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Meeting abstract

Cell adhesion-dependent trafficking and targeting of TRPC4 channels in human vascular endothelium

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Introduction

RPC4 has been suggested as a prominent Ca^{2+} signaling element of vascular endothelial cells, which governs endothelial permeability. In an attempt to identify mechanism that link TRPC4 to cell adhesion, we tested the hypothesis that TRPC4 communicates with adherens complexes by mechanisms other than generation of global cellular Ca^{2+} signals.

Results

In human microvascular endothelial cells (HMEC), TRPC4 was found to co-precipitate with VE-cadherin, indicating a physical coupling between TRPC4 and components of junctional complexes. Membrane presentation of TRPC4 as determined by surface biotinylation was found dependent on the formation of cell-cell contacts. Membrane presentation of TRPC4 was divergently affected by pro-inflammatory stimuli in cell displaying cell-cell contacts as compared to cells lacking contacts. At >90% confluency, epidermal growth factor (EGF) reduced membrane presentation of both VE-cadherin and TRPC4. By contrast, enhanced EGF-induced surface recruitment of TRPC4 was observed when cell-cell contacts were lacking. Cell adhesion-dependent targeting of TRPC4 was further analyzed by fluorescence imaging of channel localization and cellular Ca^{2+} signals in HMEC as well as in HEK293 expression system.

Conclusion

Our results suggest recruitment of TRPC4 into a junctional signaling microdomain of the vascular endothelium.

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