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LETTER

Response to 'Statins accelerate the onset of collagen type II-induced arthritis in mice'

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Statins used to treat hyperlipidemia also exhibit immunomodulatory properties. What is still unclear and a matter of debate, however, is whether these properties are of benefit or are deleterious in collagen type II-induced arthritis (CIA).

We read with great interest Vandebriel and colleagues' article about the role of statins in the induction of CIA [1]. According to the authors' conclusion, statins accelerate the onset of CIA in mice. In their study, as previously reported [2], oral atorvastatin and pravastatin had no effect on the arthritis score after CIA induction. Nonetheless, the oral route might be ineffective due to the significant hepatic first-pass metabolism of statins.

We performed a study that assessed the effects of simvastatin administrated by subcutaneous and intraperitoneal routes in CIA as previously reported [3]. Of the 60 rats included, 50 developed CIA (83.3%) and were treated by daily intraperitoneal simvastatin (n = 5), subcutaneous simvastatin (n = 9), diluted subcutaneous simvastatin (n = 9), subcutaneous saline (n = 9), and intraperitoneal saline (n = 9) for a total of 15 days. Nine rats received no treatment. A total score was calculated by grading each joint of the four limbs using a scale of 0 to 3 (0 = normal, 1 = erythema, 2 = erythema + swelling, and 3 = loss of function).

At baseline, no difference was noted in the arthritis score or weight between groups. We observed a significant weight decrease in each treatment group but no difference in weight loss between groups. After adjusting for weight, there was a significant difference in arthritis scores between intraperitoneal simvastatin and the other groups, with significantly lower arthritis scores obtained in the intraperitoneal simvastatin group (Figure 1). The difference of the arthritis score between subcutaneous simvastatin and intraperitoneal simvastatin was significant (P = 0.002) (intraperitoneal: 3.67 ± 1.32 at baseline and 4.89 ± 1.69 after 15 days vs. subcutaneous: 4.20 ± 0.84 at baseline and 7.40 ± 1.34 after 15 days). Differences in arthritis scores between the other groups, except for the simvastatin group, were not significant (Figure 1). These results obtained using linear mixed-models analysis were similar to those obtained when using PROAST, a general program for dose–response modeling, as in Vandebriel and colleagues' article.

In the intraperitoneal simvastatin group, there was a limitation in the progression of the arthritis score in rats, whereas no effect was noted in the subcutaneous simvastatin group.

Statins may therefore be a therapeutic option in CIA, provided that the substantial effects of hepatic first-pass metabolism are avoided. For CIA treatment, it might thus be interesting to administer transdermal statin patches that enhance diffusion, which have been reported to increase bone formation in rats [4]. Perhaps these patches could also be a therapeutic option in human rheumatoid arthritis.

Abbreviations
CIA, collagen-induced arthritis.

Competing interests
The authors declare that they have no competing interests.

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Published: 8 March 2013

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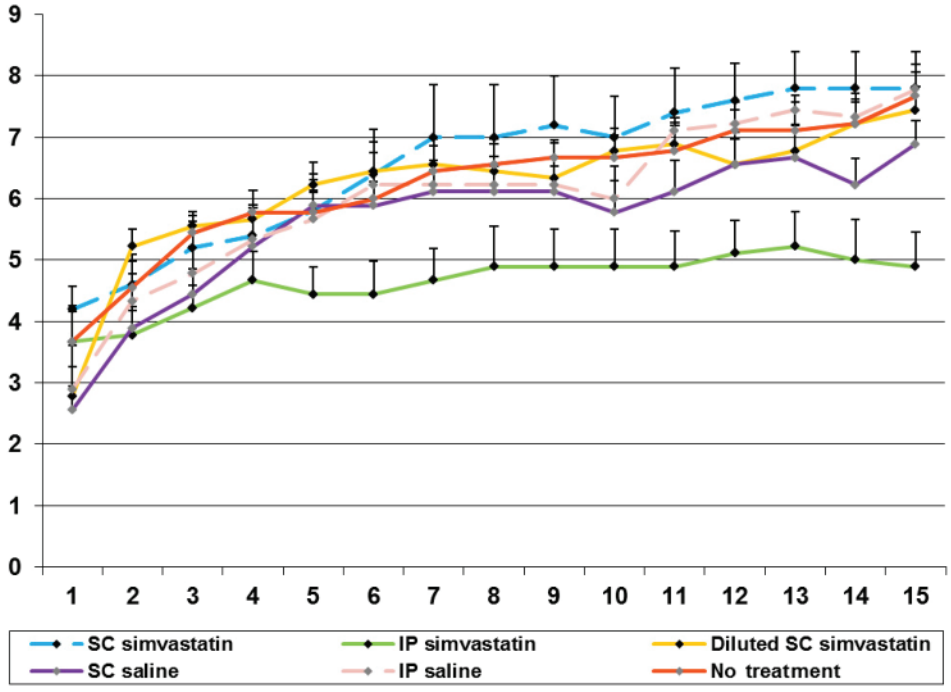

Figure 1. Arthritis score progression in the different treatment groups. IP, intraperitoneal; SC, subcutaneous.

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doi:10.1186/ar4169
Cite this article as: Mathieu S, *et al.*: Response to 'Statins accelerate the onset of collagen type II-induced arthritis in mice'. *Arthritis Research & Therapy* 2013, **15:**402.