

SOP No: AHP 87

SUBJECT: Induction of colitis in mice

POLICY: Only experienced operators are to perform this procedure.
Careful monitoring of individual mice is required when performing this procedure.

PRECAUTIONS: Gloves, mask, long-sleeve gown, closed in shoes.

Monitoring

Mice treated with 2% or 3% DSS develop diarrhoea, rectal bleeding and moderate colitis by 7 days, and when treated with 0.5% DSS remain without symptoms until 3-4 weeks of treatment when diarrhoea, rectal bleeding and chronic colitis develop . These experiments will need careful monitoring throughout the period of DSS treatment.

EQUIPMENT: Dextran Sodium Sulphate (DSS) Solution (0.5%, 2%, 3%) in drinking water
Clinical Score Sheet – for monitoring of individual mice.

PROCEDURE:

Treatment with DSS Solution:

1. Mice are treated with either Low Dose (0.5%) or High Dose (2% or 3%) DSS solution in drinking water.
2. Mice receiving low dose treatment will receive DSS for 9 weeks.
3. Mice receiving high dose treatment will receive DSS for 7 days.
4. Mice on the low dose treatment will be monitored every 3 days (for 9 weeks) using the attached score sheet. With onset of clinical signs, increase to daily monitoring.
5. Mice on the high dose treatment will be monitored twice daily (for 7 days) using the attached score sheet.
6. Any mouse receiving a score of 3 or more on the score sheet will be immediately euthanased.

Experimental conclusion

7. Mice receiving the low dose DSS or high dose DSS will be sacrificed at 9 weeks or 1 week, respectively, after commencement of DSS treatment (unless clinical scoring dictates that the animal is euthanised earlier).

- 8. 4 hours prior to sacrifice mice will be treated with bromodeoxyuridine (BrdU) i.p. (100 µg/g body weight) using a 25G needle to facilitate assessment of intestinal proliferation. BrdU will be injected in a volume no greater than 200uL.**
- 9. Prior to sacrifice, 200uL of blood will be sampled (AHT 29 or 31) for haematocrit determination as a measure of gastrointestinal bleeding and to determine leucocyte counts as a measure of leucocytosis, and to measure inflammatory cytokines and acute phase proteins.**
- 10. Mice will be sacrificed either by cervical dislocation (AHT 35) or CO2 asphyxiation (AHT36).**

RECOMMENDATIONS:

DATE ISSUED: 28 October 2009

REVISED:

REFERENCES

- 1. Heazlewood CK, Cook MC, Eri R, Price GR, Tauro SB, Taupin D, Thornton DJ, Png CW, Crockford TL, Cornall RJ, Adams R, Kato M, Nelms KA, Hong NA, Florin TH, Goodnow CC, McGuckin MA. Aberrant mucin assembly in mice causes endoplasmic reticulum stress and spontaneous inflammation resembling ulcerative colitis. PLoS Med. 2008 Mar 4;5(3):e54**

SCORE SHEET FOR ASSESSMENT OF MICE WITH INTESTINAL PATHOLOGY/DEVELOPING COLITIS/BMT
DAILY OBSERVATIONS



Experiment number: _____

Mouse number: _____

Date and time of challenge: _____

Drug (if any): _____ Dose: _____

Pre-challenge weight (g): _____

<i>DATE</i>												
Time post-challenge												
Days post-DSS/ alternative challenge	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Day 8	Day 9	Day 10	Day 11	Day 12
Observations from a distance												
Inactive												
Hunched posture												
Ruffled fur												
Rate of breathing												
Crusty Eyes												
Shivering												
Diarrhoea												
Rectal bleeding												
Rectal prolapse												
<i>On handling</i>												
Not inquisitive or alert												
Bodyweight (% change from start/score)*												
Any other abnormal behaviour or signs noted												
ACTION TAKEN^												
NOTES												
TOTAL SCORE												

Scoring Details:

0 = normal/equivocal symptoms, 1 = mild symptoms, 3 = severe symptoms. (see next page for descriptions) Total of 3 or over = mouse culled.

0 = <5% weight loss, 1 = 5-15% weight loss, 2 = 15-20%, 3 = >25% weight loss

Updated: 4.4.07

Symptom	Mild Symptoms	Severe Symptoms
Inactivity	fully mobile, but more inactive than usual	mouse moving only occasionally and largely unresponsive to prompting
Hunched posture	small change in normal posture	mouse noticeably hunched over without regaining normal posture
Ruffled fur	some restricted ruffling of fur	obvious ruffling of most fur
Rate of breathing	slightly above or below normal	excessive panting or markedly diminished rate of breathing
Crusty eyes	small build up of excretion in eyes	significant excretion in both eyes, vision likely to be impaired
Shivering	occasional shivering	constant prominent shivering
Diarrhoea	loose stools	stools have completely liquid consistency
Rectal bleeding	some blood in stool on close inspection	clear bleeding from rectum
Rectal prolapse	rectum threatening to prolapse on defecation	permanent prolapse
Not inquisitive/alert	some reduced response to stimuli	mouse largely unresponsive to stimuli