Missing-in-metastasis MIM/MTSS1 promotes actin assembly at intercellular junctions and is required for integrity of kidney epithelia.

MIM/MTSS1 is a tissue-specific regulator of plasma membrane dynamics, whose altered expression levels have been linked to cancer metastasis. MIM deforms phosphoinositide-rich membranes through its I-BAR domain and interacts with actin monomers through its WH2 domain. Recent work proposed that MIM also potentiates Sonic hedgehog (Shh)-induced gene expression. Here, we generated MIM mutant mice and found that full-length MIM protein is dispensable for embryonic development. However, MIM-deficient mice displayed a severe urinary concentration defect caused by compromised integrity of kidney epithelia intercellular junctions, which led to bone abnormalities and end-stage renal failure. In cultured kidney epithelial (MDCK) cells, MIM displayed dynamic localization to adherens junctions, where it promoted Arp2/3-mediated actin filament assembly. This activity was dependent on the ability of MIM to interact with both membranes and actin monomers. Furthermore, results from the mouse model and cell culture experiments suggest that full-length MIM is not crucial for Shh signaling, at least.
during embryogenesis. Collectively, these data demonstrate that MIM modulates interplay between the actin cytoskeleton and plasma membrane to promote the maintenance of intercellular contacts in kidney epithelia.