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## Lamellipodia-like membrane protrusions regulate the integrity of epithelial cell-cell adhesions

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Metastasis suppressor protein 1 (MTSS1) is a membrane-interacting scaffolding protein that functions as a tumour suppressor in various carcinomas. MTSS1 binds phosphoinositide-containing membranes through its I-BAR domain, and can sense and generate negative membrane curvatures; however, the mechanisms by which MTSS1 localizes to cell-cell adhesions in epithelial cells and regulates their integrity and maintenance remain elusive. Using fluorescence and electron microscopy, we found that cell-cell adhesions of Madin-Darby canine kidney (MDCK) cells harbour lamellipodia-like, dynamic actin-driven membrane folds, which exhibit negative membrane curvatures at their distal edges. BioID proteomics demonstrated that MTSS1 forms a complex with actin-binding proteins in lamellipodia-like membrane protrusions at cell-cell adhesions. Inhibition of actin filament assembly at adherens junctions leads to defects in epithelial integrity. Together, these results support a model in which membrane-associated MTSS1, together with actin-binding proteins, promotes the formation of dynamic lamellipodia-like membrane protrusions that regulate the integrity of cell-cell adhesions in epithelial monolayers.

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