

P078**Evaluating the efficacy of potential drugs for intestinal fibrosis using precision-cut tissue slices**

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Background: Intestinal fibrosis (IF) is a common complication in Crohn's disease. Currently, there are no drugs registered to treat IF and the sole therapy is intestinal resection. Transforming growth factor (TGF)-beta and platelet-derived growth factor (PDGF) play a key role in IF and are the main targets for potential treatment. Recently, we developed a novel model for the early onset of IF using precision-cut intestinal slices (PCIS). Our objective was to investigate the anti-fibrotic effect of some potential anti-fibrotic compounds, including TGF-beta and PDGF-pathway inhibitors, by using the murine PCIS fibrosis model.

Methods: Murine PCIS were incubated up to 48h. The viability was assessed by evaluating the ATP content of the PCIS. Gene expression of the fibrosis markers pro-collagen Ia1 (Colla1), heat shock protein 47 (Hsp47) and fibronectin (Fn2) were determined by qPCR.

The effects of anti-fibrotic drugs mainly inhibiting the TGF-beta pathway: valproic acid (VPA), tetracycline (Tet), pirlfenidone (Pir), and LY2109761 (LY) and mainly inhibiting the PDGF pathway: imatinib (Ima), sorafenib (Sor), and sunitinib (Sun) were determined at the maximal non-toxic concentrations.

Results: Murine PCIS remained viable up to 48h of incubation and showed increased gene expression of the fibrosis markers (Colla1, 0.6; Hsp47, 4.0 and Fn2, 6.4 fold). After 48h, VPA and Tet down-regulated Hsp47 gene expression 2.0 and 1.7 fold, respectively. Furthermore, Fn2 gene expression was also decreased 2.1 fold by Tet. Meanwhile, Pir decreased Colla1, Hsp47, and Fn2 gene expression 2.2, 1.5, and 1.2 fold, respectively. All investigated markers of fibrosis were down-regulated by LY (Colla1, 9.0; Hsp47, 1.9 and Fn2, 2.7 fold). Sun decreased the expression of Colla1, 1.6; Hsp47, 1.3 and Fn2, 1.3 fold, while Sor only down-regulated Hsp47, 1.3 fold. In contrast, Ima did not affect the expression of fibrosis markers.

Conclusions: From the compounds studied, the TGF-beta-inhibitors; Tet, Pir, and LY and only one PDGF-inhibitor, Sun, showed potential anti-fibrotic effect on gene expression of fibrosis markers in murine PCIS. Thus, PCIS is a promising model to evaluate the anti-fibrotic effect of potential drugs for intestinal fibrosis.