Guidelines Regarding Engraftment of Human Cells or Tissues into Immunodeficient Mice

Introduction

Mice whose immune systems have been altered by genetic engineering, spontaneous mutations or chemicals are widely used in biomedical studies. The immunological deficiencies that make these animals useful as models predispose them to a host of opportunistic and adventitious agents that are hazardous to immunologically competent mice. Also, special attention must be given to possible zoonotic hazards posed by transplantation of foreign tissues or cells into immunodeficient mice. The Public Health Service (PHS) published guidelines for the prevention and control of infectious diseases associated with xenotransplantation into humans (http://www.fda.gov/cber/gdlns/xenophs0101.htm); However, similar guidelines for xenografting human tissues into rodents have not been published by the USPHS.

The guidelines outlined below are intended for the introduction of human cells or tissues into immunodeficient mice. Approval is required from the Animal Care and Use Committee and the Institutional Biosafety Committee prior to initiating any studies involving animals and infectious agents.

Recommended Procedure

In an effort to protect the staff members working with animal models that have been exposed to human cells or tissues, the NCI-Frederick ACUC recommends that all human samples be pre-screened for the following pathogens prior to use in animal studies: HIV 1-2, EBV, HTLV 1-2, JCV, MoMuLV, CMV, Hepatitis B and C. In addition, all cell lines and tissues utilized in research studies at the NCI-Frederick must undergo Mouse Antibody Production (MAP) testing prior to use in animals. As soon as the sample has been found to be free of selected infectious agents, the sample may be used in the animal facility.

Contact Information:	*Human Pathogen Testing Lab of Molecular Technology 301-846-5676*
MAP Testing	*Animal Health Diagnostic Lab 301-846-1134*

Since the testing requirements can take anywhere from a few days (human pathogen testing) to several weeks (MAP testing), the NCI-Frederick ACUC encourages investigators to utilize DTP tumor cell lines [some are available from the DCTD repository] as a primary source of human tumor cell lines for use in animal research studies. These lines have already been MAP tested and pre-screened for human pathogens allowing for immediate use in research studies. Please click here for a listing of human tumor cell lines available. If your cell line was originally obtained or derived from a DTP/DCTD repository line, the ACUC Coordinator can obtain the test results on your behalf and no additional human pathogen testing is required if the cell line has not been purposely infected. For MAP testing, no additional testing is required provided the cell line has not been exposed to rodents either through transplantation or through exposure to rodent derived materials in vitro (e.g. mouse serum, ascites-derived monoclonal antibodies). However, if the human tumor cell line you require is not available through DTP, the

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human pathogen and/or MAP testing should be coordinated through your animal facility manager as soon as possible.

The ACUC recognizes that there are special circumstances for which an investigator may not be able or willing to conduct pathogen testing on human samples. As a result, the ACUC will review these requests on a case-by case basis to determine if pathogen testing may be waived. Some examples include:

- The use of primary human samples that require immediate transfer into mice (once the human sample is received at the NCI-Frederick, a portion may be submitted for pathogen testing to potentially limit the period of time for which the study would require special housing procedures and practices as described below)
- The investigator chooses to implement the special housing procedures and practices required for untested human samples (as described below) in lieu of pathogen testing (i.e., short-term experiments). Please keep in mind that the NCI-Frederick animal facilities have limited resources to support these types of requests at this time.

In cases where pathogen testing is waived or if human tissues are known or shown to be infected, the NCI-Frederick Biosafety Office will provide the level of containment and procedures for the handling and disposal of materials. Investigators working with such materials must have an approved *Pathogen Registration** on file. The study will be conducted in a quarantined area within a designated facility (where such isolation facilities exist). The room should be posted indicating that untested/infected human tissues are being used. Persons working with infectious agents or potentially infected material must be aware of the potential hazards and must be trained and proficient in the practices and techniques required for handling such material safely. The facility manager in charge of the area in which the study is being conducted in coordination with a member of the Biosafety Office is responsible for providing the appropriate training and the S.O.P. All mice will be maintained in microisolator cages or negatively ventilated units *(NOTE: Positive Individually ventilated (PIV) cage units must be operated as a negative pressure unit. Operation of a PIV as a positive pressure unit is not only unacceptable; it poses a risk of environmental contamination if the mice are harboring an infectious agent. If negative ventilation is used it is important to remember that the air drawn into the cage should be filtered to avoid unnecessary exposure to mouse pathogens.)* All of the cages will be changed in a Biosafety Level 2 (BSL2) hood or cage changing station. The Biosafety Office will provide procedures for disposing of potentially contaminated material.

**Registration of Research with Pathogens, Oncogenes, and Toxins* form is available for download at: http://web.ncifcrf.gov/campus/safety/usedocs.stm

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