Author's response to reviews

Title: In vitro prediction of stop-codon supression by by intravenous gentamycin in patients with cystic fibrosis; a pilot study.

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Author's response to reviews: see over
Dear Editor,

We apologize for mistakes that were in our first revised version. In the current version have pay attention to answer to all remarks of the reviewer. The detailed description of changes is listed below.

Looking forward to hear from you

Sincerely

Aleksander Edelman

Response to reviewer

We apologize for the mistakes that were in the revised version. In the present version we took into account all remarks of the reviewer.

1. Table 1 has been clarified. “w” and “c” refer to the sense and antisense strands respectively. Footnotes have been added (Table 1 new version).

2. IC has been changed to ICC which means immunocytochemistry and has been defined in the legend of Table 3 (new version).

3. We precise in the legend of Figure 1 that the data corresponds to the measurements obtained in Y122X patients and healthy controls (legend of figure 1, new version).

4. We apologize for the mistake. The abscissa for Figure 2a and 2b are now correctly labeled in seconds. In our hands, a NPD experiment lasts for 10 to 20 minutes, that is between 600 and 1200 seconds, i.e. within the period indicated in the figures a and b.

5. We apologize for the confusion between the text regarding Figure 2. We corrected this point (p. 9 line 16,new version).

6. We have modified the Figure 2c and 2d according to the reviewer’s remarks, and removed Figure 3. These figures show CFTR immunostaining with MATG 1061 monoclonal antibody of nasal ciliated cells before and after gentamicin treatment in a Y122X homozygous CF patient. Figure 2c corresponds to immunostaining of CFTR before gentamicin treatment.
Figure 2d corresponds to immunostaining of CFTR after gentamicin treatment. An insert representing immunostaining of nasal ciliated cells from a healthy control subject has been added in Figure 2d for ease of comparison. MATG 1061 monoclonal antibody recognizes amino acids 503-515 in the first nucleotide-binding domain of CFTR. This information is included in the new version of the manuscript (p.7, line 2). The 24-1 monoclonal antibody recognizes the amino acids 1377-1480 at the C-terminus domain of CFTR. This information is also included in the new version of the manuscript (p.7, line 1). These two antibodies were chosen given their accuracy for CFTR detection in nasal epithelial cells using immunocytochemistry (reference 14, new version). This precision has been added in the revised version of the manuscript (page 7, line 3).

A detailed legend is given in the revised manuscript including the antibody used and scale bars. Scale bars are 40, 20 and 60 microns for Figure 2c, 2d and insert, respectively.

A detailed description of both PD tracing and the immunostaining has been added in the legend of Figure 2.

7. The data of the R1162X patient has been indicated as data not shown.