

GUIDELINES FOR THE USE OF RODENTS IN EXPERIMENTAL NEOPLASIA

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Background

Tumor development in rodents evokes a range of effects that depend on the experiment, tumor line, and the response of the individual animal. This document provides guidelines for designing and conducting procedures that will accomplish the experimental objectives while ensuring the welfare of animals used in tumor development studies and of animals with spontaneous tumors.

Guidelines

- Experimental neoplasia procedures and associated details (e.g., injection site location, tumor cell source, monitoring, endpoints) must be described and justified in the Animal Use Protocol (AUP) and approved by the ACUC.
- The Office of Laboratory Animal Care (OLAC) and the Office of Environment, Health and Safety (EH&S) must be consulted when developing protocols involving inoculation with cells as all implants may harbor viruses or transmissible agents. Both primary and cultured human cell lines may harbor human pathogens that may proliferate in permissive or immunodeficient rodents. Appropriate testing of cell lines and biohazard containment procedures are required for rodents when implanted with human cells. Tumors from rodent cell lines or any cell lines that have been passaged through rodents must be tested prior to use *in vivo* to avoid inadvertent introduction of rodent pathogens into vivaria. OLAC must be contacted prior to use of all human or rodent-derived biological materials in live rodents. Please refer to the Animal Care and Use Committee (ACUC)'s Testing Biologicals Used in Laboratory Rodents Policy.
- Tumor implantation sites should be chosen to minimize interference with normal body functions, such as ambulation, eating, drinking, defecation, or urination. Subcutaneous implantation is considered the least disruptive with the flank as the preferred location. All tumor injection sites must be justified and approved in the AUP.
- Animals must be observed with sufficient frequency to ensure that they are euthanized according to established end-points. All animals should be inspected at least three times a week until the tumor development becomes evident. Observations (and measurements) must occur daily once tumors are evident.

- As per the *Guide for the Care and Use of Laboratory Animals (Guide)*, criteria for euthanasia (i.e., endpoints of experimental neoplasia) must be determined and justified in the AUP. These criteria must include:
 - Ulcerated tumors
 - Tumors that interfere with normal activity
 - Weight loss greater than 10% of baseline weight
 - Body condition score of two or less (on a scale of one to five)
 - Clinical signs of illness such as hunched posture, respiratory difficulties, or reticence to move
 - Tumors exceeding 1.5 cm (mice) or 2.5 cm (rats)
 - Multiple tumors – The diameters of all tumors totaled must not exceed 1.5 cm (mice) or 2.5 cm (rats). These should be considered maximum size; earlier size end-points should be used if possible.
- These guidelines apply to experimental tumors and cell lines as well as tumors which arise spontaneously. The development of spontaneous tumors is considered a humane endpoint unless otherwise specifically approved in the AUP.
- Laboratory staff must label all cages that contain rodents undergoing experimental neoplasia with:
 - The date and site of injection
 - The cell line identity
 - The name and phone number of the individual primarily responsible for monitoring the animals
- Animals must be observed with sufficient frequency to ensure that they are euthanized according to established end-points. All animals should be inspected at least three times a week until the tumor development becomes evident. Observations (and measurements) must occur daily once tumors are evident.

References

- Ullman-Culleré, M.H., & Foltz, C.J. (1999). Body condition scoring: a rapid and accurate method for assessing health status in mice. *Lab Animal Science*, 49(3), 319-23.
(http://labanimals.stanford.edu/resources/pdfs/Body_Condition_Scoring_in_Mice.pdf).
- Institute of Laboratory Animal Research (ILAR). National Research Council (2011). *Guide for the Care and Use of Laboratory Animals* (8th edition). Washington, D.C.: The National Academies Press.