity driven size filtration from 24h supernatants of thymocytes and splenocytes isolated from BALB/c and DBA1 mice. The amount of the extracellular vesicles was standardized to protein content by a microBCA assay. BALB/c mice were immunized intraperitoneally by the emulsion of human fetal aggrecan (partially deglycolysated by chondoitinase ABC digestion) and DDA. Furthermore, in DBA1 mice arthritis was induced by a peptide of glucose-6-phosphate isomerase (GPI) and CFA. At the time of antigen injection, some groups of mice were co-injected intravenously with extracellular vesicles secreted by either syngeneic thymus or spleen cells. The course of clinical arthritis was characterized by cumulative acute arthritis scores. Total and antigen-specific IgG and IgM levels were determined by ELISA at different stages of arthritis induction.

Results: We observed the development of characteristic symptoms of arthritis after immunization with aggrecan or GPI peptide. According to our results, co-injection with thymus extracellular vesicles partially prevented the development of the arthritis. The clinical symptoms were slightly reduced (the cumulative arthritis scores were lower), and the aggrecan-specific and total IgM values were lower in the group co-injected with extracellular vesicles. In the arthritis model induced by GPI peptide we could almost fully prevent the development of the inflammatory symptoms by co-injection of extracellular vesicles secreted by splenocytes.

Conclusion: Our data suggest that extracellular vesicles may modulate immune responses and clinical symptoms in arthritis.