Reviewer's report

Title: Membrane Sealant Poloxamer P188 Protects Against Isoproterenol Induced Cardiomyopathy in Dystrophin Deficient Mice

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Reviewer: Thomas Meyer

Reviewer's report:

Spurney and colleagues examined the effect of chronic intermittent intraperitoneal administration of poloxamer 188 on isoproterenol-induced cardiomyopathy in dystrophin-deficient mdx mice. The authors state that P188 treatment of mdx mice prevented the decrease in cardiac function induced by isoproterenol administration. Interestingly, however, despite the beneficial effects of P188 administration on left ventricular ejection fraction, blood pressure was unaffected and heart rate even increased as compared to mice treated with isoproterenol only. Such a hemodynamic behavior (increased shortening fraction, stable or even decreased blood pressure, and increased heart rate) would be expected, when a highly immunogenic substance such as the P188 co-polymer will induce an immune response in the treated mice. In line, the authors report that the drug did not affect skeletal muscle strength, which was measured in vitro using the extensor digitorum longus muscle model. In contrast to what has been published before, P188 treatment did not ameliorate cardiac fibrosis in hearts chronically exposed to the β1 receptor agonist. This observation furthermore suggests that P188 had no direct effects on skeletal or cardiac contractility, but acts as an unspecific stimulator of the immune system.

To exclude that the hemodynamic effects in the P188-treated mice do not simply result from unspecific immune stimulation, the authors must include P188-treated control mice for their data interpretation. If wild-type mice expressing functional dystrophin also show similar hemodynamic responses, the in vivo effects of P188 are unspecific rather than being pharmacologically induced.

Note: To me it is unclear whether in Tables 2 and 3 the authors give all significant differences between individual groups. At least, in Table 3B the p value for comparison between MDX-Untx versus MDX-Iso+P188 is missing. I rather suggest that the authors should additionally present data from Tables 2 and 3 in histograms and indicate all significant differences between groups by brackets.

Level of interest: An article of importance in its field

Quality of written English: Acceptable

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.