TANKYRASE REGULATES ACTIN POLYMERIZATION VIA ARP2/3 COMPLEX' INHIBITOR ARPIN

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Cell migration promotes a variety of crucial processes like embryogenesis, immune cell trafficking, tissue homeostasis and wound healing. Central feature of cell migration is the formation of cell membrane protrusions and cell adhesions. In response to extracellular signals, branched actin networks start to polymerize at the leading edge of cells. The growing branched actin network provides a force to protrude the membrane and form structures called lamellipodia and filopodia at the cell leading edge that enables a cell to protrude its membrane and establish new contacts with its environment. Actin-related protein 2 and 3 (Arp2/3) complex is one of the major actin nucleators that generates the branched actin filaments network via formation of so called branch junction between two actin filaments [1]. Activity of the Arp2/3 complex is tightly regulated by Nucleation Promoting Factors (NPF) and inhibitors. Inactivator of Arp2/3 complex in lamellipodia is a recently found protein called Arpin [2][3]. Arpin decreases the amount of branched junctions. Interestingly, Arpin is recruited and activated by small GTPase Rac1 at the lamellipodium tip, where Rac1 also stimulates NPF WAVE complex. Co-existence of positive Rac-WAVE-Arp2/3 and negative Rac-Arpin-Arp2/3 regulatory circuits displays that Arpin has to be itself tuned by the cell. We found two binding partners of Arpin – Tankyrase1 and Tankyrase2 and made an analysis of Tankyrases binding importance for Arpin activity in vivo via point mutation in the binding site of Tankyrase. It appeared that Tankyrase is necessary for Arpin-Arp2/3 complex interaction. Furthermore, we used Transmission Electron Microscopy to depict the details of Arpin-Tankyrase interaction using purified proteins. We found that Tankyrase undergoes significant conformational changes in the presence of Arpin, which could reveal the mechanism of Arp2/3 complex inhibition and actin polymerization regulation.

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