IMPLEMENTING HUMANE ENDPOINTS IN MICE USED IN CANCER RESEARCH

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OBJECTIVES

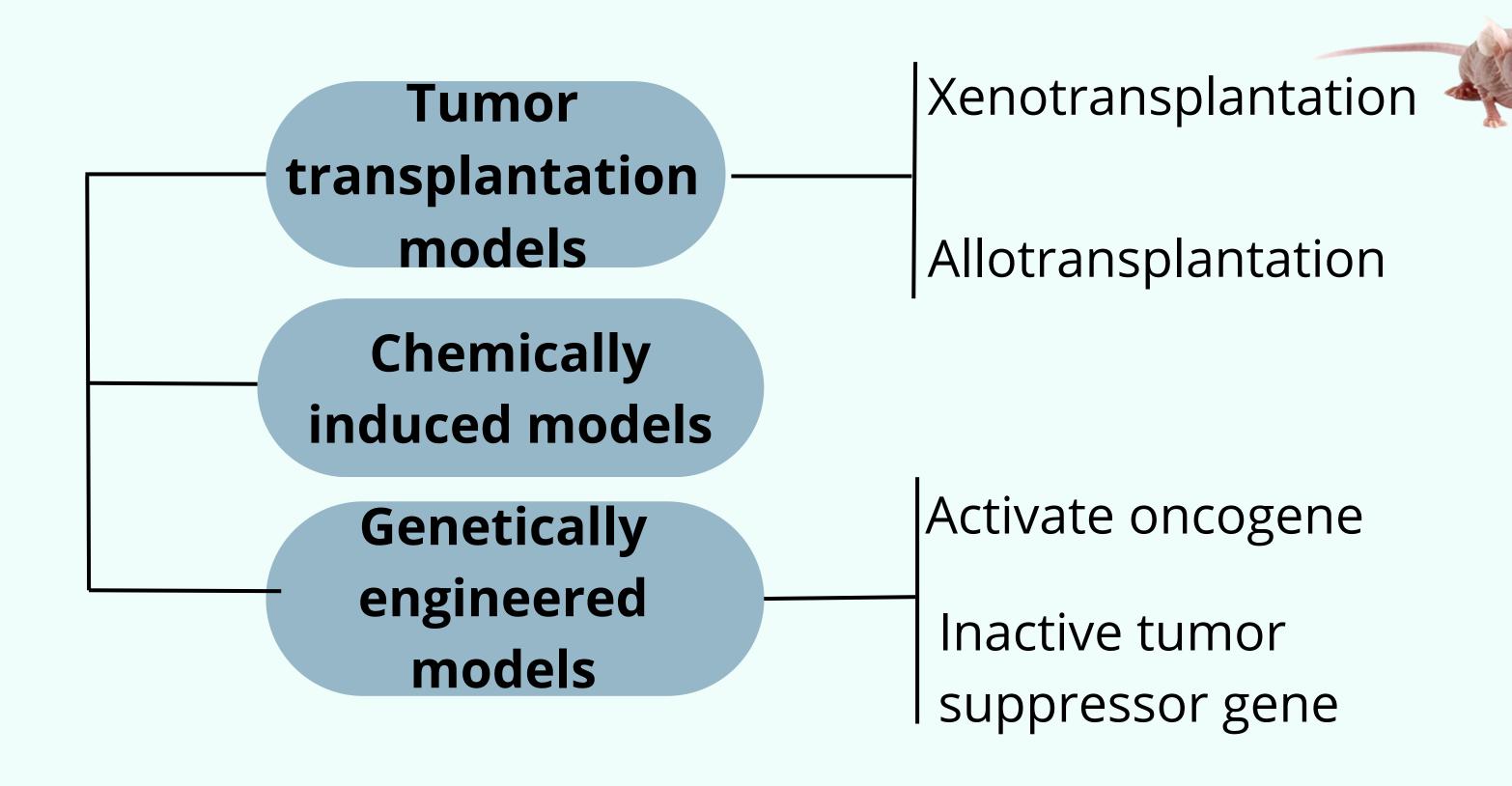
- Definition of the main **murine models** in **cancer research**.
- Development of the concept of **humane endpoints** and the **circumstances** they should be applied.
- Recognition of **clinical signs** using a **scoring sheet** to facilitate decision making based in real experiment.

INTRODUCTION

Humane endpoints are defined as "those clear, predictable and irreversible criteria that can be used as a substitute for a more severe experimental result" (Brønstad, 2021; Morton, 1999). "Death as an endpoint to a procedure should be avoided as far as possible and replaced by earlier, humane endpoints". (Directive 2010/63/EU art 13.3.)

2. WHEN TO APPLY THEM

1.MURINE MODEL FOR CANCER



Unexpected disease unrelated to the experiment

Scientific objectives have been reached

Action points do not relieve pain and suffering

Suffering has become more severe than anticipated

3.CLASSIFICATION OF SEVERITY

Tumor induction

MILD model without

harmful clinical effect

Tumor induction

MODERATE model expected to

cause moderate pain

SEVERE Model for metastasis

4. SCORING SHEET AND ENDPOINT CRITERIA

ANIMAL: Number							OBSERVER								
BASELINE WEIGHT (DAY 0)															
Day of experiment	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14
GENERAL															
CLINICAL															
SIGNS															
Body weight															
General aspect															
Temperature															
Breathing rate															
Gait															
BEHAVIORAL SIGNS															
Provoked behavior															
Non-provoked behavior															
SPECIFIC CLINICAL SIGNS															
Tumor size															
Ulceration															
Bleeding															
Ascites															

Table 1. Numerical scoring sheet with scores of 0-3.

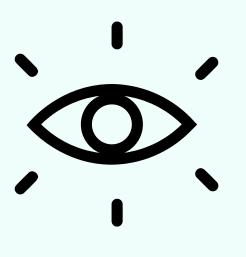
Body condition Loss > 20%Diarrhea General aspect Change of >2-3°C **Temperature** Tachypnea/bradypnea 40% **Breathing rate** with cyanosis Ataxia Gait Inmobile during >4h Mental status Comatose Tumor diameter >2.0 cm Specific clinical Ascites Ulceration signs Hemorrhage

Table 2. Endpoint criteria with a score of 3 in the experimental study of Lim *et al.* (2020). This criteria and the sum of scores of 15-21 will be considered euthanasia. Scores between 1-14 intervention points will be implemented.

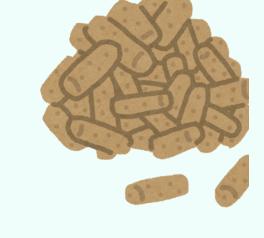
CONCLUSIONS

- Endpoint criteria must be applied once the data necessary for the research has been obtained, anticipating animal suffering as much as possible.
- Refinement methods must be applied (analgesia).
- Combine clinical evaluation with translacional imaging methods to get greater objectivity.

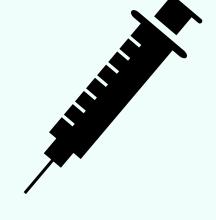
INTERVENTION POINTS



Increase monitory frequency



Stimulate food intake



Analgesia