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Inhibition of IL-6 production from rheumatoid synovial fibroblasts by isoform-specific histone deacetylase (HDAC) inhibitor

Abstract

The purpose of this study is to clarify the epigenetic abnormality of rheumatoid arthritis. We have examined the effect of various HDAC inhibitors on the production of IL-6 from rheumatoid synovial fibroblasts (RSF).

RSF, osteoarthritis synovial fibroblasts (OSF), and human fibroblast cell line 293 (HEK 293) were treated with various histone deacetylase (HDAC) inhibitors. Both the IL-6 mRNA and protein expression levels were examined using the quantitative reverse-transcription polymerase chain reaction (qRT-PCR) and an enzyme-linked immuno sorbent assay (ELISA). To examine cell viability, we used WST-1 assay.

Pan-HDAC inhibitor suppressed the IL-6 production from RSF and OSF. However, class-specific inhibitors augmented the IL-6 gene expression from both RSF and OSF. RSF was more susceptible for the class I HDAC-specific inhibitor 4SC-202 and class I HDAC isoform 8 inhibitor PCI34051.

Importantly, we observed significant inhibition of IL-6 mRNA and protein production with class II HDAC isoform 6-specific inhibitor CAY10603.

These observations suggest the feasibility of specific epigenetic anti-RA therapy using specific HDAC inhibitors.