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Characterizing Cannabinoid Receptors for Novel Targeted Therapeutic Approaches in Rheumatoid Arthritis

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Abstract

Rheumatoid arthritis (RA) is an autoimmune disease characterized by chronic inflammation and progressive destruction of the articular joints. The endocannabinoid system is a group of evolutionary conserved endogenous cannabinoid receptors 1 and 2 (CB1 and CB2). While CB1 is found more in the central and peripheral nervous system, CB2 is preferentially expressed in the immune cells, suggesting that CB2 may regulate the immune responses. Indeed, previous studies in cancer biology have shown CB2 may have a role in various diseases involving the immune system such as experimental autoimmune encephalomyelitis, diabetes, and cancer. However, CB2's role in the disease progression of RA has not been well characterized yet. Preliminary studies show CB2, not CB1, expression is upregulated at both the mRNA and protein level in RA synovial fibroblasts as compared to the normal synovial fibroblasts. Additionally, the use of specific CB2 agonists has been shown to attenuate the pro-inflammatory response. However, both the underlying molecular mechanism for increased CB2 expression and its implications in the RA disease progression remains unknown. This presentation highlights the current understanding of the endocannabinoid system, its implications in RA, and future strategies to decipher the molecular mechanisms that govern its expression to exploit this system for therapeutic gains.