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Two novel diagnostic tests assess disease activity and predict therapeutic benefit of a novel antifibrotic drug in patients with collagenous colitis in contrast to Crohn's and ulcerative colitis

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The diagnostic screening test "Drug Inhibition Index (DII)" was developed here at Dalhousie University and is used to test drugs in vitro to see if they can inhibit the stimulatory effect of selected patient's blood samples on proliferation of selected cell targets e.g., intestinal smooth muscle cells (ISMCs) as the target in the intestinal fibrosis diagnostic test. We will show that DII predicts the inhibitory effect of pentoxifylline in this diagnostic test and thus show that pentoxifylline will have a have a beneficial effect on fibrosis, regardless of the form of fibrosis and ultimately pentoxifylline will control scarring. Our research indicates another diagnostic test, the FSI or fibroproliferative stimulation index is an excellent tool to predict fibrosis. Our data suggests that FSI correlates with P-III-P or pro-collagen type 3 peptide in experimental models (TNBS) and is a positive predictor of fibrosis in specific forms of fibrosis including HCV related hepatic fibrosis.

Objectives: We assessed the DII of pentoxifylline and the in vivo effect of pentoxifylline (Trental^{R}) in a small group of patients with collagenous colitis. We report the FSI results obtained in the cohort of collagenous colitis patients and explore the role of IL-18 and the molecular mechanism in an experimental model (TNBS).

Results: The results indicate that the FSI was elevated in the cohort of collagenous colitis patients and that pentoxifylline had a significant DII in those collagenous colitis patients who ultimately derived benefit from Trental^{R} treatment.

Conclusions: We have shown that patient sera stimulated ISMC proliferation and that pentoxifylline treatment decreased collagenous colitis sera-stimulated ISMC proliferation. Our results suggest that the FSI is an effective measure of fibrosis in collagenous colitis and have previously demonstrated this in HCV and NASH fibrosis and in experimental models of fibrosis. The DII may prove to be of significant utility in the development of novel therapeutics to treat collagenous colitis and other forms of IBD. The molecular changes support a potential role for pentoxifylline in the treatment of fibrosis associated with IBD. (supported by CIHR).

Biography

Dr. Theresa C. Hemsworth-Peterson completed her Ph.D at the age of 28 and conducted postdoctoral studies at National Institutes of Health, in the National Institute of Child Health and Human development in Dr. Dan Nebert's Developmental Pharmacology lab. She is an Affiliate Scientist at the QEII in Halifax and a Professor of Medicine in the GI Division at Dalhousie University in Halifax, Canada. She is past Chair of the Dalhousie Medical Research Foundation SAC and holds several US patents and has published extensively in reputed journals and has served on their editorial board.