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Mechanics of composite actin networks: in vitro and cellular perspectives

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Actin filaments and associated actin binding proteins play an essential role in governing the mechanical properties of eukaryotic cells. Even though cells have multiple actin binding proteins (ABPs) that exist simultaneously to maintain the structural and mechanical integrity of the cellular cytoskeleton, how these proteins work together to determine the properties of actin networks is not well understood. The ABP, palladin, is essential for the integrity of cell morphology and movement during development. Palladin coexists with alpha-actinin in stress fibers and focal adhesions and binds to both actin and alpha-actinin. To obtain insight into how mutually interacting actin crosslinking proteins modulate the properties of actin networks, we have characterized the micro-structure and mechanics of actin networks crosslinked with palladin and alpha-actinin. Our studies on composite networks of alpha-actinin/palladin/actin show that palladin and alpha-actinin synergistically determine network viscoelasticity. We have further examined the role of palladin in cellular force generation and mechanosensing. Traction force microscopy revealed that TAFs are sensitive to substrate stiffness as they generate larger forces on substrates of increased stiffness. Contrary to expectations, knocking down palladin increased the forces generated by cells, and also inhibited the ability to sense substrate stiffness for very stiff gels. This was accompanied by significant differences in the actin organization and adhesion dynamics of palladin knock down cells. Perturbation experiments also suggest altered myosin activity in palladin KD cells. Our results suggest that the actin crosslinkers such as palladin and myosin motors coordinate for optimal cell function and to prevent aberrant behavior as in cancer metastasis.