Activin A induces erythroid gene expressions and inhibits mitogenic cytokine-mediated K562 colony formation by activating p38 MAPK

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Abstract

Activin A, a member of the transforming growth factor (TGF)-beta superfamily, is involved in the regulation of erythroid differentiation. Previous studies have shown that activin A inhibited the colony-forming activity of mouse Friend erythroleukemia cells, however, the mechanism remains unknown. First, we show herein that activin A induced the expression and activated the promoters of alpha-globin and zeta-globin in K562 cells, confirming that activin A induces erythroid differentiation in K562 cells. The p38 mitogen activated protein kinase (MAPK) inhibitor, SB203580, inhibited and the extracellular signal regulated kinase (ERK) inhibitor, PD98059, enhanced the expression and promoter activities of alpha-globin and zeta-globin by activin A, indicating that p38 MAPK and ERK are crucial for activin A-induced erythroid genes expression. Second, SB203580 inhibited the inhibitory effect of activin A on the colony-forming activity of K562 cells using the methylcellulose colony assay, indicating that activin A inhibits K562 colony formation by activating p38 MAPK. In addition, mitogenic cytokines SCF, IL-3, and GM-CSF induced colony formation of K562 cells that could be inhibited by PD98059 or enhanced by SB203580, respectively, indicating that these mitogenic cytokines induce K562 colony formation by activating ERK and inactivating p38 MAPK. Furthermore, activin A reduced the induction effect of these mitogenic cytokines on K562 colony formation in a dose-dependent manner. The inhibition of p38 MAPK reverted the inhibitory effect of activin A on mitogenic cytokine-mediated K562 colony formation. We conclude that activin A can regulate the same pathway via p38 MAPK to coordinate cell proliferation and differentiation of K562 cells. 2006 Wiley-Liss, Inc.