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Saccharomyces boulardii CNCM I-745 Restores intestinal Barrier Integrity by Regulation of E-cadherin Recycling.

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Abstract

BACKGROUND AND AIMS: Alteration in intestinal permeability is the main factor underlying the pathogenesis of many diseases affecting the gut, such as inflammatory bowel disease [IBD]. Characterization of molecules targeting the restoration of intestinal barrier integrity is therefore vital for the development of alternative therapies. The yeast Saccharomyces boulardii CNCM I-745 [Sb], used to prevent and treat antibiotic-associated infectious and functional diarrhea, may have a beneficial effect in the treatment of IBD.

METHODS: We analyzed the impact of Sb supernatant on tissue integrity and components of adherens junctions using cultured explants of colon from both IBD and healthy patients. To evaluate the pathways by which Sb regulates the expression of E-cadherin at the cell surface, we developed in vitro assays using human colonic cell lines, including cell aggregation, a calcium switch assay, real-time measurement of transepithelial electrical resistance [TEER] and pulse-chase experiments.

RESULTS: We showed that Sb supernatant treatment of colonic explants protects the epithelial morphology and maintains E-cadherin expression at the cell surface. In vitro experiments revealed that Sb supernatant enhances E-cadherin delivery to the cell surface by re-routing endocytosed E-cadherin back to the plasma membrane. This process, involving Rab11A-dependent recycling endosome, leads to restoration of enterocyte adherens junctions, in addition to the overall restoration and strengthening of intestinal barrier function.

CONCLUSION: These findings open new possibilities of discovering novel options for prevention and therapy of diseases that affect intestinal permeability.

KEYWORDS: Adherens junction; inflammatory bowel disease; intestinal permeability

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