



OTTO VON GUERICKE  
UNIVERSITÄT  
MAGDEBURG



MEDIZINISCHE  
FAKULTÄT

Medizinische Fakultät, Leipziger Str. 44, 39120 Magdeburg

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**Klinik für Gastroenterologie,  
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Direktor: Prof. Dr. med. Ali Canbay

**PD Dr. med. Alexander Link**

Leiter des Forschungslabors/Head of GI  
Research Laboratory

Otto-von-Guericke-Universität  
Medizinische Fakultät  
Leipziger Str. 44  
39120 Magdeburg

Telefon: +49 391 67-13745  
Telefax: +49 391 67-13105

alexander.link@med.ovgu.de  
[www.med.uni-magdeburg.de](http://www.med.uni-magdeburg.de)

Ihre Zeichen, Ihre Nachricht vom:

Unsere Zeichen:  
AL

Durchwahl:  
+49391-6713745

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### **Biostatistics statement**

Authors of the manuscript have a long-standing research experience with sufficient training and skills in Biostatistics, which is necessary for the high-quality analysis in this work.

Statistical analysis was performed using GraphPad Prism 6 (GraphPad Software Inc., La Jolla, CA, USA). All data are presented as mean  $\pm$  SD. Chi square test and Fisher's exact test were used for contingency tables. The Mann-Whitney U-test and the Kruskal-Wallis analyses of variance were used to analyze the statistical significance for two unpaired groups or multiple groups, respectively. Post hoc analyses were performed using Dunn's multiple comparison tests. Correlation analyses were performed using Spearman's test. Two-sided p-values  $<0.05$  were considered as statistically significant.