

Chronic liver damage models

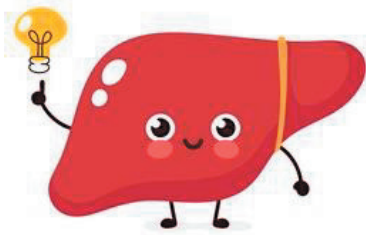
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Background

The purpose of our chronic liver damage model is to understand how normal and malignant stem cells (marked by fluorescent reporters) behave in response to the liver damaging agent diethoxy carbonyl 1,4-dihydrocolidine (DDC) in mouse models.



Here we discuss our methodologies and impact on the mouse models with suggestions for improvement in Animal Welfare.

Method

Diet administration

Mice were given three pellets of DDC diet each in a petri dish that was placed on the cage floor and refreshed if soiled or eaten.



Mice were rotated 1 week on DDC and 1 week off (provided with normal diet) for 4 weeks. This was to help their bodyweights stabilise as we believed the diet was not very palatable.

Weighing

All the mice were weighed daily and when a 10% body weight loss was reached, they received diet mash (80% DDC diet + 20% normal diet soaked in water).

Bodyweights were taken during the morning which provided sufficient time to address any concerns found.



Mice were weighed at the same time each day to ensure consistency.

Blood sampling

The mice on this study were split into two groups.

- Group 1 mice had blood sampled on Tuesday every week and group 2 mice on Wednesday every week.
- 20 microlitres of blood was sampled (from the tail vein) from each mouse at the same time and day to ensure consistency.
- Mice were placed in a tube restrainer to collect the blood sample. All mice appeared to respond well to the restrainer which could be due to the result of being handled daily throughout the study.
- Weighing and diet administration were performed at the same time as blood sampling to prevent over handling the mice (Figure 1).

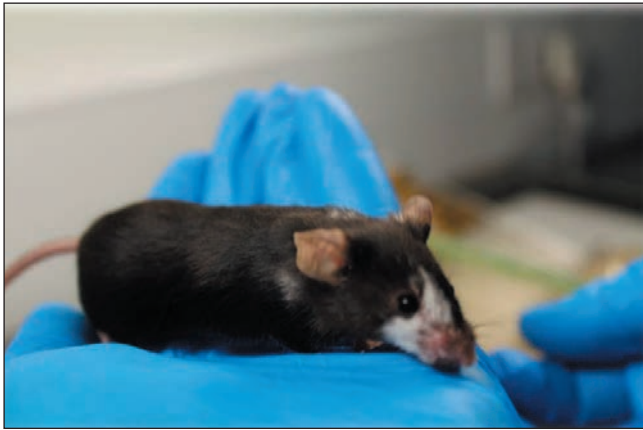


Figure 1. Mouse being handled daily.

Acknowledgements

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Findings and what we would change

Bodyweight significantly decreased when placed on DDC diet and significantly increased when placed back on normal diet. The graph below (Figure 2) reflects this from one of the study mice.

We could introduce DDC diet gradually to counteract the weight loss when moved to DDC diet.

Weight decrease was possibly linked to the palatability of diet.

Mash with Nesquik could improve the palatability (has worked in other diet studies at the Cambridge Institute).

Other sampling alternatives could have been using the saphenous vein as a refinement.

A cone restrainer could be used rather than a tube restrainer as the tube restrainers can have implications relating to stress with the mouse being confined. With a cone restrainer the mouse is not confined to a small area.

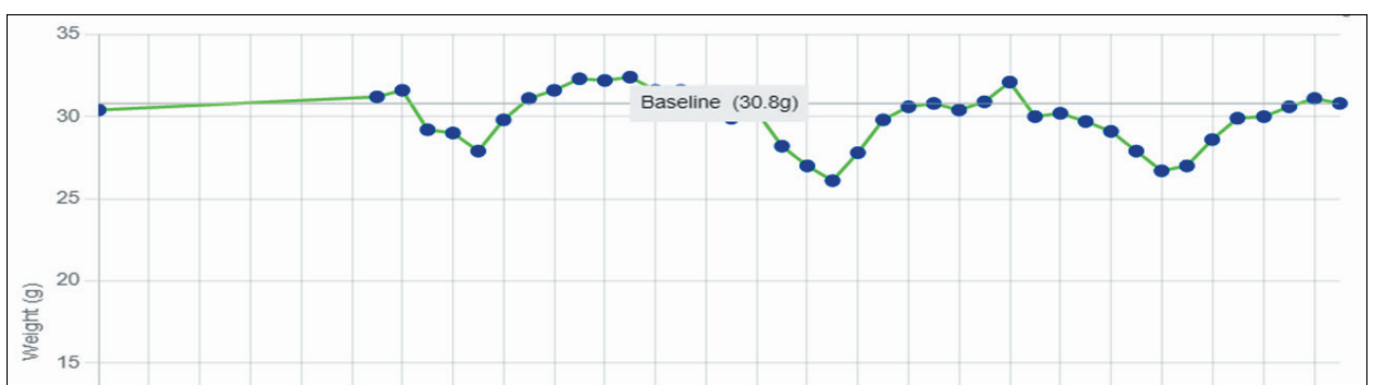


Figure 2. Bodyweights of mice.