

## ESPS Peer-review Report

**Name of Journal:** World Journal of Gastroenterology

**ESPS Manuscript NO:** 3593

**Title:** Synergistic effect of interleukin-10-receptor variants in a case of early-onset Inflammatory Bowel Disease

**Reviewer code:** 00503539

**Science editor:** Zhai, Huan-Huan

**Date sent for review:** 2013-05-08 13:50

**Date reviewed:** 2013-05-15 20:47

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A (Excellent)	<input type="checkbox"/> Grade A: Priority Publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B (Very good)	<input type="checkbox"/> Grade B: minor language polishing	<input type="checkbox"/> Existed	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C (Good)	<input type="checkbox"/> Grade C: a great deal of language polishing	<input type="checkbox"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D (Fair)		BPG Search:	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)	<input type="checkbox"/> Grade D: rejected	<input type="checkbox"/> Existed	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

## COMMENTS TO AUTHORS

ESPS Manuscript No. 3593 Ms. Title: Synergistic effect of interleukin-10-receptor variants in a case of early-onset ulcerative colitis

**GENERAL COMMENTS:** The authors investigated the molecular cause such as down- or over-expression of IL-10 receptors,  $\beta$ -catenin, and TNF receptors of very early-onset inflammatory bowel disease in a 18-months old child as well as his relatives, other IBD patients, FAP/colorectal cancer patients, and healthy donors. They concluded that a synergistic effect of several variant alleles of the IL10 receptor genes, inherited in a Mendelian manner, is involved in IBD onset in this young child. These results are interesting and have the significance of the research contents, although this is basically a single-case report.

**SPECIFIC COMMENTS:** 1) There are some confuses in using the terms "inflammatory bowel disease" and "ulcerative colitis". The authors should properly use both terms, respectively. 2) There are some minor misspellings. 3) Discussion: "According to our hypothesis, we found TNFR1 down-expression and TNFR2 and IL-10RB over-expression in primary fibroblasts incubated with mesalazine and azathioprine, both in the IBD and in FAP patients. In IBD patient only, azathioprine, but not mesalazine induces a TNF $\alpha$  decrease." Further explain the significance of TNFR1 down-expression and TNFR2 and IL-10RB over-expression in primary fibroblasts in ulcerative colitis. 4) Conclusion: "In addition, we suggest that  $\beta$ -catenin and TNFR1 protein expressions could represent molecular markers of sub-clinical disease in apparently healthy relatives of patients." Discuss the relationship between  $\beta$ -catenin and TNFR1 protein expressions in ulcerative colitis.

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**Name of Journal:** World Journal of Gastroenterology

**ESPS Manuscript NO:** 3593

**Title:** Synergistic effect of interleukin-10-receptor variants in a case of early-onset Inflammatory Bowel Disease

**Reviewer code:** 00039467

**Science editor:** Zhai, Huan-Huan

**Date sent for review:** 2013-05-08 13:50

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CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A (Excellent)	<input type="checkbox"/> Grade A: Priority Publishing	Google Search:	<input checked="" type="checkbox"/> Y] Accept
<input checked="" type="checkbox"/> Y] Grade B (Very good)	<input checked="" type="checkbox"/> Y] Grade B: minor language polishing	<input type="checkbox"/> Existed	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C (Good)	<input type="checkbox"/> Grade C: a great deal of	<input type="checkbox"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D (Fair)	language polishing	BPG Search:	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)	<input type="checkbox"/> Grade D: rejected	<input type="checkbox"/> Existed	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

## COMMENTS TO AUTHORS

The present study claims an association between an inherited novel IL10RA polymorphism along with a compound heterozygosity of IL10RB and a very early onset of inflammatory bowel disease. Furthermore, Beta catenin, TNFRI and TNFRII were overexpressed in the proband. It does exist a special enthusiasm about the potential power of genomics to define the etiology and/or phenotype of diseases, this also because associations that arise from genetic studies may be less likely to be confounded or biased than other types of studies. When epidemiologic studies are performed the number of patients and controls reported are crucial to support strong genotype/phenotype associations. However, when a single specific case or family is studied the discovery of new functional polymorphisms specially when the authors make efforts to examine the functional consequences of these mutations deserves more attention even if the functional characterization and the real pathogenic contribution of susceptible genes are hard to assess in complex disorders such as IBD. Overall the study raises numerous important issues that still remain to be solved in the attempt to correlated genotype/phenotype association in early onset IBD.