

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/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/Xenotransplantation/ucm074727.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 Frederick National Lab 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 Frederick National Lab must undergo Mouse Antibody Production (MTBM) 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:
Molecular Technology
MTBM Testing

Human Pathogen Testing Lab of
301-846-5676
Animal Health Diagnostic Lab 301-846-1134

Since the testing requirements can take anywhere from a few days (human pathogen testing) to several weeks (MTBM testing), the Frederick National Lab 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 MTBM tested and pre-screened for human pathogens allowing for immediate use in research studies. 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 MTBM 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

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available through DTP, the human pathogen and/or MTBM 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 Frederick National Lab, 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 Frederick National Lab 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 Frederick National Lab 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/Ehs/lbc/Research.aspx>

**DTP TUMOR CELL LINES AVAILABLE FOR USE IN
ANIMAL STUDY PROPOSALS
[Some are available from the DCTD Repository]**

LINE	MTBM TEST	VIRAL SCREEN TEST	NOTES
10.5	NR	Yes	Human In Vitro Cell Line
11-9-1-4	NR	Yes	Human In Vitro Cell Line
1-9-13-93	NR	Yes	Human In Vitro Cell Line
6.03	NR	Yes	Human In Vitro Cell Line
786-0	Yes	Yes	Anticancer Screen Panel
A-204	Yes	Yes	Human In Vitro Cell Line
A-2780	Yes	Yes	Human In Vitro Cell Line
A-498	Yes	Yes	Anticancer Screen Panel
A-549	Yes	Yes	Anticancer Screen Panel
A-704	Yes	Yes	Human In Vitro Cell Line
ACHN	Yes	Yes	Anticancer Screen Panel
NCI/ADR-RES	Yes	Yes	Human In Vitro Cell Line
ASPC-1	Yes	Yes	Human In Vitro Cell Line
BG-1	Yes	Yes	Human In Vitro Cell Line
BOW-G	Yes	Yes	Human Melanoma Xenograft

NR = No report found, but a MTBM test may be available. Please contact the ACUC Coordinator (301-846-7544) if you are interested in using this line to determine if testing is required.

** Requestor must obtain permission from the source BEFORE ordering
** Commercial Entities – These lines are only available through licensing:
Contact John Stansberry at stansbej@mail.nih.gov*

LINE	MTBM TEST	VIRAL SCREEN TEST	NOTES
BT-549	Yes	Yes	Anticancer Screen Panel
CAKI-1	Yes	Yes	Anticancer Screen Panel
CALU-1	Yes	Yes	Human In Vitro Cell Line
CALU-3	Yes	Yes	Human In Vitro Cell Line
CALU-4	NR	Yes	Human In Vitro Cell Line
CCRF-CEM	Yes	Yes	Anticancer Screen Panel
CCRF-SB	Yes	Yes	Human In Vitro Cell Line
CHA-59	Yes	Yes	Human In Vitro Cell Line
CL10	Yes	Yes	Human In Vitro Cell Line
COLO-205	Yes	Yes	Anticancer Screen Panel
COX	NR	Yes	Anticancer Screen Panel
CP-70	Yes	Yes	Human In Vitro Cell Line
CWR-22	Yes	Yes	Human Prostate Adenocarcinoma Xenograft
CWR-33 BREI	NR	Yes	Human In Vitro Cell Line
CX-1 (HT-29)	Yes	Yes	Anticancer Screen Panel
CX-2	Yes	Yes	Human Colon Xenograft
CX-3	Yes	Yes	Human Colon Xenograft

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CX-5	Yes	NR	Human Colon Xenograft
DAU	Yes	Yes	Human Burkitt's Lymphoma Xenograft
DAUDI	Yes	Yes	Human In Vitro Cell Line
DEAC-1	Yes	Yes	Human Epidermoid Xenograft
DEAC-7	Yes	Yes	Human Melanoma Xenograft
DEL-G	Yes	Yes	Human Sarcoma Xenograft
DLD-1	Yes	Yes	Anticancer Screen Panel
DMS-114	Yes	Yes	Human In Vitro Cell Line
DMS-273	Yes	Yes	Anticancer Screen Panel
DU-145	Yes	Yes	Anticancer Screen Panel
ECV-304	NR	Yes	Human In Vitro Cell Line
EJ6	Yes	Yes	Human In Vitro Cell Line
EKVX	Yes	Yes	Anticancer Screen Panel
FO-1	NR	NR	Human Melanoma Xenograft
G289L	Yes	Yes	Anticancer Screen Panel
GOB-G	NR	NR	Human Colon Xenograft
H1299	NR	Yes	Human In Vitro Cell Line

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H5V	NR	Yes	Human In Vitro Cell Line
HAB-18	Yes	Yes	Human In Vitro Cell Line
HAB-68	Yes	Yes	Human In Vitro Cell Line
HAB-85	Yes	Yes	Human In Vitro Cell Line
HAB-92	Yes	Yes	Human In Vitro Cell Line
HCC-2998	Yes	Yes	Anticancer Screen Panel
HCC-M1544	NR	Yes	Human In Vitro Cell Line
HCT-116	Yes	Yes	Anticancer Screen Panel
HCT-15	Yes	Yes	Anticancer Screen Panel
HELA	Yes	Yes	Human In Vitro Cell Line
HEP-3	Yes	NR	Human Epidermoid Xenograft
HEPG2	Yes	Yes	Human In Vitro Cell Line
HL-3	Yes	Yes	Human In Vitro Cell Line
HL-4	Yes	Yes	Human In Vitro Cell Line
HL-60	Yes	Yes	Anticancer Screen Panel
H-MESO-1	Yes	Yes	Human In Vitro Cell Line
H-MESO-1A	Yes	Yes	Human Lung Xenograft

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HOP-18	NR	Yes	Human In Vitro Cell Line
HOP-19	NR	Yes	Anticancer Screen Panel
HOP-27	Yes	Yes	Anticancer Screen Panel
HOP-62	Yes	Yes	Anticancer Screen Panel
HOP-72/02	Yes	Yes	Anticancer Screen Panel
HOP-92	Yes	Yes	Anticancer Screen Panel
HS-1	NR	NR	Human Sarcoma Xenograft
HS-578T	Yes	Yes	Anticancer Screen Panel
HS-913T	Yes	NR	Human In Vitro Cell Line
HT-29 (CX-1)	Yes	Yes	Anticancer Screen Panel
HUH-7	Yes	Yes	Human In Vitro Cell Line
IGR-OV1	Yes	Yes	Anticancer Screen Panel
IM-9	Yes	Yes	Human In Vitro Cell Line
JEG-3	NR	Yes	Human In Vitro Cell Line
JURKAT	Yes	Yes	Human In Vitro Cell Line
K-562	Yes	Yes	Anticancer Screen Panel
KB-ADL 12	Yes	Yes	Human In Vitro Cell Line

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KD488 IS	Yes	Yes	Human In Vitro Cell Line
KLO-G	Yes	NR	Human Colon Xenograft
KM-12	Yes	Yes	Anticancer Screen Panel
KM12LX	Yes	Yes	Human In Vitro Cell Line
KM-20L2	Yes	Yes	Human In Vitro Cell Line
KSY-1	NR	Yes	Human In Vitro Cell Line
KSY-1FNA	Yes	Yes	Human In Vitro Cell Line
L1210	NR	Yes	Human In Vitro Cell Line
L1210JF	NR	Yes	Human In Vitro Cell Line
LNCAP-FNA	Yes	Yes	Human In Vitro Cell Line
LNCAP-HIGH	Yes	Yes	Human In Vitro Cell Line
LNCAP-MS	NR	Yes	Human In Vitro Cell Line
LOVO	Yes	NR	Human In Vitro Cell Line
LOVO I	NR	NR	Human Colon Xenograft
LOVO II	NR	NR	Human Colon Xenograft
LOX-IMVI	Yes	Yes	Anticancer Screen Panel
LS174Y	NR	Yes	Human In Vitro Cell Line

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LXFL 529 *	Yes	NR	Human In Vitro Cell Line
M14	Yes	Yes	Anticancer Screen Panel
M19-MEL	Yes	Yes	Human In Vitro Cell Line
M5076	Yes	Yes	Human In Vitro Cell Line
M5076 LIVER	Yes	Yes	Human In Vitro Cell Line
MALME-3M	Yes	Yes	Anticancer Screen Panel
MCF-7	Yes	Yes	Human In Vitro Cell Line
MDA-MB-231	Yes	Yes	Anticancer Screen Panel
MDA-MB-361	Yes	Yes	Human In Vitro Cell Line
MDA-MB-435	Yes	Yes	Anticancer Screen Panel
MDA-MB-468	Yes	Yes	Human In Vitro Cell Line
MHEC5T	Yes	Yes	Human In Vitro Cell Line
MHM-25	Yes	Yes	Anticancer Screen Panel
MHM-8	Yes	Yes	Anticancer Screen Panel
MLI-076 IS	NR	Yes	Human In Vitro Cell Line
MOLT-4	Yes	Yes	Anticancer Screen Panel
MRI-H-121	Yes	Yes	Human Kidney Xenograft

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MRI-H-121B	Yes	Yes	Human Melanoma Xenograft
MRI-H-130	Yes	Yes	Human Cervix Xenograft
MRI-H-147	Yes	Yes	Human Endometrium Xenograft
MRI-H-1579	Yes	NR	Human Prostate Adenocarcinoma Xenograft
MRI-H-165	Yes	Yes	Human Lung Xenograft
MRI-H-166	Yes	Yes	Human Kidney Xenograft
MRI-H-171	Yes	Yes	Human Endometrium Xenograft
MRI-H-177	Yes	Yes	Human Cervix Xenograft
MRI-H-1834	NR	NR	Human Ovary Xenograft
MRI-H-186	Yes	Yes	Human Cervix Xenograft
MRI-H-187	Yes	Yes	Human Melanoma Xenograft
MRI-H-194	Yes	Yes	Human Colon Xenograft
MRI-H-196	Yes	Yes	Human Cervix Xenograft
MRI-H-207	Yes	Yes	Human Ovary Xenograft
MRI-H-215	NR	NR	Human Cervix Xenograft
MRI-H-220	Yes	Yes	Human Endometrium Xenograft
MRI-H-221	Yes	Yes	Human Melanoma Xenograft

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MRI-H-227	Yes	Yes	Human Ovary Xenograft
MRI-H-250	NR	NR	Human Colon Xenograft
MRI-H-253	Yes	Yes	Human Endometrium Xenograft
MRI-H-254	Yes	Yes	Human Stomach Adenocarcinoma Xenograft
MRI-H-255	Yes	Yes	Human Melanoma Xenograft
MRI-H-258	Yes	Yes	Human Ovary Xenograft
MRI-H-266	Yes	Yes	Human Lung Xenograft
MRI-H-273	NR	NR	Human Ovary Xenograft
MX-1	Yes	Yes	Human In Vitro Cell Line
NC-37	NR	NR	Human In Vitro Cell Line
NCI/ADR-RES	Yes	Yes	Anticancer Screen Panel
NCI-H125	Yes	NR	Human In Vitro Cell Line
NCI-H146	Yes	Yes	Anticancer Screen Panel
NCI-H226 **	Yes	Yes	Anticancer Screen Panel
NCI-H23 **	Yes	Yes	Anticancer Screen Panel
NCI-H28	NR	Yes	Human In Vitro Cell Line
NCI-H292	Yes	NR	Human In Vitro Cell Line

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NCI-H322M **	Yes	Yes	Anticancer Screen Panel
NCI-H358M	Yes	NR	Human In Vitro Cell Line
NCI-H460 **	Yes	Yes	Anticancer Screen Panel
NCI-H520	Yes	Yes	Anticancer Screen Panel
NCI-H522 **	Yes	Yes	Anticancer Screen Panel
NCI-H69	Yes	Yes	Human In Vitro Cell Line
NCI-H82	Yes	Yes	Human In Vitro Cell Line
NCI-H9	NR	Yes	Anticancer Screen Panel
NIS-G	Yes	Yes	Human Melanoma Xenograft
OGL-G	Yes	Yes	Human Sarcoma Xenograft
OV	NR	NR	Human In Vitro Cell Line
OVCAR-3	Yes	Yes	Anticancer Screen Panel
OVCAR-4	Yes	Yes	Anticancer Screen Panel
OVCAR-5	Yes	Yes	Anticancer Screen Panel
OVCAR-8	Yes	Yes	Anticancer Screen Panel
PC3	Yes	Yes	Anticancer Screen Panel
PC-3/M	Yes	NR	Human In Vitro Cell Line

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PC3-GFP	Yes	Yes	Human In Vitro Cell Line
PPC-1 IS	NR	Yes	Human In Vitro Cell Line
PSN-1	Yes	Yes	Human In Vitro Cell Line
RD IS	NR	Yes	Human In Vitro Cell Line
RG-2	NR	Yes	Human In Vitro Cell Line
RPMI-7951	Yes	Yes	Human In Vitro Cell Line
RPMI-8226	Yes	Yes	Anticancer Screen Panel
RXF-393	Yes	Yes	Anticancer Screen Panel
RXF-631	Yes	Yes	Human In Vitro Cell Line
SF-268	Yes	Yes	Anticancer Screen Panel
SF-295	Yes	Yes	Anticancer Screen Panel
SF-539	Yes	Yes	Anticancer Screen Panel
SHP-77	Yes	Yes	Human In Vitro Cell Line
SKBR3	NR	Yes	Human In Vitro Cell Line
SK-MEL-2	Yes	Yes	Anticancer Screen Panel
SK-MEL-28	Yes	Yes	Human In Vitro Cell Line
SK-MEL-5	Yes	Yes	Anticancer Screen Panel

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SK-MES-1	Yes	Yes	Human In Vitro Cell Line
SK-OV-3	Yes	Yes	Anticancer Screen Panel
SKOV-3IPL	Yes	Yes	Human In Vitro Cell Line
SLC-11	NR	Yes	Anticancer Screen Panel
SN-1251	NR	Yes	Anticancer Screen Panel
SN-12-A1	Yes	Yes	Human In Vitro Cell Line
SN-12-C	Yes	Yes	Anticancer Screen Panel
SN-12-K1	Yes	Yes	Human In Vitro Cell Line
SN-12-L1	Yes	Yes	Human In Vitro Cell Line
SN-12-S1	Yes	NR	Human In Vitro Cell Line
SNB-19	Yes	Yes	Anticancer Screen Panel
SNB-56	NR	Yes	Anticancer Screen Panel
SNB-7	Yes	Yes	Human In Vitro Cell Line
SNB-75	Yes	Yes	Anticancer Screen Panel
SNB-78	Yes	Yes	Human In Vitro Cell Line
SR	Yes	NR	Anticancer Screen Panel
SW-620	Yes	Yes	Anticancer Screen Panel

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LINE	MTBM TEST	VIRAL SCREEN TEST	NOTES
SWA-G	Yes	Yes	Human Ovary Xenograft
T24	Yes	Yes	Human In Vitro Cell Line
T24-E7	NR	Yes	Human In Vitro Cell Line
T-47D	Yes	Yes	Anticancer Screen Panel
T50	NR	Yes	Human In Vitro Cell Line
TBD-1211	Yes	NR	Human In Vitro Cell Line
TE-671	Yes	Yes	Anticancer Screen Panel
TK10	Yes	Yes	Anticancer Screen Panel
TRI-G	Yes	NR	Human Melanoma Xenograft
U-251	Yes	Yes	Anticancer Screen Panel
U251-HRE	Yes	Yes	Human In Vitro Cell Line
U251-PGL3	Yes	Yes	Human In Vitro Cell Line
U251-PGL3 CLONE	Yes	Yes	Human In Vitro Cell Line
U373	Yes	Yes	Human In Vitro Cell Line
U87	Yes	Yes	Human In Vitro Cell Line
UABLG22 IS	NR	Yes	Human In Vitro Cell Line
UACC-257	Yes	Yes	Anticancer Screen Panel

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UACC-62	Yes	Yes	Anticancer Screen Panel
UCSD-242L	NR	Yes	Human In Vitro Cell Line
UCSD-354L	Yes	Yes	Human In Vitro Cell Line
UCSD-535L	NR	Yes	Anticancer Screen Panel
UIISO-KCA-1 IS	NR	Yes	Human In Vitro Cell Line
UO-31	Yes	Yes	Anticancer Screen Panel
WIDR	Yes	NR	Human In Vitro Cell Line
WIL-G	Yes	Yes	Human Melanoma Xenograft
WSU-HN-31	Yes	Yes	Human In Vitro Cell Line
XF-498	Yes	Yes	Human In Vitro Cell Line

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