New Results

The ER tether VAPA is required for proper cell motility and anchors ER-PM contact sites to focal adhesions

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ABSTRACT

Cell motility processes highly depend on the membrane distribution of Phosphoinositides (PInst), giving rise to cytoskeleton reshaping and membrane trafficking events. Membrane contact sites serve as platforms for lipid exchange and calcium fluxes between two organelles. Here, we show that VAPA, an ER membrane-resident contact site tether, plays a crucial role during cell motility. CaCo2 adenocarcinoma epithelial cells depleted for VAPA exhibit several collective and individual motility defects, disorganized actin cytoskeleton and altered protrusive activity. During migration, VAPA is required for the maintenance of PI(4,5)P2 levels at the plasma membrane, but not for PI(4)P homeostasis in the Golgi and endosomal compartments. Importantly, we show that VAPA regulates the dynamics of focal adhesions (FA) through its MSP domain, and is essential to stabilize and anchor ventral ER-PM contact sites to FA, thus mediating microtubule-dependent FA disassembly. To conclude, our results reveal unprecedented functions for VAPA-mediated membrane contact sites during cell motility and provides a dynamic picture of ER-PM contact sites connection with FA mediated by VAPA.

Competing Interest Statement

The authors have declared no competing interest.

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