

哈尔滨医科大学生物医学研究

## 伦理审查报告

审查编号: HMUIRB20180015

哈尔滨医科大学 生物化学及分子生物学教研室 拟开展 非结合型胆红素对 DSS 诱导的溃疡性结肠炎的保护作用 的科研工作。该项目是以 动物 为研究对象的 随机对照试验 研究。哈尔滨医科大学医学伦理委员会对该项目的相关伦理问题进行了审查。

### 一、项目信息

研究项目名称: 非结合型胆红素对葡聚糖硫酸钠诱导的溃疡性结肠炎的保护作用

承担单位: 哈尔滨医科大学

项目负责人: 郑嘉东

职称: 硕士生

研究起止日期: 2016 年 01 月 至 2017 年 12 月

### 二、主要研究方案

**背景及目的:** 炎症性肠病是一种病因尚不明确的慢性肠道炎症性疾病, 包括溃疡性结肠炎和克罗恩病, 其具体机制尚不明确。非结合型胆红素 (UCB) 作为内源性的抗炎、抗氧化物质, 备受研究者们关注。本研究旨在探讨非结合型胆红素对葡聚糖硫酸钠 (DSS) 诱导的溃疡性结肠炎的保护作用及其潜在机制。

**方法:** 以浓度为 3% 的葡聚糖硫酸钠为化学诱导剂饮用 6 天后, 恢复正常饮水 2 天, 建立实验性 C57BL/6 小鼠实验性 UC 动物模型, 从实验周期第 1 天开始, 进行 UCB (400  $\mu$ M) 灌胃给药持续 7 天, 每天观察记录实验动物体重、毛色、粪便粘稠度及隐血, 于实验第 8 天进行取材, 留取实验动物血清、脾脏、结肠组织及肠道内容物, 运用 H&E、ELISA、WB、酶-底物催化方法、qPCR 等实验技术检测相关指标。

**结果:** 与模型组比较, UCB 给药明显改善实验动物疾病活动指数, 维持肠道正常生理结构, 提高肠组织紧密连接蛋白表达, 降低肠道通透性, 同时 UCB 显著灭活实验动物肠道内消化蛋白酶, 维持肠道内微生物群落组成的稳定性, 降低肠组织炎症因子表达水平, 显著下调 TLR4-MyD88-TRAF6-NF- $\kappa$ B 通路, 抑制肠道免疫-炎症反应。

实验当中所有手术均在戊巴比妥钠麻醉中进行以尽量减少实验动物的痛苦。

### 三、审查评议意见

哈尔滨医科大学医学伦理审查委员会审议认为: 在动物研究部分, 该研究必须用实验动物进行实验, 无法用计算机模拟、细胞培养等非生命方法替代动物或用低等动物替代高等动物进行实验; 所用动物的品种品系、质量等级、规格数量合适, 研究者已通过改进实验方法、调整实验观测指标等方法来优化实验方案、善待动物, 切实保证了动物福利措施的落实。

### 四、结论

该研究在研究设计中充分考虑了相关的伦理原则与规范, 项目实施中严格遵守了伦理委员会批准的研究方案, 符合《赫尔辛基宣言》等国内外规范性文件的伦理要求。本报告中英文各一式两份, 以中文作为标准文本。

哈尔滨医科大学医学伦理审查委员会

2018 年 9 月 24 日



**Harbin Medical University**  
**Institutional Research Board Approval Report**

No.: HMUIRB20180015

Harbin Medical University Jiadong Zheng proposes to conduct a research on animal specimens, which is The protective effect of unconjugated bilirubin on DSS-induced ulcerative colitis. This project takes C57BL/6 mice as the research subjects. HMU Medical Science Ethics Committee has examined the ethical issues involved in the project.

**I . Basic Information**

Project name The protective effect of unconjugated bilirubin on DSS-induced ulcerative colitis

Investigator affiliation Harbin Medical University

Principle investigator Jiadong Zheng Academic title Master

Date of start 2016.01 Date of completion 2017.12

**II . Introduction**

**Background and Purpose:** UCB has attracted attention as endogenous anti-inflammatory factor and antioxidant. We studied the protective effect of UCB on DSS-induced ulcerative colitis. **Methods:** Colitis was induced by putting 3% DSS in drinking water for 6 days, followed by another 2 days of regular water. UCB (400 $\mu$ M) was administered by intra-gastric gavage for 1 week. Some indicators of experimental animals were recorded daily. On the 8th day, spleen, colon tissue and intestinal contents were collected for further exploration. **Results:** UCB relieves the DSS-induced ulcerative colitis of mice. The experiments are all performed in anesthesia of pentobarbital sodium to minimize the pain of experimental animals.

**III . Comments**

HMU Medical Science Ethics Committee has the following comments. With respect to the section related to human research, the design and procedure of this study has fully addressed issues of security and justice. The trade-offs between risks and benefits are appropriately assessed. The recruitment of participants is based on the principle of voluntarily and participation on consent. Participant credentials are protected to the fullest extent. No conflict of interests is envisaged between the research content and the results. With respect to the section of animal research, it is necessary for this study to do experiments on animals, which are irreplaceable by inanimate means such as computer simulation or cell culture. Neither can lower animals replace higher animals in the experiments.

The species, quality, and quantity of the animals to be used are appropriate. Research design has been optimized through methods improvement and adjustment of the observation protocols. Animals will be kindly-treated and the protection of animal welfare is ensured.

**IV . Conclusion**

This study has fully concerned relevant ethical principles and codes in the research design. The enactment of the study has strictly conformed to the plan approved by the ethics committee. Ethical requirements stated by **Declaration of Helsinki** and other international regulations are met by this study. The report is written in English and Chinese, with Chinese as the standard text.

**Institutional Research Board of Harbin Medical University**

September 24<sup>th</sup>, 2018

