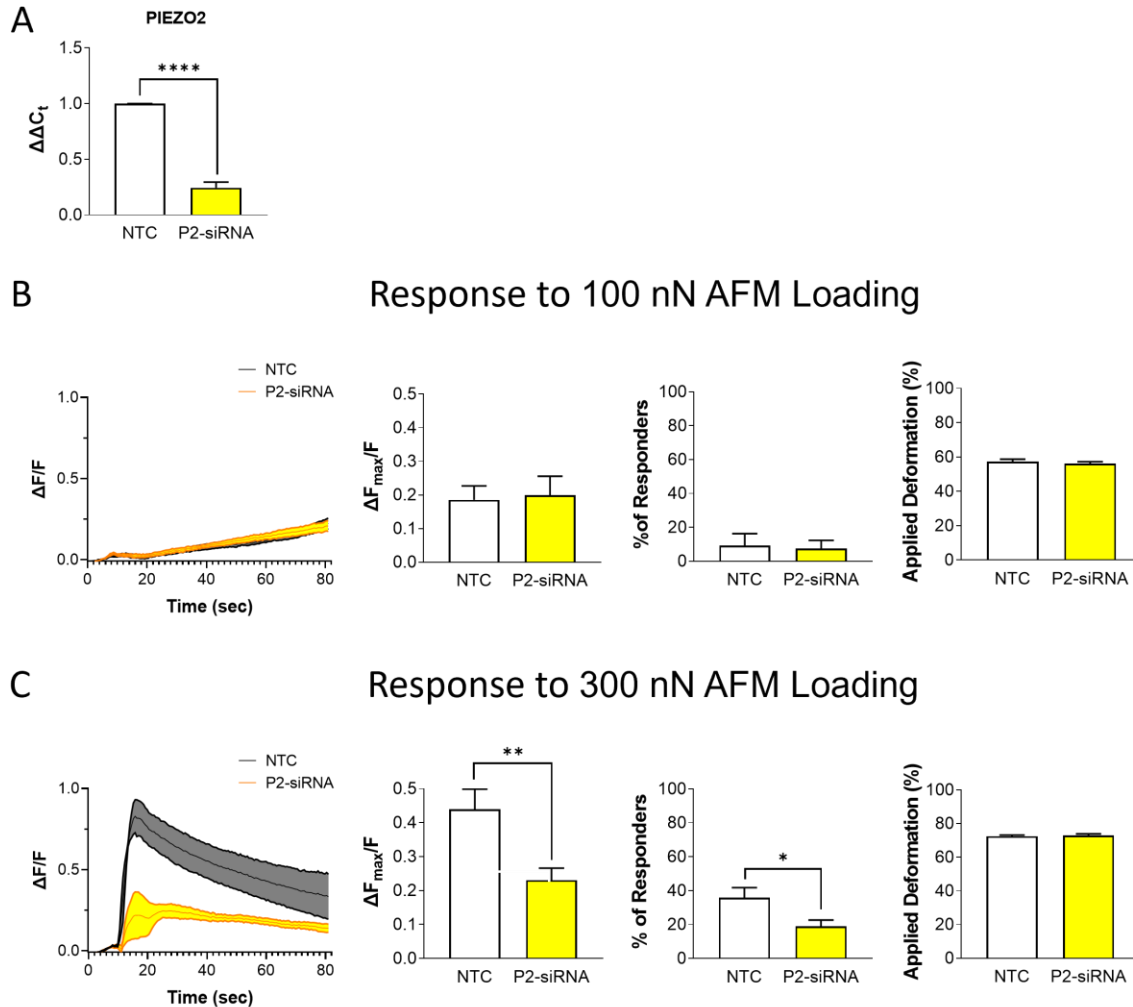


1 **Supplementary Figure 1. NTC and P2-siRNA chondrocyte intracellular Ca²⁺ response to**
 2 **100 and 300 nN force. A)** mRNA levels of *PIEZO2* (P2) normalized to ACTB expression level
 3 in non-targeting control (NTC) and P2-siRNA chondrocytes, in a separate group of pigs from
 4 those in the 500 nN experiments in Figure 1. AFM loading response of P2-siRNA cells
 5 compared to their respective NTCs showing representative cells signaling trend, normalized
 6 intracellular Ca²⁺ fluorescence intensity $\Delta F_{max}/F$, the percentage of the responding cells, and
 7 deformation after loading cells to **B)** 100 nN, and **C)** 300 nN. Data presented as mean \pm SEM.
 8 For A, n=5 samples; for B and C, percentage of responders, n=4-6 test batches, for applied
 9 deformation and Ca²⁺ response to AFM mechanical loading, n=49-96 cells; for group comparison
 10 A, B, C, t-test, * p<0.05, ** p<0.005, **** p<0.0001.



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18 **Supplementary Video 1. NTC (for P1-siRNA) chondrocytes intracellular Ca²⁺ response to**
19 **500 nN of AFM loading.** Response of chondrocytes treated with NTC for P1-siRNA to 500 nN
20 of mechanical compression. Green fluorescence indicates an increase in the Ca²⁺ concentration in
21 the cell.

22 **Supplementary Video 2. P1-siRNA chondrocytes intracellular Ca²⁺ response to 500 nN of**
23 **AFM loading.** Response of chondrocytes treated with P1-siRNA to 500 nN of mechanical
24 compression. Green fluorescence indicates an increase in the Ca²⁺ concentration in the cell.

25 **Supplementary Video 3. NTC (for P2-siRNA) chondrocytes intracellular Ca²⁺ response to**
26 **500 nN of AFM loading.** Response of chondrocytes treated with NTC for P2-siRNA to 500 nN
27 of mechanical compression. Green fluorescence indicates an increase in the Ca²⁺ concentration in
28 the cell.

29 **Supplementary Video 4. P2-siRNA chondrocytes intracellular Ca²⁺ response to 500 nN of**
30 **AFM loading.** Response of chondrocytes treated with P2-siRNA to 500 nN of mechanical
31 compression. Green fluorescence indicates an increase in the Ca²⁺ concentration in the cell.

32 **Supplementary Video 5. NTC (for P1-siRNA) chondrocytes intracellular Ca²⁺ response to 5**
33 **µM Yoda1 addition.** NTC for P1-siRNA cells response to yoda1 addition. Green fluorescence
34 indicates an increase in the Ca²⁺ concentration in the cell.

35 **Supplementary Video 6. P1-siRNA chondrocytes intracellular Ca²⁺ response to 5 µM**
36 **Yoda1 addition.** P1-siRNA cells response to yoda1 addition. Green fluorescence indicates an
37 increase in the Ca²⁺ concentration in the cell.

38 **Supplementary Video 7. NTC (for P2-siRNA) chondrocytes intracellular Ca²⁺ response to 5**
39 **µM Yoda1 addition.** NTC for P2-siRNA cells response to yoda1 addition. Green fluorescence
40 indicates an increase in the Ca²⁺ concentration in the cell.

41 **Supplementary Video 8. P2-siRNA chondrocytes intracellular Ca²⁺ response to 5 µM**
42 **Yoda1 addition.** P2-siRNA cells response to yoda1 addition. Green fluorescence indicates an
43 increase in the Ca²⁺ concentration in the cell.

44 **Supplementary Video 9. Chondrocyte intracellular Ca²⁺ response to different levels of**
45 **mechanical loading.** Representative cells' Ca²⁺ signaling to 50 nN force in iso-osmotic
46 condition. Green fluorescence indicates an increase in the Ca²⁺ concentration in the cell.

47 **Supplementary Video 10. Chondrocyte intracellular Ca²⁺ response to different levels of**
48 **mechanical loading.** Representative cells' Ca²⁺ signaling to 100 nN force in iso-osmotic
49 condition. Green fluorescence indicates an increase in the Ca²⁺ concentration in the cell.

50 **Supplementary Video 11. Chondrocyte intracellular Ca²⁺ response to different levels of**
51 **mechanical loading.** Representative cells' Ca²⁺ signaling to 300 nN force in iso-osmotic
52 condition. Green fluorescence indicates an increase in the Ca²⁺ concentration in the cell.

53 **Supplementary Video 12. Chondrocyte intracellular Ca²⁺ response to different levels of**
54 **mechanical loading.** Representative cells' Ca²⁺ signaling to 500 nN force in iso-osmotic
55 condition. Green fluorescence indicates an increase in the Ca²⁺ concentration in the cell.

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