

## ANSWERING REVIEWERS



August 12, 2013

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: WJG editorial manuscript R1.doc).

**Title:** Molecular classification of colorectal carcinomas: the genotype to phenotype relation

**Author:** Elke Kaemmerer, Christina Klaus, Min Kyung Jeon, Nikolaus Gassler

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

**ESPS Manuscript NO:** 4117

The manuscript has been improved according to the suggestions of reviewers:

1 Format has been updated

[This is done.](#)

2 Revision has been made according to the suggestions of the reviewer

[The help of the reviewers for improving the manuscript is highly acknowledged. We have changed the manuscript according to their insightful comments.](#)

### Reviewer #1

1. For certain, there is clear correlation between mutant alleles and phenotypes. But this is not straightforward as my colleague attempted to conclude in his article under review. There are different factors that govern the expression of pathogenic mutations; such as: the location of the mutation within the gene, the degree to which aspects of aberrant phenotype are aberrated in the heterozygote, the degree to which expression of mutant phenotype is influenced by the other gene products, the proportion and nature of cells in which the mutant gene is present and the parental origin. In addition, environmental factors play significant major essential roles in the induction and then in the development of tumours. This means that the existence of further predisposing environmental factors is quite necessary for phenotype expression. Therefore, publication of this article will certainly mislead other investigators who determine to use its conclusion as basis for further research in the same direction.

[We do absolutely agree with the reviewer that the genotype to phenotype correlation of CRCs is not straightforward. The phenotype is determined by several additional circumstances and quite varibale. These facts are further addressed in the revised version of the manuscript. In addition, the priority of molecular CRC tissue analysis \(definition of the genotype\) to define prognostic and therapeutic tumour groups is highlighted.](#)

## Reviewer #2

1. Classes of molecular events targeting colorectal carcinogenesis. The article addresses directly the issue of genotype to phenotype relation in CRC. A brief report (or maybe a table) of genotype classification that can categorize patients with CRC in prognostic groups would be valuable for the readers. Moreover, targeted groups of patients can be identified for targeted therapy. I would also expect authors to give some future perspectives.

The importance of CRC genotyping to define prognostic and therapeutic groups is now addressed. At present, for only some genotypes the prognostic value is clearly characterized. In the overwhelming number of cases tumour stage is the most important variable in patient's prognosis. Therefore we would prefer the manuscript without your proposed table.

Thank you again for publishing our manuscript in the *World Journal of Gastroenterology*.

Sincerely yours,

*Nikolaus Gassler*

Prof. Dr. Nikolaus Gassler (M.A.)

Institute of Pathology

RWTH Aachen University

Pauwelsstrasse 30

52074 Aachen, Germany

Fax: +49 241 80 82439

E-mail: ngassler@ukaachen.de