NSG = Notoriously sensitive guys: handling with care

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Introduction

NSG (NOD scid gamma) mice are a key model in biomedical research due to being immunodeficient. They lack functional T, B and NK cells, which enable the successful engraftment of human cells and tissues. As a result, NSG mice are used to create humanised models that allow for the study of human-specific diseases and the implementation and assessment of different therapies.

Prior to the injection of human hematopoietic stem cells (HSCs), the mice are conditioned via gamma irradiation to enhance the efficacy of the HSC engraftment. Here, we highlight two key health concerns related to post-irradiation morbidity: dental issues and tendinitis. We address how refinements and early interventions are critical for the welfare of NSG mice post-irradiation. The aim of this poster is to highlight recommendations for project licenses and the Animal Welfare Ethical Review Body (AWERB).

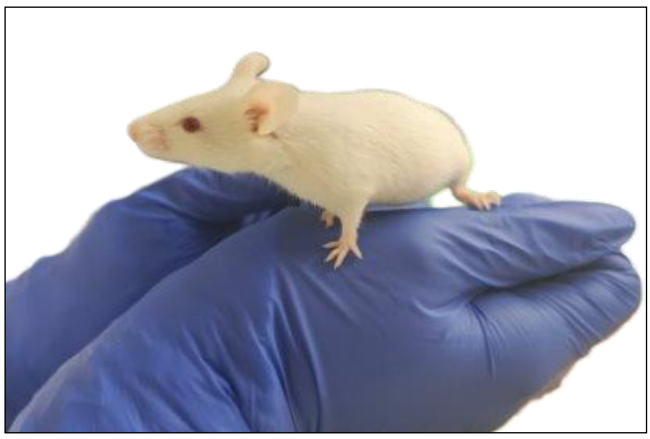

Figure 1. NSG NOD.Cg-PrkdcscidIl2rgtm1Wjl/Sz, common name: NSG Mouse (NOD scid gamma), also known as: NOD-scid IL2Rgammanull, NOD-scid IL2Rgnull, NOD scid gamma.

Tendinitis

What is tendinitis?

Tendinitis is an emerging welfare concern in NSG mice, with limited understanding of its mechanisms and long-term management. Tendinitis is a progressive condition affecting the tarsal joint. Early clinical signs include swelling (rounding) of the hock, limping and curling of the toes. This then progresses to redness, development of a small lesion on the hock and eventually, ulceration of the heel. Beatty *et al*. (2024) hypothesise the cause of tendinitis to be endochondral ossification due to mesenchymal cell expansion in response to a trauma.

Previous management of tendinitis involved 5 days of oral NSAID (Metacam), with Sudocrem applied to dry or dimpled hocks. However Sudocrem has been linked to zinc toxicity and gastrointestinal upset in small animals (Siow, 2018) and was not seen to be an effective treatment.

In collaboration with a Named Veterinary Surgeon (NVS), a revised protocol was introduced. Metacam is now given at the first clinical signs of tendinitis and continued for 5 days, with Lyonsleaf, a 100% natural topical product, used as supportive care. This approach is not curative but aims to slow disease progression.

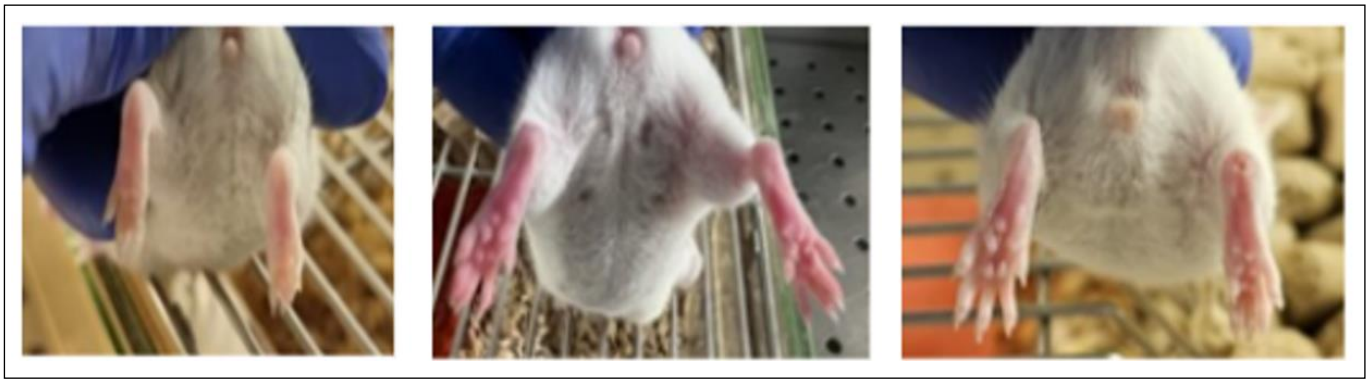

Figure 2: Examples of different stages of tendinitis. (left) and (middle) display rounding of the hock. (right) shows ulceration of the hock – a humane endpoint.

Although we had seen results, these had not been quantified. We carried out a small trial on two mice with the same experimental history, both identified with early signs of tendinitis. Mouse 1 received Metacam alone, while Mouse 2 received Metacam plus Lyonsleaf. Daily photographs were taken over 5 days to monitor disease progression.

Handling and husbandry

In addition to the revised treatment plan, we have refined how we handle NSGs. As mentioned, Beatty *et al.* (2024) believe tendinitis occurs in response to a trauma. We therefore want to reduce the risk of any trauma to the back legs. We do this by scruffing mice on a sponge or by supporting the back legs with our hands. Please

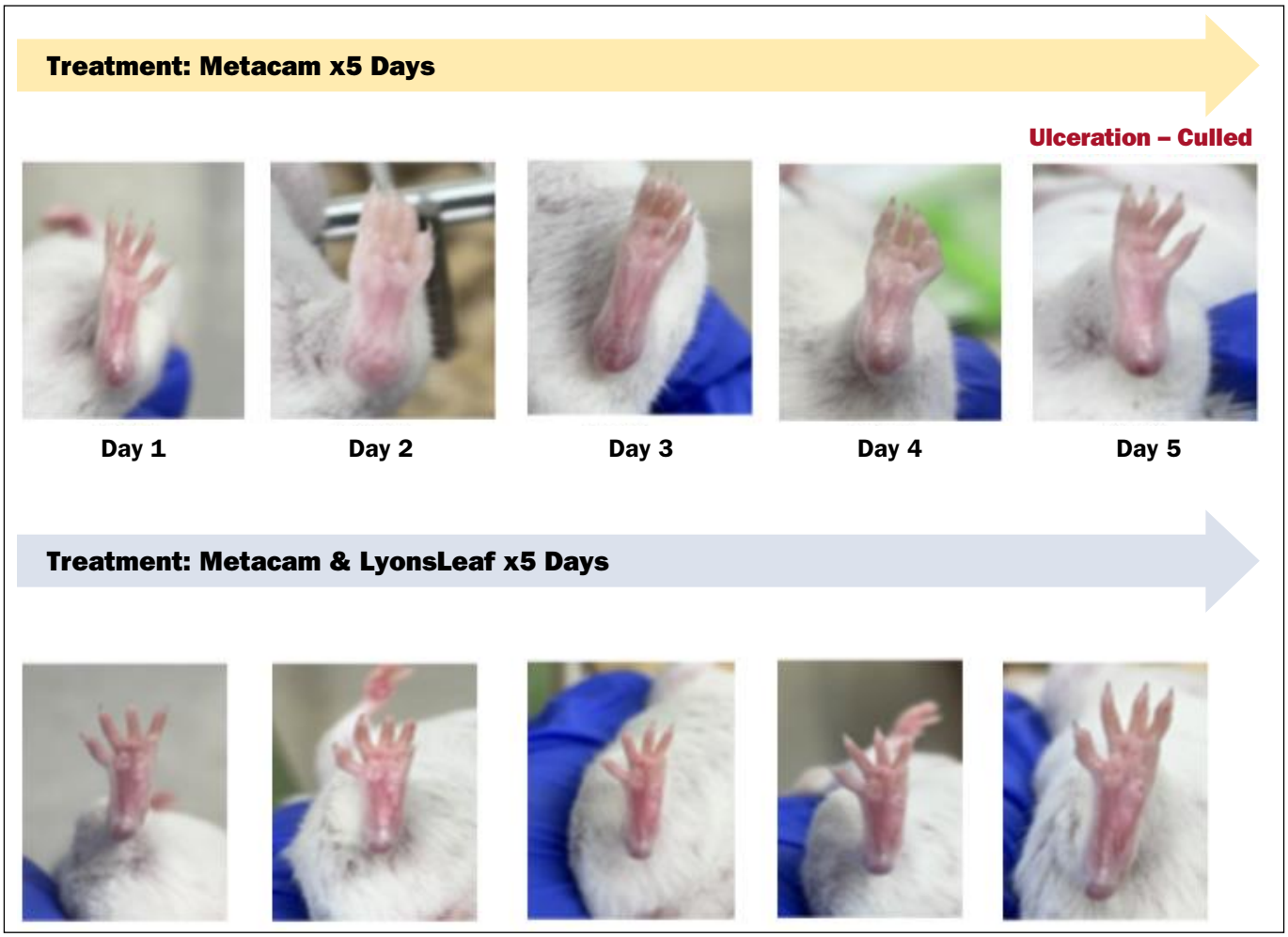

Figure 3: (Top) Mouse receiving Metacam alone displayed a marked increase in swelling on day 2, 3 and 4. By day 5, although swelling appears to have decreased, the hock ulcerated. Hock ulceration is a humane endpoint and accordingly this mouse was culled. (Below) Mouse 2 receiving both Metacam and Lyonsleaf showed a gradual decrease in swelling across day 2, 3 and 4, with swelling completely reduced by day 5.

follow the QR codes to see how we have refined our handling.

All mice were housed in IVC cages and housed under SOPF conditions. Enrichment included red plastic tunnels, nesting pucks with small wooden chew blocks and a sawdust substrate.

Conclusion

This case study provides preliminary evidence for a practical treatment and monitoring approach for tendinitis in NSG mice, improving welfare and informing further research. In addition, it highlights the importance of preventative care and husbandry. Further data collection is needed to confirm the efficacy of this treatment plan in slowing disease progression and to support these initial findings.

Dental impairments post-irradiation

NSG mice receiving 2–2.5 Gray (Gy) of gamma irradiation have been observed to develop dental problems (Figure 4), often preceded by a decline in body condition score. Affected mice present as hunched with poor body condition and often overgrooming. We hypothesise weeks 5-10 to be a critical timepoint for dental issues to occur. Although these trends have been noted, there is limited data to confirm them.

Methodology

A total of 56 female NSG mice (approximately 6 weeks old) received a single 2 Gy dose of total body gamma irradiation in accordance with their experimental protocol. Following irradiation, mice were monitored twice weekly. Assessments included body condition scoring using the Ullman-Cullere and Foltz descriptive BCS system, evaluation of posture (including hunching) and grooming behaviour, and dental checks twice a week for changes in translucency, mobility and fracture. Mice received gel pots between weeks 5-10.

Results

The results from this case study confirmed our hypothesis that weeks 5-10 are when the highest incidents of dental issues occur, with 20% of animals having an incident by week 7. This demonstrates that weeks 5-10 are a critical window for monitoring and supportive care. This is demonstrated in Figure 5.

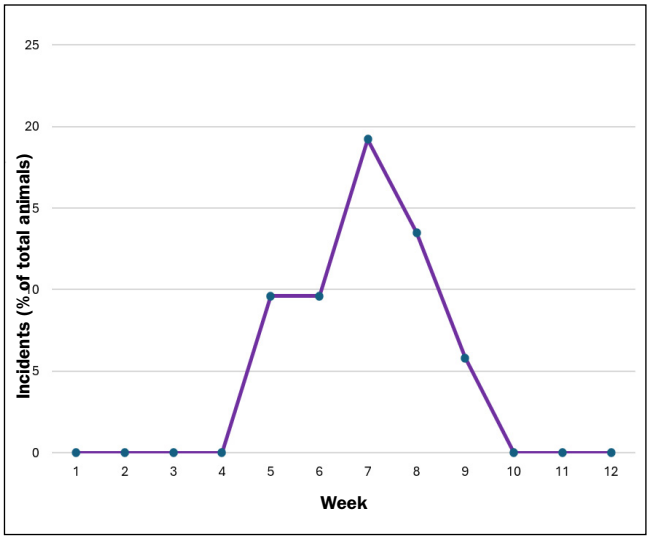

Figure 5. Incidents of dental issues against time.

Figure 4. Two mice exhibiting dental problems.

Conclusion

From this case study we can conclude that there is a need for supportive care for NSG mice that have been irradiated via gamma irradiation between 2-2.5 gy. Although mice presented with fractured or missing teeth, their weights did not exceed humane endpoints and no mice within the cohort were culled due to weight loss.

This case study supports our hypothesis that weeks 5-10 are critical time points for supportive care and increased monitoring. By increasing monitoring and providing a form of wet diet, we can enhance Animal Welfare and perpetuate the 3Rs. By reducing the risk of morbidity, we are reducing the need for repeat experiments due to data loss from mice exceeding humane endpoints.

How can we help these notoriously sensitive guys?

Refined handling and monitoring

Scan the QR code (Appendix 1) for videos on refined handling techniques. These include the sponge scruff and the back leg support scruff. These have been developed to reduce the amount of pressure applied to the hind legs of NSGs, ultimately reducing the risk of trauma and inducing tendinitis.

Gamma-irradiated mice

Review current procedural frameworks. Pitcher *et al.* (2025) demonstrate that NSG mice can be successfully reconstituted at 100 Gy, with 0 dental implications. Therefore irradiating at 100 Gy as opposed to 200-250 Gy would refine procedural frameworks and reduce the number of health concerns observed in mice post-irradiation. We would therefore encourage a review of experimental protocols with NSG mice being irradiated at over 100Gy.

Week 5-10 post-irradiation is a critical window, where enhanced monitoring and supportive care is required. During this time, weights should be closely monitored, along with body condition. Providing mice with a wet or soft diet will encourage eating if teeth breakage does occur. Pitcher *et al.* (2025) also provided a higher fat diet and found a reduction in weight loss post-irradiation.

Consider using alternative mouse models. NSGs have high radio-sensitivity. There are other immunodeficient models that can be considered that are less radio-sensitive and can therefore reduce the likelihood of health concerns post-irradiation (Table 1).

Monitoring and scoring

Early identification is key. Staff should be trained to identify early clinical signs of both tendinitis & dental issues post-irradiation. This is supported by the development of accurate and standard clinical monitoring systems. Standardised clinical scoring are essential for the early detection of tendinitis and dental abnormalities. These allow clear identification of intervention points.

Future studies

Although preliminary evidence supports the proposed treatment plan for tendinitis and dental issues post-irradiation, it is not enough data to statistically confirm these findings. Further studies are needed with larger cohorts and more longitudinal data (past week 12 post-irradiation).

References

1 **Pitcher, J.L., Harman, B., Strake, B., Nungesser, D. & Emmell, E.** (2025). *Establishment and Optimization of the NSG Mouse Model for Antibody Development* [Poster] Biologics Toxicology & Biologics Research, Janssen Research & Development, LLC, Available at: https://clearh2o.com/cdn/shop/files/NSG-Mouse-model-antibody_a267e1c4-928b-4a29-a242-c79f5600b0e5.pdf?v=2489108839822687686[Accessed: 01/03/2026]

Model	Background	Key mutations	Immune phenotype	Robustness
Model 1	NOD	*Prkdc*^scid + *112rg*^null	No T, B, NK cells	High radiosensitivty (DNA repair defect)
Model 2	NOD	*Rag*^null + *112rg*^null	No T, B, NK cells	Improved tolerance to irradiation
Model 3	BALB/c ≠ *Sirpa*^NOD	*Rag2*^null + *112rg*^null + *Fit3*^null	No T, B, NK cells + reduced myeloid	Highly robust

Table 1. Alternative immunodeficient models.

[2] **Siow, J.W.** (2018). *Zinc toxicosis in a dog secondary to prolonged zinc oxide ingestion,* Open Veterinary Journal, 8(4), 458–462, https://doi.org/10.4314/ovj.v8i4.17

[3] **Beatty, C., Garnham, S., Brown, K., Caunce, S., Keeley, J., O'Mahony, T., Parnell, J., Foster, M. & Warner, A.** (2024). *Development of a monitoring and treatment regimen for NSG mice displaying phenotypic tarsal joint swelling and hock lesions* [Poster presented at the LASA Annual Conference 2024] RxCelerate Ltd & University of Cambridge, Available at: https://www.rxcelerate.com/wp-content/uploads/2024/11/RxC-Poster_LASA-2024-NSGs_vFINAL.pdf [Accessed: 01/03/2026]

[4] The Jackson Laboratory (2026). *NSG® Variants Portfolio* [online] The Jackson Laboratory, Available at: https://www.jax.org/jax-mice-and-services/find-mice/nsg-portfolio [Accessed: 01/032026]

Appendices

Appendix 1:
QR code (videos on refined handling techniques)