References:


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SAT0025

NEUROMEDIN U SUPPRESSES COLLAGEN-INDUCED ARTHRITIS THROUGH ACTIVATION OF ILC2

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Background: Reduction and dysregulation of ILC2 was linked to delayed resolution of arthritis. The neuropeptide Neuromedin U (NMU) has been reported to rapidly activate ILC2 and initiate a Th2 type immune response through NMR1 expressed on the surface of ILC2. However, one previous study reported that NMU promoted autoantibody-mediated arthritis.

Objectives: The aim of this work was to investigate the effect of NMU on collagen-induced arthritis (CIA) mice and the potential mechanisms.

Methods: CIA was induced in C57BL/6 WT and C57BL/6 Nmu deficient mice on day 1. WT mice were treated i.p. daily by NMU-23 (20ug/mice) or by PBS for 10 days from day 1 to 5 and day 21 to 25. The clinical scores of CIA mice were assessed every two days from day 22 and determined on a scale of 0–4 for each paw. The proportion of ILC2 as well as Th1, Th2, Th17 and Treg in spleen, mesenteric lymph node (mLN) and joints of arthritic mice were analyzed by flow cytometry on day 42.

Results: NMU-23 dramatically inhibited clinical onset and severity of arthritis in treated WT mice compared with control mice. Interestingly, NMU-deficient mice also developed significantly less severe arthritis compared with WT control (Fig 1). Flow cytometry analyses showed that the proportion of ILC2, which defined as Lin-CD45+CD127+KLRG1+ICOS+ST2+, was elevated in the joint but not in the spleen and mLN of arthritic mice treated with NMU-23. In contrast, the proportion of ILC2 was significantly lower in the spleen of NMU-deficient mice than WT control. The percentage of Th2 cells in the spleen and mLN tend to be higher in NMU-23 treated mice, but there is no statistical significance. Surprisingly, Th1 cells were increased in the mLN of NMU-23 treated and NMU-deficient mice compared with control whereas Th17 was comparable among groups. In addition, the proportion of Treg was decreased in the joint of NMU-23 treated and NMU-deficient mice compared with control mice.

Conclusion: Our preliminary results show that repeated injection of NMU-23 during induction (early) and development (late) stage of CIA strongly suppressed clinical onset and severity of arthritis, which might be ascribed to activation of ILC2 in the joint. Further study is needed to explore other cellular and molecular mechanisms in the effect.

References:


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