3-P1-35

Poster Sessions

Differentiation-inducing factor 1 activates AMP-regulated kinase/Cofilin pathway to regulate the actin cytoskeleton.

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Differentiation-inducing factor 1 (DIF-1) is a polyketide produced by *Dictyostelium discoideum* which inhibits growth and migration and promotes differentiation of prestalk cells. In *Dictyostelium* AX2 cells, DIF-1 regulates phosphorylation of signaling molecules involved in rearrangement of actin cytoskeleton and induces cell rounding. Here, we found that DIF-1 regulates actin cytoskeleton in mammalian cells by activating Cofilin, an actin depolymerization factor. In mouse immortalized endothelial cells (SVECs), DIF-1 rapidly induced cell spreading and dephosphorylation, and activation of Cofilin. Knockdown of cofilin suppressed the cell spreading by DIF-1. AMP-activated protein kinase (AMPK), an upstream of Cofilin, was found to be phosphorylated and activated by DIF-1. On the other hand, Compound C, an AMPK inhibitor, inhibited dephosphorylation of Cofilin by DIF-1, indicating that DIF-1 dephosphorylates and activates Cofilin via AMPK. Knockdown of LKB1, an upstream kinase of AMPK, suppressed phosphorylation and activation of AMPK by DIF-1 in SVECs, indicating the involvement of LKB1 in AMPK activation by DIF-1. Activation of AMPK and Cofilin were also observed in other mammalian cells including HUVECs and PANC-1 cells, suggesting that AMPK and Cofilin are common downstream molecules of DIF-1 signaling. We propose that AMPK/Cofilin pathway is a new signaling pathway in the regulation of actin cytoskeleton by DIF-1.