**Supplementary Table 1**

Supplementary Table 1A: 1st ATP-vehicle-2nd ATP treatments

|  |  |  |
| --- | --- | --- |
| Classification | Number of cell | (%) |
| Total | 190 | 100 |
| 1st ATP (−) VH (+) 2nd ATP (+) | 0 | 0 |
| 1st ATP (−) VH (+) 2nd ATP (−) | 0 | 0 |
| 1st ATP (−) VH (−) 2nd ATP (+) | 1 | 0.5 |
| 1st ATP (−) VH (−) 2nd ATP (−) | 67 | 35.3 |
| 1st ATP (+) VH (+) 2nd ATP (+) | 0 | 0 |
| 1st ATP (+) VH (+) 2nd ATP (−) | 0 | 0 |
| 1st ATP (+) VH (−) 2nd ATP (+) | 90 | 47.4 |
| 1st ATP (+) VH (−) 2nd ATP (−) | 32 | 16.8 |

Supplementary Table 1B: 1st ATP-histamine-2nd ATP treatments

|  |  |  |
| --- | --- | --- |
| Classification | Number of cell | (%) |
| Total | 263 | 100 |
| 1st ATP (−) His (+) 2nd ATP (+) | 13 | 4.9 |
| 1st ATP (−) His (+) 2nd ATP (−) | 33 | 12.5 |
| 1st ATP (−) His (−) 2nd ATP (+) | 29 | 11.0 |
| 1st ATP (−) His (−) 2nd ATP (−) | 31 | 11.8 |
| 1st ATP (+) His (+) 2nd ATP (+) | 72 | 27.4 |
| 1st ATP (+) His (+) 2nd ATP (−) | 15 | 5.7 |
| 1st ATP (+) His (−) 2nd ATP (+) | 60 | 22.8 |
| 1st ATP (+) His (−) 2nd ATP (−) | 10 | 3.8 |

**Supplementary Table 1. Number and percentage of cells classified by the reactivity of the first ATP, drugs (vehicle or histamine), and second ATP in NHEKs.**

Eight groups classified by reactivity to the first ATP, drugs (vehicle [Supplementary Table 1A] or histamine [Supplementary Table 1B]), and second ATP are shown. The number and percentage of the responding cells in relation to the total number of analyzed cells are shown. (+) indicates a positive reaction, and (−) indicates a negative reaction. VH, vehicle. His, histamine.

**Supplementary Table 2**

|  |  |  |
| --- | --- | --- |
| Classification | Number of cell | (%) |
| Total | 293 | 100 |
| 1st ATP (−) His-CPM (+) 2nd ATP-CPM (+) | 0 | 0 |
| 1st ATP (−) His-CPM (+) 2nd ATP-CPM (−) | 0 | 0 |
| 1st ATP (−) His-CPM (−) 2nd ATP-CPM (+) | 16 | 5.5 |
| 1st ATP (−) His-CPM (−) 2nd ATP-CPM (−) | 91 | 31.1 |
| 1st ATP (+) His-CPM (+) 2nd ATP-CPM (+) | 1 | 0.3 |
| 1st ATP (+) His-CPM (+) 2nd ATP-CPM (−) | 0 | 0 |
| 1st ATP (+) His-CPM (−) 2nd ATP-CPM (+) | 169 | 57.7 |
| 1st ATP (+) His-CPM (−) 2nd ATP-CPM (−) | 16 | 5.5 |

**Supplementary Table 2. Effects of (+)-chlorpheniramine maleate on histamine-induced and second ATP-induced [Ca2+]i changes**

Eight groups classified by reactivity to the first ATP, histamine, and second ATP are shown. Chlorpheniramine maleate at a final concentration of 100 µM was added after recording the first ATP (3 µM) treatment. In the presence of chlorpheniramine maleate, histamine-induced [Ca2+]i elevation was almost completely suppressed. The number and percentage of the responding cells in relation to the total number of analyzed cells are shown. (+) indicates a positive reaction, and (−) indicates a negative reaction. CPM, chlorpheniramine maleate. His, histamine.