Reviewer's report

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

**Version:** 1  **Date:** 21 January 2011

**Reviewer:** Rainer Ng

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General
When applied to injured cells, P188 repairs disrupted membranes and enhances the recovery of a variety of cell types against a myriad of injury-inducing protocols. In this study, the authors add to the work done by Yatsuda et. al and demonstrate the protective effects of P188 on cardiac function in dystrophin-deficient mice. The authors tested a chronic dosage regimen of P188 in isoproterenol-challenged mdx mice and report improvement in several parameters of cardiac function. In essence, the study is similar to Yatsuda et. al with two major distinctions: the dosage regimen of P188 (chronic vs acute) and the methods used to assess cardiac function (echocardiography vs PV catheter). The comparisons between these methodologies may be of interest to some.

Major:
The manuscript correctly notes that cardiomyopathy in mdx mice becomes evident at ~9mths of age. The authors should provide clarification as to why 2-3 mth mdx mice were used instead. Might the protective effects of P188 have been more dramatic in older mdx mice?

There is some discrepancy in the reported numbers in the collagen/fibrosis section of the paper. Some of the percentages reported on page 13 do not match up with the legend of Fig 1.

Readers will benefit from a graph/table that represents data from the in-vitro muscle studies (both mdx and BL10). In addition to the specific force, the authors should also report EDL masses at the 0, 4 week timepoints to establish the effects of chronic dosage of P188 on skeletal muscle (if not in the main paper, at least in supp. Materials).

Minor:
The authors may want to further motivate their manuscript by citing Townsend et al (Mol Ther. 2008 May;16(5):832-5). That study highlights the crucial need for including the heart as a target when designing therapies for DMD.

Citation for the 460 mg/mg/dose of P188 is needed (Lee R.C. PNAS, 1992).

**Level of interest:** An article of limited interest
Quality of written English: Acceptable

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

Declaration of competing interests:

Am a member of a group of who have filed a patent for the use of P188 in preventing skeletal muscle deficiencies. U.S. Patent Application No. 12/747,073