Author's response to reviews

Title: Removal of urothelium affects bladder contractility and release of ATP but not release of NO in rat urinary bladder

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Author's response to reviews:

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Dear Ms. Neilan.

Please find enclosed the corrected manuscript of MS 2930467973133430 (Removal of bladder urothelium...)

We added one additional author to the paper (Timothy B. Boone, MD), and we replaced the micrograph of bladder strips with one that shows a clearer and more convincing picture of the suburothelium in the swabbed preparations. In addition we dealt with all of the criticisms of the Reviewers as detailed below.

Response to Dr. Alison Brading:

Thank you for the constructive criticism of our paper:

In response to your major concern, we I replaced the micrographs of the intact and swabbed strips. This time we used paraffin embedding, and the slices were thinner (5 µm instead of 50 µm) and the magnification was 5 times higher (200 times). The micrograph shows that the suburothelium has been preserved after swabbing, thus the conclusion we draw in the paper stands. However, we included the possibility of the species-related differences in the discussion, since the referenced findings were observed in other species (guinea-pig, pig, human). We also added? The major difference between those species and the rat is that the urothelium is not strongly attached to the muscular layer and can be easily peeled down without extensive use of sharp instruments.

Minor Revisions:
We eliminated the reference to methodology from the Result section.
In Figure 3 we changed “transactional” to “cross-sectional.”
In figs 5-6 we placed the asterisks above the proper columns.

Response to Dr. Russ Chess-Williams:

Thank you for the helpful and constructive criticism.

1. For the replaced microscopic pictures we used different embedding (paraffin vs. OTC), cut thinner slides (5 µm vs. 50 µm) and used higher magnification (200 times vs. 40 times). The microscopic pictures clearly show the difference between the intact and swabbed preparations and also show that the suburothelial layer is present after swabbing. In the light of this result we did not basically change the conclusion of the paper. However, we included the possibility of the species difference for the discussion (pg 9, end of 1st para) and we mentioned the possibility that ATP but especially NO can be derived from the smooth muscle layer.

2. I corrected the figs 4, 5, 6, and placed the asterisks above the proper column.

3. The averaged cross sectional area is calculated from the length and weight of the strips, with the knowledge that the specific density of the muscle is 1.06 g/cm³. The volume of the strip can be calculated from the weight and specific density. Dividing the volume by the length will give the cross sectional area. This calculation is widely used by muscle physiologists. Because the calculation is relatively straightforward I did not detail it in the Methods but I included the specific density of the muscle.

4. Reference 11 has been corrected, and I cited two additional papers regarding the contractile response of urothelium intact and –free preparations.

5. The legend for figure 2 is revised as suggested to indicate the concentrations of the applied drugs.