The primary cilium contributes to mechanically induced changes in actin organization and TAZ translocation

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Due to insufficient pharmacological treatment strategies for osteoporosis, it is critical to further elucidate mechanisms of bone mechanotransduction. Separately, the osteocyte actin cytoskeleton and primary cilium have been shown to be important for osteogenic fluid-flow response [1,2,3,4]. Whether these two apparently distinct systems function cooperatively is unknown. We hypothesize that the primary cilium influences mechanically induced actin adaptation and TAZ translocation.

Figure 1. A) Flow induced an increase in cell area in control but not KD cells B) Cell morphology distribution depended on flow condition and cilia impairment (Test of Independence, P < 0.01) C) Dendrites of primary cilia impaired cells are organized closer to the center of the cell and there are fewer long dendrites over 65 µm compared to controls (Wilcoxon matched-pairs test, P = 0.03) D) TAZ translocated to the nucleus in control cells. E) Fold-increase in TAZ nuclear translocation is inhibited in the KD group. (*"+" intergroup comparison, "**"intrgroup comparison; **/+ + P < 0.01, +++/**/+ P < 0.001; mean ± S.E is shown; F-actin based data from 4 experimental repeats; TAZ data from 2 experimental repeats).

With an IFT88 siRNA-mediated knockdown (KD) to inhibit primary cilia formation in MLO-Y4 osteocyte-like cells, we applied oscillatory fluid-flow for 1 hr at 1 Hz and 1 Pa peak shear stress. We stained for primary cilia (acetylated alpha-tubulin), F-actin (AF488-conjugated phalloidin), and TAZ. Primary cilia KD prevented a flow-induced increase in the area of actin staining (Fig.1A), altered the distribution of cell morphologies and response to flow in the KD group (Fig 1B), and resulted in shorter actin-based dendrites (Fig.1C). Additionally, the KD inhibited TAZ translocation, an actin-dependent mechanoresponse (Fig.1D and 1E). These data implicate the osteocyte primary cilium as a potential mechano-responsive regulator of actin dynamics and indicate these two modes of mechanosensing may be more interrelated than previously thought.