CELLULAR AND MOLECULAR IMPACT OF THE MELANOCORTIN RECEPTOR AGONIST PL8177 IN DEXTRAN SULFATE SODIUM–INDUCED COLITIS IN RATS

John Dodd

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The melanocortin 1 receptor agonist PL8177 demonstrated significant improvement in anatomical markers of colitis and shifted macrophage populations from inflammatory M1 to pro-resolution M2 phenotype in a dextran sulfate sodium-induced rat model.

KEY POINTS

- Oral PL8177 at 50 µg showed significant improvement in colon weight (53% reduction), stool consistency, and fecal occult blood score compared to vehicle control, and the 100 µg dose significantly improved the total colitis index.
- All PL8177 dose groups showed greater improvement in the total colitis index compared to mesalazine-treated rats, which showed marked colon length reduction but only moderate (35%) improvement in colon weight.
- Single nuclei RNA-seq analysis revealed that PL8177 100 µg treatment shifted macrophage populations from primarily M1 (inflammatory) in vehicle-treated colons to primarily M2 (pro-resolution) phenotype, with cell populations and gene expression closer to healthy controls.
- Proteomic analysis showed PL8177-treated colons were more similar to sham colons than vehicle-treated colons, with expression of proteins promoting intestinal homeostasis resembling healthy tissue.
- This study may be of interest to researchers investigating novel anti-inflammatory mechanisms in inflammatory bowel disease; authors are employees of Palatin Technologies, Inc.

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