

## **Description of Additional Supplementary Files**

File Name: Supplementary Movie 1

Description: TIRF imaging showing the effect of TPC2-A1-N (30  $\mu$ M) on subcellular Ca<sup>2+</sup> levels of individual HEK cells loaded with Cal-520. # denotes agonist addition.

File Name: Supplementary Movie 2

Description: TIRF imaging showing the effect of TPC2-A1-P (30  $\mu$ M) on subcellular Ca<sup>2+</sup> levels of individual HEK cells loaded with Cal-520. # denotes agonist addition.

File Name: Supplementary Movie 3

Description: TIRF imaging showing the effect of a combination of TPC2-A1-N (30  $\mu$ M) and TPC2-A1-P (30  $\mu$ M) on subcellular Ca<sup>2+</sup> levels of individual HEK cells loaded with Cal-520. # denotes agonist addition.

File Name: Supplementary Movie 4

Description: Epifluorescence imaging showing the effect of TPC2-A1-N (30  $\mu$ M) and TPC2-A1-P (60  $\mu$ M) on lysosome motility of HeLa cells loaded with Fluorescein-dextran. Agonist addition is denoted by N and P, respectively.