Title: **Microtubules regulate mechanosensitive cell migration**

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Cells sense the mechanical properties of the substrate through integrin-mediated focal adhesions and transduce these mechanical cues into biochemical signals by a process known as mechanotransduction. In turn, cells adapt and perform specific functions that regulate various cellular processes such as cell migration. Although the role of microtubules in cell adhesion and migration has been well established, their involvement in mechanotransduction remains unclear. Using a combination of microfabrication methods, biophysical approaches and imaging techniques, we show that substrate rigidity affects a tubulin post-translational modification, namely acetylation, through β_1 integrin-mediated downstream signalling in astrocytes. The enzyme responsible for microtubule acetylation, αTAT1, interacts with focal adhesion protein Talin in a tension-dependent manner. Moreover, we demonstrate that αTAT1 reorganizes the actomyosin network, increases traction force generation and promotes cell migration on stiff substrates. Our results suggest a feedback mechanism involving microtubules and actin in mechanotransduction at focal adhesions whereby, cells sense the rigidity of the substrate through integrin-mediated adhesions, modulate their levels of microtubule acetylation, which then controls the actomyosin cytoskeleton, force transmission on the substrate and promotes cell migration.