Reviewer's report

Title: Muscle wasting associated with pathologic change is a risk factor for the exacerbation of joint swelling in collagen-induced arthritis in cynomolgus monkeys

Version: 2 Date: 9 April 2013

Reviewer: Junya Ozawa

Reviewer's report:

Comments
This manuscript describes an investigation analyzing joint swelling, food consumption, body weight, serum biochemical parameters and the quadriceps femoris muscle histology in collagen-induced arthritis using cynomolgus monkeys. I appreciated this conscientious work is well organized. However, I have some question and suggestion as below.

Major Compulsory Revisions

Methods
# Please describe the method of statistical analysis in detail about data in Figure 6 in Methods.
# How did you sampled from the quadriceps muscle for histological study? It is important to isolate tissues from the identical portion of each sample, because the distribution of muscle fiber type is non uniform (e.g., slow fibers at deeper zone were greater than those at superficial zone in the rat rectus femoris muscle).

Tables/Figures
# Table 1: Please show the criteria for distinguishing atrophied fibers or not. It is difficult to judge the muscle fiber size in longitudinal section because it is determined by the cut level.
# Lower arrow in figure 2D indicate a regenerating fiber (or myotube), not atrophied myofiber.

Minor Essential Revisions

Introduction
# Is there a hypothesis for the current investigation? If there is, please describe in Introduction.

Methods
# I feel the data in Figure 1 should be done statistical analysis. Please consider it.
# I feel the data from pimonidazole staining in Fig 4 is not necessarily sound because sample number is too small (n = 1).
Discretionary Revisions

Overall
# Cachexia is defined as an accelerated loss of skeletal muscle in the context of a chronic inflammatory response. If this model mimics rheumatoid cachexia, you should show us data that the skeletal muscle volume is reduced in this model.

Title
# This study is not necessarily enough to clarify muscle wasting associated with pathologic change is a risk factor for the exacerbation of joint swelling in CIA. Your data just indicate the relationship between severity of joint swelling and creatinine, not pathological change. In fact, the authors described that “muscle wasting might exacerbate …” in Abstract.

Discussion
# Temporal changes in muscle injury marker (CPK) and inflammation markers (CRP and IL6) are not synchronized. Please provide your opinion what is a trigger to induce skeletal muscle injury at 2 weeks after 2nd immunization?

Level of interest: An article of limited interest

Quality of written English: Acceptable

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests:

I declare that I have no competing interests.