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TARGETING ADAMTS-7 METALLOPROTEINASE: A PROMISING APPROACH FOR MANAGING RHEUMATOID ARTHRITIS

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ADAMTS-7 is a promising molecular target for the diagnosis and treatment of rheumatoid arthritis. It plays an important role in the destruction of cartilage in joint syndrome, especially in the active stage of the disease. Further clinical studies are needed to confirm its diagnostic and prognostic significance, as well as to develop targeted therapy aimed at inhibiting ADAMTS7 activity.

Keywords
rheumatoid arthritis, ADAMTS-7, joint syndrome, diagnostic marker

Rheumatoid arthritis (RA) is a systemic inflammatory disease characterized by the destruction of articular cartilage and the development of severe joint syndrome. A key participant in these destructive processes is the metalloproteinase ADAMTS-7, which can break down extracellular matrix proteins, including cartilage oligomeric matrix protein (COMP) [7,10]. This article presents current data on the role of ADAMTS-7 in joint structure damage, its mechanisms of action, diagnostic significance, and potential as a therapeutic biomarker. RA is accompanied by chronic inflammation of the synovial membrane, pannus formation, and destruction of both articular cartilage and bone tissue [1,4]. Joint syndrome reflects the severity and activity of the disease. At the core of RA pathogenesis lies the activation of immune-mediated inflammation involving metalloproteinases. ADAMTS-7 exhibits specific activity toward COMP, the degradation of which accelerates the breakdown of cartilage integrity [6,8,12].

Rheumatoid arthritis accounts for approximately 1% of rheumatological diseases in the adult population and is characterized by a chronic inflammatory process that primarily affects the small joints. Progressive destruction of articular cartilage and bone leads to disability. Joint syndrome—which includes pain, swelling, ankylosis, and joint deformities—reflects the activity and severity of the disease [2,13].

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Metalloproteinases, including members of the ADAMTS family, play a crucial role in remodeling the extracellular matrix and in the destruction of articular cartilage. ADAMTS-7 is a zinc-dependent metalloproteinase expressed in various tissues, including the synovial membrane. Its main substrate is COMP (cartilage oligomeric matrix protein), a protein essential for maintaining the structural integrity of cartilage [1,3,9,11].

Table 1.

Structural domains of ADAMTS-7 and their functions:

Domain	Function
Signal peptide	Extracellular secretion
Catalytic domain	Proteolytic activity, breakdown of matrix proteins
Integrin-like cysteine-rich domain	Binding to the cell surface and interacting with other proteins
Thrombospondin-1 domain	Binding to COMP and extracellular matrix components

From a pathogenetic perspective, it is important to note that ADAMTS-7 contributes to the degradation of cartilage matrix components, the exacerbation of inflammation, the proliferation of synoviocytes, and the activation of fibroblast-like cells in the synovial membrane [3,4,10,12]. Animal studies have shown that blocking the ADAMTS-7 gene slows down cartilage destruction in models of experimentally induced arthritis [12,14].

According to literature data, elevated levels of ADAMTS-7 expression have been detected in the synovial tissue and blood serum of patients with active-stage rheumatoid arthritis (DAS28 > 5.1). A positive correlation has been observed between enzyme activity and the severity of clinical manifestations of joint syndrome, as well as with levels of inflammatory markers such as IL-1β, IL-6, and TNF-α. Some studies suggest that ADAMTS-7 levels are particularly elevated during the early and active stages of RA, highlighting its potential as a promising biomarker for early diagnosis and monitoring of disease activity [2,4,5,10].

Specifically, ADAMTS-7 is considered one of the key indicators of cartilage tissue destruction, and its potential as a therapeutic target for slowing disease progression is currently under investigation. Given its high sensitivity to changes in immuno-inflammatory processes, ADAMTS-7 holds diagnostic value as a potential biomarker, particularly in cases of high RA activity [1,4,7,13].

The activity of this metalloproteinase can be used to assess disease prognosis, the risk of structural tissue damage, and the effectiveness of treatment. Currently,

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the development of ADAMTS-7 inhibitors is underway, with the potential for use in combination with conventional immunosuppressive and anti-inflammatory therapies such as methotrexate, hydroxychloroquine (Plaquenil), leflunomide, and sulfasalazine. Studies have also shown that targeting ADAMTS-7 can help halt cartilage destruction and reduce inflammatory responses [4,12,14].

Table 2.

Advantages of ADAMTS-7 inhibitors in targeted therapy for rheumatoid arthritis:

Approach	Effect	Stages of conducted research
ADAMTS-7 inhibitors	Decreased cartilage destruction and inflammation	Preclinical stage
Anti-ADAMTS-7 antibody	Suppression of RA progression	Experimental models
siRNA to ADAMTS7	Decreased expression in synoviocytes	In vitro

In particular, specific ADAMTS-7 inhibitors—similar to matrix metalloproteinase (MMP) inhibitors used in autoimmune systemic diseases—are currently under development. Their use in combination with conventional disease-modifying antirheumatic drugs (DMARDs) has shown effectiveness in reducing tissue-destructive processes and improving the course of the disease [1,4,10,13].

ADAMTS-7 is considered a key predictor of cartilage structural damage in rheumatoid arthritis, as it breaks down essential structural proteins in the extracellular matrix and contributes to the exacerbation of joint syndrome. Elevated levels of ADAMTS-7 in blood serum are directly correlated with disease activity, highlighting its potential as both a promising diagnostic biomarker and an effective target for targeted therapy [7,10,12].

Thus, ADAMTS-7 is regarded as a promising molecular marker for the diagnosis and treatment of rheumatoid arthritis, playing a critical role in cartilage degradation associated with joint syndrome, particularly during the active phase of the disease. Comprehensive clinical studies are needed to validate its diagnostic and prognostic value and to support the development of targeted therapeutic strategies aimed at inhibiting ADAMTS-7 activity.

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