

Title: Nebulized hypertonic saline triggers nervous system-mediated active liquid secretion in cystic fibrosis swine trachea

Authors and affiliations

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Table 1: ASL measurements in wild-type swine *in vivo*

| Group | ASL layer height (μm) Mean \pm SEM | | | | | | |
|----------------------|---|-----------------------|-------------------------------|-----------------------|--------------------------------|-----------------------|--------------------------------|
| | Initial (-3 min) | 6 min | Δ height (-3 to 6 min) | 12 min | Δ height (-3 to 12 min) | 18 min | Δ height (-3 to 18 min) |
| HTS n=6 | 142.29 \pm 30.66 | 165.29 \pm 23.53 | 23.00 \pm 10.92 | 197.42 \pm 27.88 | 55.13 \pm 9.63 | 237.25 \pm 26.12 | 94.96 \pm 18.56 |
| ITS n=6 | 176.83 \pm 29.93 | 188.54 \pm 33.93 | 11.71 \pm 5.07 | 198.42 \pm 35.22 | 21.58 \pm 6.59 | 210.83 \pm 34.30 | 34.00 \pm 5.58 |
| HTS+Atro+Lido n=6 | 180.13 \pm 26.42 | 192.58 \pm 30.43 | 12.46 \pm 7.22 | 220.42 \pm 30.90 | 40.29 \pm 9.36 | 242.38 \pm 28.50 | 62.25 \pm 8.65 |
| ITS+Atro+Lido n=5 | 161.45 \pm 30.44 | 165.85 \pm 29.07 | 4.40 \pm 2.69 | 171.55 \pm 29.92 | 10.10 \pm 3.52 | 186.05 \pm 30.40 | 24.60 \pm 6.66 |
| HTS+Capsaicin n=6 | 121.00 \pm 20.93 | 152.50 \pm 18.96 | 31.50 \pm 10.97 | 192.67 \pm 27.93 | 71.67 \pm 19.94 | 228.13 \pm 25.64 | 107.13 \pm 15.02 |
| ITS+Capsaicin n=5 | 118.10 \pm 35.30 | 135.65 \pm 38.05 | 17.55 \pm 5.06 | 151.00 \pm 38.82 | 32.90 \pm 6.44 | 181.25 \pm 34.05 | 63.15 \pm 4.59 |

Table 2: ASL measurements in wild-type swine *ex vivo*

| Group | ASL layer height (μm) mean \pm SEM | | | | | | |
|--|---|-----------------------|-------------------------------|-----------------------|--------------------------------|-----------------------|--------------------------------|
| | Initial (-3 min) | 6 min | Δ height (-3 to 6 min) | 12 min | Δ height (-3 to 12 min) | 18 min | Δ height (-3 to 18 min) |
| HTS n=45 | 93.61 \pm 5.83 | 99.42 \pm 5.97 | 5.81 \pm 0.63 | 105.53 \pm 5.78 | 11.92 \pm 0.58 | 112.53 \pm 5.80 | 18.92 \pm 0.74 |
| ITS n=49 | 84.14 \pm 4.17 | 86.70 \pm 4.28 | 2.55 \pm 0.37 | 91.46 \pm 4.27 | 7.32 \pm 0.46 | 95.54 \pm 4.25 | 11.39 \pm 0.59 |
| Control n=12 | 71.53 \pm 7.60 | 73.65 \pm 7.56 | 2.12 \pm 0.41 | 79.33 \pm 7.41 | 7.80 \pm 0.46 | 82.76 \pm 7.34 | 11.23 \pm 0.81 |
| HTS+Amiloride n=12 | 100.77 \pm 15.48 | 106.60 \pm 15.81 | 5.83 \pm 1.65 | 111.71 \pm 15.62 | 10.94 \pm 1.14 | 119.73 \pm 14.83 | 18.96 \pm 1.81 |
| HTS+Lido+TTX n=18 | 100.50 \pm 5.97 | 105.36 \pm 5.70 | 4.86 \pm 1.06 | 108.27 \pm 5.55 | 7.78 \pm 1.20 | 113.13 \pm 5.99 | 12.64 \pm 1.06 |
| ITS+Lido+TTX n=9 | 109.47 \pm 17.03 | 112.39 \pm 17.43 | 2.92 \pm 1.46 | 115.31 \pm 17.54 | 5.83 \pm 1.46 | 119.19 \pm 16.91 | 9.72 \pm 1.75 |
| HTS+172 n=59 | 89.56 \pm 4.33 | 93.37 \pm 4.35 | 3.81 \pm 0.44 | 97.67 4.29 | 8.11 \pm 0.46 | 102.88 \pm 4.30 | 13.32 \pm 0.50 |
| ITS+172 n=29 | 85.58 \pm 5.49 | 87.39 \pm 5.46 | 1.81 \pm 0.55 | 88.77 \pm 5.49 | 3.20 \pm 0.62 | 90.71 \pm 5.57 | 5.13 \pm 0.63 |
| HTS+172+Lido+TTX n=9 | 88.21 \pm 8.11 | 91.13 \pm 8.46 | 2.92 \pm 1.46 | 93.07 \pm 9.20 | 4.86 \pm 1.54 | 95.99 \pm 8.00 | 7.78 \pm 0.97 |
| ITS+172+Lido+TTX n=21 | 86.67 \pm 6.83 | 88.75 \pm 6.76 | 2.08 \pm 0.83 | 90.83 \pm 6.63 | 4.17 \pm 0.98 | 92.50 \pm 6.52 | 5.83 \pm 1.10 |
| HTS+NK-1 blocker n=36 | 112.79 \pm 10.48 | 118.23 \pm 10.40 | 5.44 \pm 0.60 | 123.33 \pm 10.51 | 10.55 \pm 1.07 | 128.17 \pm 10.75 | 15.39 \pm 1.16 |
| ITS+NK-1 blocker n=16 | 71.48 \pm 7.46 | 75.30 \pm 7.37 | 3.83 \pm 1.12 | 80.77 \pm 7.38 | 0.30 \pm 0.70 | 83.51 \pm 7.75 | 12.03 \pm 1.57 |
| HTS+172+NK-1 blocker n=10 | 88.73 \pm 7.74 | 91.35 \pm 7.74 | 2.63 \pm 1.34 | 96.60 \pm 7.56 | 7.88 \pm 0.88 | 101.85 \pm 7.58 | 13.13 \pm 1.96 |
| ITS+172+NK-1 blocker n=17 | 113.75 \pm 13.61 | 115.29 \pm 13.68 | 1.54 \pm 0.83 | 117.35 \pm 13.86 | 3.60 \pm 1.08 | 119.41 \pm 13.94 | 5.66 \pm 1.05 |
| HTS+Atropine n=22 | 104.71 \pm 6.71 | 108.29 \pm 6.71 | 3.58 \pm 0.94 | 112.66 \pm 6.63 | 7.96 \pm 1.14 | 117.44 \pm 6.94 | 12.73 \pm 1.49 |
| ITS+Atropine n=11 | 96.93 \pm 10.42 | 100.90 \pm 11.36 | 3.98 \pm 1.38 | 105.68 \pm 11.12 | 8.75 \pm 1.18 | 109.65 \pm 10.98 | 12.73 \pm 1.38 |
| HTS+172+Atropine n=18 | 98.02 \pm 6.92 | 100.93 \pm 7.23 | 2.92 \pm 1.00 | 104.34 \pm 6.66 | 6.32 \pm 1.19 | 107.25 \pm 6.71 | 9.24 \pm 1.32 |
| ITS+172+Atropine n=19 | 92.11 \pm 9.13 | 93.03 \pm 9.28 | 0.92 \pm 0.63 | 95.33 \pm 9.67 | 3.22 \pm 1.00 | 97.63 \pm 9.40 | 5.53 \pm 1.20 |
| HTS+Bumet+NA+172+HCO ₃ ⁻ -free n=24 | 97.34 \pm 4.99 | 99.71 \pm 4.93 | 2.37 \pm 0.56 | 103.21 \pm 5.01 | 5.87 \pm 0.72 | 106.53 \pm 5.05 | 9.19 \pm 0.69 |
| ITS+Bumet+NA+172+HCO ₃ ⁻ -free n=18 | 120.90 \pm 12.78 | 122.16 \pm 12.81 | 1.26 \pm 0.20 | 123.67 \pm 12.80 | 2.77 \pm 0.29 | 125.13 \pm 12.77 | 4.23 \pm 0.50 |

Table 3: ASL measurements in CFTR^{-/-} swine *ex vivo*

| Group | ASL layer height (μm) Mean ± SEM | | | | | | |
|--------------------------|----------------------------------|-------------------|-----------------------|-------------------|------------------------|-------------------|------------------------|
| | Initial (-3 min) | 6 min | Δheight (-3 to 6 min) | 12 min | Δheight (-3 to 12 min) | 18 min | Δheight (-3 to 18 min) |
| HTS n=6 | 226.04 ± 77.65 | 234.79 ± 80.18 | 8.75 ± 5.53 | 261.04 ± 78.08 | 35.00 ± 7.14 | 268.33 ± 78.25 | 42.29 ± 8.28 |
| ITS n=4 | 144.38 ± 16.17 | 146.56 ± 15.72 | 2.19 ± 2.19 | 148.75 ± 15.16 | 4.38 ± 2.53 | 155.31 ± 19.03 | 10.94 ± 4.19 |
| HTS+Lido+TTX+Atro n=4 | 137.81 ± 32.03 | 142.19 ± 29.54 | 4.38 ± 2.53 | 148.75 ± 30.52 | 10.94 ± 2.19 | 161.88 ± 28.24 | 24.06 ± 5.51 |