Nagoya City University Academic Repository

学位の種類	博士（医学）
報告番号	甲第１６０６号
学位記番号	第１１４１号
氏名	立松　尚衛
授与年月日	平成 30 年 3 月 26 日
学位論文の題名	Mithramycin has inhibitory effects on gliostatin and matrix metalloproteinases expression induced by gliostatin in rheumatoid fibroblast-like synoviocytes (関節リウマチ線維芽細胞様滑膜細胞においてミスラマイシンはグリオスタチンによって誘導されたグリオスタチンとマトリックスメタロプロテイナーゼ発現を抑制する) Modern Rheumatology. 2017 Jul 25 (Published online)
論文審査担当者	主査：　和田 郁雄 副査：　山崎 小百合，大塚 隆信

Mithramycin has inhibitory effects on gliostatin and matrix metalloproteinase expression induced by gliostatin in rheumatoid fibroblast-like synoviocytes

ABSTRACT

Gliostatin (GLS) has angiogenic and arthritogenic activities and enzymatic activity as thymi- dine phosphorylase. Aberrant GLS production has been observed in the synovial membranes of patients with rheumatoid arthritis (RA). Matrix metalloproteinases (MMPs) are involved in joint destruc- tion. Promoters of GLS and some MMP genes contain Sp1 binding sites. We examined the inhibitory effect of the Sp1 inhibitor mithramycin on GLS-induced GLS and MMP expression in cultured fibro- blast-like synoviocytes (FLSs). Synovial tissue samples were obtained from patients with RA. FLSs pretreated with mithra- mycin were cultured with GLS. The mRNA expression levels of GLS and MMP-1, MMP-2, MMP-3, MMP- 9, and MMP-13 were determined using reverse transcription polymerase chain reactions. Protein levels were measured using enzyme immunoassay and gelatin zymography. GLS upregulated the expression of GLS itself and of MMP-1, MMP-3, MMP-9, and MMP-13, an effect significantly reduced by treatment with mithramycin. GLS and mithramycin had no effect on MMP-2 expression. Mithramycin downregulated the increased expression of GLS and MMP-1, MMP-3, MMP- 9, and MMP-13 in FLSs treated with GLS. Because GLS plays a pathological role in RA, blocking GLS stimulation using an agent such as mithramycin may be a novel approach to antirheumatic therapy.