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Epithelial-to-Mesenchimal Transition (EMT) in experimental intestinal fibrosis

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Inflammatory Bowel Diseases (IBD) are chronic and progressive inflammatory disorders that may result in intestinal fibrosis, characterized by excessive and uncontrolled deposition of extracellular matrix components (ECM). Other than Smad-dependent the profibrotic effects of TGFβ signaling that leads to a phenotype switch of intestinal mesenchymal cells, resulting in proliferation and collagene deposition (1), source of fibrotic tissue comes from the process called Epithelial-to-Mesenchymal Transition (EMT), in which also epithelial cells acquire fibroblastic phenotype and related function (2). The purpose of our study was to evaluate the expression of protein markers of EMT in a mouse model of intestinal fibrosis and their changes after the administration of the experimental drug GED- 0507-34 Levo, that is able to inhibit and revert the fibrotic phenotypic switch. Immunohistochemistry (IHC) and immunofluorescence (IF) evalutations for E-cadherin and β-catenin were performed in three groups of C57BL/6 mice: Dextran Sulphate Sodium (DSS) colitis group, DSS+GED group and controls. In the same groups E-cadherin, β-catenin, p-GSK3-beta and GSK3-beta were evaluated by immunoblotting. In IHC and IF analysis, was observed a significant decrease of E-cadherin and β-catenin expression in DSS group compared to control. GED administration was able to revert the DSS effect by increasing the expression of both proteins to levels similar to the control. Comparable results were obtained by immunoblotting. Furthermore the immunoblotting assay showed that the known EMT inhibitor GSK3-beta is activated in the DSS+GED group suggesting that GSK3-beta activity is required for the restoration of the epithelial phenotype exerted by GED. Taken together, our results indicates that the EMT is another cause of collagen deposition in our mouse model and thus it could be a valid target for the development of a treatment for intestinal fibrosis.

References

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Keywords

Intestinal Fibrosis; EMT; E-cadherin; β-catenin; GSK3-beta.