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MED28 (magicin/EG-1) modulates MEK1 (MAP2K1)-dependent cellular migration in human breast cancer cells

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The objective of this study is to understand the role of MED28 (magicin/EG-1) in the aspect of cellular migration in human breast cancer cells. MED28 exhibits several cellular roles, including a mammalian Mediator subunit (MED28), a Grb2 and cytoskeleton-associated protein, a repressor of smooth muscle cell differentiation, and an endothelial-derived gene (EG-1). The association of MED28 with multiple proteins, including Grb2, Src, merlin, and actin, strongly suggests that MED28 is involved in many cellular signaling pathways. Specifically, several tumors, including breast cancer, highly express MED28; however, the fundamental mechanism is unclear at present. Using RNA interference (RNAi) technology, we found that suppression of MED28 blocked cellular migration and invasion with concomitant reduced expression levels of matrix metalloproteinase-2 (MMP2) and mitogen-activated protein kinase kinase 1 (MEK1; MAP2K1). In contrast, overexpression of MED28 enhanced cellular migration and up-regulated MMP2 and MEK1 expression. Moreover, MEK1 knockdown blocked MED28-induced MMP2 activation, cellular migration, and invasion as shown by gelatin zymography, wound-healing, and Matrigel invasion assays. Our data indicate that MED28 modulates cellular migration in a MEK1-dependent manner in human breast cancer cells, reinforcing the important cellular function of MED28.

Funding:
This work was supported by the National Science Council grant, NSC 98-2320-B-309-002-MY3, to M.-F.L.