Reviewer's report

Title: Can the disorder of immune response in bone cause the steroid-induced femoral head osteonecrosis? The investigation on Toll-like receptor 4 signaling pathway

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Reviewer: SHUNICHIRO OKAZAKI

Reviewer's report:

The following are the major concerns regarding this manuscript.

1. Could the authors perform RNA isolation and protein isolation with same femoral head? Size of rat femoral head was under #5mm.
2. To my knowledge, TLR4, MyD88, NF-kB and MCP-1 are not cytokines.
3. TAK 242 can't purchase from Takeda Pharm Co.
4. The authors defined osteonecrosis as the diffuse presence of empty lacunae or pyknotic nuclei of osteocytes in the bone trabeculae, accompanied by surrounding bone marrow cell necrosis or myelofibrosis. However, I could not recognize these findings in Figure 3. Higher power magnification is needed. And histopathological appearance in Figure 3 is different from that of previous reports (Ichiseki et al. 2011, Okazaki et al. 2012, Janke et al. 2013).
5. Why are TLR4, MyD88, NF-kB p65 and MCP-1 (positive staining, mRNA and protein) of Group A higher than Group N? Group A rats received TLR4 inhibitor, TAK242. Please discuss. It is well known that steroids suppress NF-kB activation.
6. In conclusions, the authors described that TLR4 signaling pathway plays a role in the pathogenesis of steroid-induced femoral head osteonecrosis. It was already reported previously (Okazaki et al. 2009, 2012). There is no priority.
7. More references are needed in discussion.

Should be rejected.

Level of interest: An article of insufficient interest to warrant publication in a scientific/medical journal

Quality of written English: Needs some language corrections before being published

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:
I declare that I have no competing interests.