

Mouse Model for Inflammatory Bowel Diseases



DESCRIPTION

This is a transgenic double-knockout (DKO) mouse (*Gpx1* and *Gpx2*). Both GPX1 and GPX2 belong to a selenium-dependent glutathione peroxidase (GPXs) family, which are enzymes that are efficient in the reduction of hydroperoxides. *Gpx1* is expressed ubiquitously, and *Gpx2* is highly expressed in the epithelium of the gastrointestinal (GI) tract. *Gpx1/2*-DKO mice have early-onset spontaneous ileocolitis beginning around weaning. These mice are an excellent model for human inflammatory bowel diseases (IBD) because they share similar disease etiology, which includes that the disease severity is highly influenced by genetic background, gut microflora, diet, and higher cancer risk in the distal GI tract. Unlike most mouse IBD models which have disrupted genes playing an important role in regulation of adaptive immunity, these *Gpx1/2*-DKO mice have intact immunity- which resembles human IBD.

KEY ASPECTS

- Homozygous disruption of both the endogenous *Gpx1* and *Gpx2* genes.
- Disease characteristics include ileitis, colitis, hypothermia, growth retardation, runting, perianal ulceration, diarrhea, wasting syndrome,, IBD histopathology, tumors/cancer in the ileum or colon

PUBLISHED DATA

- Esworthy RS, Binder SW, Doroshov JH, and Chu FF, Microflora trigger colitis in mice deficient in selenium-dependent glutathione peroxidase and induce *Gpx2* gene expression. *Biol. Chem.* 384: 597-607, 2003
- Lee D-H, Esworthy RS, Chu, C, Pfeifer GP, and Chu, F-F. Mutation accumulation in the intestine and colon of mice deficient in two intracellular glutathione peroxidases. *Cancer Res.* 66: 9845-9851, 2006
- Hahn MA, Hahn T, Lee DH, Esworthy RS, Kim B, Riggs AD, Chu F-F, and Pfeifer GP. Methylation of Polycomb target genes in intestinal cancer is mediated by inflammation. *Cancer Res.* 68:10280-9, 2008
- Esworthy RS, Kim BW, Larson GP, Yip MLR, Smith DD, Li M, Chu F-F. A colitis locus on chromosome 2 impacting the severity of early-onset disease in mice deficient in GPX1 and GPX2. *Inflammatory Bowel Diseases.* In press, 2010

INTELLECTUAL PROPERTY

Title	US Patent Number	Issued
Mice with Combined Disruption of GPX1 and GPX2 Gene have Growth Retardation, Hypothermia, and Colitis and Provide a Mouse Model for Cancer	6,762,343	7/14/2004

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