**Step 3. Please provide the Scientific Research Process write-up.** Authors are asked to submit a report that describes the entire [scientific research process](https://f6publishing.blob.core.windows.net/customuploadedfiles/Format_for_Scientific_Research_Process.pdf) that was used to obtain the data and findings presented in their submitted manuscript. Once the manuscript is accepted for publication, this report will be released together with the manuscript to promote further in-depth reading by the article’s attracted audience, ultimately improving the academic influence of the article.

This report should answer the following questions:

1. What did this study explore?

1. Stable gastric pentadecapeptide BPC 157 combines treatment of colitis and ischemia and reperfusion in rats and provides new insights.

2. How did the authors perform all experiments?

2. Medication (/kg, 1ml bath/rat) at the blood deprived colon segment (25mm, 2 ligations on left colic artery and vein, 3 arcade vessels within ligated segment), includes BPC 157 (10µg), L-NAME (5mg), L-arginine (100mg) alone or combined and saline (controls). During reperfusion, medication was BPC 157 (10µg) and saline (controls).  We recorded (USB microscope camera) vessel presentation between arcade vessel interconnections at the ventral and dorsal side, through next 15 minutes of ischemic colitis (*IC*-rats) or reperfusion (removed ligations) (*IC+RL*-rats). Upon colon opening gross presentation was noted, oxidative stress measured by quantifying thiobarbituric acid (TBA) reactivity as malonedialdehide equivalents (MDA) (increased (*IC*- and *IC+RL*–rats)) and NO levels (decreased (*IC*-rats); increased (*IC+RL*–rats)) in colon tissue samples by  Griess reaction. *IC+OB-*rats (*IC-*rats had additional colon obstruction (*OB*) for the first 3 days (*IC+OB-*rats)) immediately after obstruction removal, received BPC 157 bath. Vessel presentation was recorded for next 15 minutes. At day 10 ligation time, gross surface presentation, number of gross mucosal defects and colon diameters were assessed upon colon opening, and the adhesion increased severity was scored.

3. How did the authors process all experimental data?

3. In general, we obtained results that showed the presence of increasing/decreasing collaterization between the arcade vessels inside and outside ligations or previous ligations. Subsequently, we demonstrated a markedly attenuated course of ischemic colitis in BPC 157-treated rats, IC rats, IC+RL rats, and IC+OB rats; conversely, an aggravated course of ischemic colitis was observed in L-NAME- treated rats, L-arginine-treated rats, and in IC rats. Commonly, in *IC-, IC+RL-, IC+OB*-rats, BPC 157 bath increased vessel presentation, inside/outside arcade interconnections quickly reappeared, mucosal folds were preserved and the pale areas were small and markedly reduced. BPC 157 counteracted worsening effects induced by L-NAME and L-arginine. MDA- and NO-levels were normal in BPC 157 treated *IC*-rats and *IC+RL*-rats. Thus, in BPC 157-treated rats, we revealed the maintenance of vessel function upon the first innate reperfusion in IC rats, in animals that had been subjected to additional bowel obstruction (IC+OB rats) and, subsequently, upon massive reperfusion occurring after the removal of the vascular obstruction(s) (IC+RL rats).

4. How did the authors deal with the pre-study hypothesis?

4. In this work, we focused on the prototype cytoprotective anti-ulcer peptide stable gastric pentadecapeptide BPC 157, which has been used in trials for ulcerative colitis and now for multiple sclerosis, in the treatment of colitis and ischemia in rats, seeking new insights into ischemic colitis (IC), ischemia and reperfusion and therapy. The harmful events were on the left colic artery and vein, such as two ligations (IC rats) or injuries from removed ligations (RL) (IC+RL rats) (there was always gross vessel presentation failure), and the combination of two obstructions, ligation of the vessels and additional colon obstruction (OB) (IC+OB rats). IC was assessed at short (minutes) (IC rats, IC+RL rats) or more prolonged (3- and 10-day) intervals (IC+OB rats). The main focus of the intervention was that BPC 157 rapidly activates collaterals due to its particular direct and rapid effect on vessel presentation, the bypassing of one or more of the vascular obstructions and thereby achieving a therapeutic effect.

5. What are the novel findings of this study?

We rescued rat ischemic colitis. The gastric pentadecapeptide BPC 157, which has been used in clinical trials for ulcerative colitis, exerted rapid cytoprotective endothelium rescue against the disabled left colic artery and vein after blood deprivation via two ligations and during reperfusion (ligations removed). By bypassing obstructions, quickly rescuing blood supply, rapidly activating collaterals, and restoring arcade interconnections, as a new integrative beneficial effect, BPC 157 prevented the occurrence of pale lesions without mucosal folds and normalized the levels of NO and MDA, two oxidative stress markers, in tissues. BPC 157 showed effectiveness over the NO-system background, immobilized (L-NAME+L-arginine), (over)stimulated (L-arginine) or blocked (L-NAME). Likewise, later application of BPC 157 in a bath treatment to rats with pertinently obstructed vessels that underwent additional colon obstruction for three days produced a similar beneficial effect.

Thus, BPC 157 is fundamental treatment that quickly restores blood supply to the ischemically injured area and rapidly activates collaterals. This effect involves the NO system.