Ezh2 Controls Integrin-Dependent Adhesion and Migration through Direct Methylation of Talin

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Abstract

Cell migration is a highly dynamic process requiring temporal and spatial coordination between integrin activation and disassembly of adhesion complexes. Talin, a key molecule that controls these processes by linking integrins to the actin cytoskeleton, is functionally regulated by various post-translational modifications. Here we show that the lysine methyltransferase, Ezh2, critically regulates integrin signaling and governs the adhesion dynamics of neutrophils and dendritic cells (DCs). Ezh2 deficiency impaired integrin-dependent transendothelial migration of innate leukocytes and restricted disease progression in an experimental autoimmune encephalomyelitis model of multiple sclerosis. Ezh2 recruitment by the guanine nucleotide exchange factor, Vav, resulted in reduced talin binding to F-actin through Ezh2-mediated talin methylation and thereby was essential for the regulation of adhesion structure turnover. Our data demonstrates for the first time that leukocyte migration and adhesion dynamics are critically regulated by the polycomb group protein Ezh2 through talin methylation.