PRIMARY CILIA MECHANICS REGULATES CELL MECHANOSENSITIVITY

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Introduction

Primary cilia (PC) are solitary, nonmotile hair-like organelles of the cell that are linked to the cytoskeleton and act as an antenna collecting biomechanical signals from the extracellular space [Singla, 2006]. The mechanosensory role of the PC has been reported in many tissues such as kidneys, cartilage, tendons and bone where the malfunction of PC is associated with many human diseases [Hoey, 2011]. Experiments have shown that the removal of the PC changes cells' response to mechanical stimuli, such that cells become less sensitive to fluid flow [Malone, 2007]. However, the mechanisms behind this change in cell mechanosensitivity is unclear. We hypothesise that the PC deflection under fluid flow induces strains on the cell which are responsible for regulating cell mechanosensitivity. Moreover, this study investigates how PC interacts with the cytoskeleton components of cells under fluid flow stimulation.

Methods

A three-dimensional FE model of a single cell was created in Abaqus consisting of a nucleus, cytoplasm, cortex, microtubules, actin bundles and primary cilium (Fig 1A) [Barreto, 2012]. The cell was assumed to be semi-ellipsoidal in shape (19µm long, 8µm wide) and the PC was modelled as 5µm long and 200nm in diameter. The PC was attached on top of the cell and linked to the microtubules and actins bundles of the cell, protruding into the extracellular environment. Fluid pressure of 0.35 Pa, corresponding to that created under bioreactor perfusion flow of 1 mm/s, was applied as a surface traction force on the cell. Simulations were performed of a cell *with* PC and one *without* PC.

Results

The shear forces on the cell, created by the fluid flow, induced cell deformations and activated the cytoskeleton components. The PC was deflected under the flow, which created strains on its surface, highest at the cilia base (Fig 1B). The deflection of the cilia also created higher local strains in the cytoplasm of the cell, compared to those observed in the cell without PC (Fig 1C and 1D). Bending of the cilia also doubled the strains on the actin bundles under fluid flow.

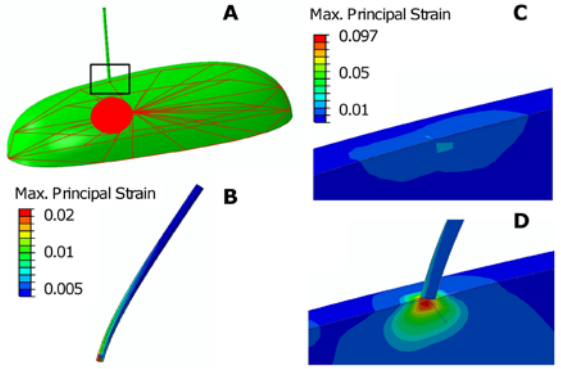

Figure 1: A) The cell model where the cytoskeleton components are highlighted in red. B) Illustrates the strains on the PC under fluid flow. C) Magnified cross section of the cell without PC and D) with PC).

Discussion

The results suggested that the PC is changing the mechanosensory response of cells to fluid flow, by influencing the transmitted strain profile inside cells. Different stretch-activated channels located on the cilia and at its base, responsible for intracellular signalling [Singla, 2006], are likely to be activated by the strains caused by the ciliary deflection. The cytoplasm and actin strains created by the PC deflection could also influence other cellular mechanisms such as activities of the Golgi apparatus located close to the base of the cilia [Satir, 2010]. The results indicate that cell mechanosensitivity can be altered by targeting PC mechanics.

References

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