

Athymic Nude Mouse

The nu mutation was discovered in 1962 in a closed outbred stock of albino mice in the Virus Laboratory, Ruchill Hospital, Glasgow, Scotland. Harlan obtained the model from the National Cancer Institute, National Institutes of Health, Maryland. This athymic nude model is maintained as an outbred colony, produced within flexible-film isolators and monitored for microbiologic integrity. Athymic nude mice are suitable for use in oncology, immunology*, and other fields of biomedical research. Harlan was renamed Envigo in 2015. Envigo was acquired by Inotiv in 2021.

Athymic Nude Mouse - Hsd:Athymic Nude-Foxn1^{nu}

CHARACTERISTICS

- Autosomal recessive mutation on nu locus on chromosome 11
- Thymic aplasia
- Phenotypically hairless (sparse hair growth possible)
- T-cell deficient
- Normal B-cell function
- Accepts xenograft and allograft transplantation
- Insusceptible to graft-versus-host disease
- No generation of cytotoxic effector cells

RESEARCH USE

GENERAL

- Tumor imaging (1,13,15,21,29,32,35,70,)
- Spontaneous tumors (17)
- Xenograft transplantation (5,11,13, 15,24,41,45,47,51,55,58,70,73)
- Tumor angiogenesis (4,14,33,37,54,59)
- Cancer cell tumorigenesis (2,6,18,20,31,43,44,46,56,66,67,68,69)
- Tumor inhibition (22, 25, 30, 53)
- Carcinogenesis regulation (5,10,23,40)
- Radiotherapy (34)

OVARIAN CANCER

- Vitamin D analogue (71)
- (NIS)-mediated radioiodide
- Tumor imaging (15)
- Antigen-specific mAb-based
- Immunotherapy (16)
- Adenovirus-mediated introduction of tumor suppressor genes (36, 42)
- IL-2 plasmid therapy of murine ovarian
- Carcinoma (27)

COLON CANCER

- Meloxicam (COX-2 Inhibitor) treatment (19)
- Gene targeting in colorectal cancer cells (45, 52)
- Epidermal growth factor receptor (egfr)
- Expression inhibition (48)
- *In vivo* microscopy tumor imaging (32)

SKIN CANCER

- Vitamin e succinate treatment (38)
- Antitumor activity of tnf- α in human melanoma xenografts (41)
- Dynamic fluorescence optical
- Tumor imaging (21)

PANCREATIC CANCER

- Identification of MnSOD tumor suppressor gene (54)





BREAST CANCER

- Bioluminescent tumor imaging (13, 29)
- Therapeutic electromagnetic field and gamma irradiation (7)
- Reversal of tamoxifen resistance of human breast carcinomas (3)
- α -difluoromethylornithine (DFMO)
- Treatment to attenuate metastasis (50)
- Inhibitory effects of arzoxifene on breast cancer carcinomas (65)
- Proapoptotic gene bik therapy (75)
- Reduced tumorigenicity of MDA-MB-231 cells by TGF- β RIII (57)

LUNG CANCER

- Bioluminescent tumor imaging (13)
- Aromatase inhibitors (63)
- Methadone treatment (64)
- Gene therapy utilizing plasmid DNA (26)
- Liposome-p53 administration in early endobronchial cancer (74)

PROSTATE CANCER

- PET tumor imaging (70)
- Peptide-doxorubicin prodrug treatment (11)
- Genistein therapy combined with irradiation (25)
- Identification of MnSOD tumor Suppressor gene (61)
- Thapsigargin prodrug treatment (12)
- Alendronate drug treatment (60)

BRAIN CANCER

- Adenovirus-mediated introduction of tumor suppressor genes (9)
- Celecoxib and its analog, DMC downregulate survivin expression (49)
- Suicide gene-transducing replication-competent foamy virus vector therapy (24)
- Identification of CuZuSOD tumor suppressor gene (72)
- Antineoplastic effects of hydralazine and valproic acid drug therapy (8)
- Iodine-125 seed irradiation (62) Squamous Cell Cancer
- Modulation of radiation response (28)

References:

- Alauddin, Miah M, Shahinian, Antranik, Park, Ryan, Tohme, Michael, Fissekis, John D, Conti, Peters. 2007. Biodistribution and PET Imaging of [18F]-Fluoroadenosine derivatives. *Nucl Med Biol*, 34(3), 267-72.
- Arteaga, C. L., Carty-Dugger T., Moses, H.L., Hurd, S.D., and Pietenpol, J.A. 1993. Transforming growth factor β 1 can induce estrogen-independent tumorigenicity of human breast cancer cells in athymic mice. *Cell Growth & Diff*, 4, 193-201.
- Arteaga, C. L., Koli, K.M., Dugger T.C., and Clarke, R. 1999. Reversal of Tamoxifen resistance of human breast carcinomas *in vivo* by neutralizing antibodies to transforming growth factor- β . *J Natl Cancer Inst*, 91, 46-53.
- Benjamin, L. E. and Keshet, E. 1997. Conditional switching of vascular endothelial growth factor (VEGF) expression in tumors: Induction of endothelial cell shedding and regression of hemangioblastoma-like vessels by VEGF withdrawal. *Proc Natl Acad Sci*, 94, 8761-6.
- Buckley, S., Shi, W., Driscoll, B., Ferrario, A., Anderson, K., and Warburton, D., 2004. BMP4 signaling induces senescence and modulates the oncogenic phenotype of A549 lung denocarcinoma cells. *Am J Physiol Lung Cell Mol Physiol*, 286, L81-6.
- Calaf, G. and Hei, T.K. 2001. Oncoprotein expression in human breast epithelial cells transformed by high-LET radiation. *Int J Radiat Biol*, 77, 31-40.
- Cameron, I.L., Sun, L., Short, N., Hardman, W.E. and Williams, C.D. 2005. Therapeutic electromagnetic field (TEMF) and gamma irradiation on human breast cancer xenograft growth, angiogenesis and metastasis. *Cancer Cell Intl*, 5, 23.
- Chavez-Blanco, A., Perez-Plasencia, C., Perez-Cardenas, E., Carrasco-Legleu, C., Rangel-Lopez, E., Segura-Pacheco, B., et al. 2006.
- Antineoplastic effects of the DNA methylation inhibitor hydralazine and the histone deacetylase inhibitor valproic acid in cancer cell lines. *Cancer Cell Intl*, 6, 2.
- Chen, J., Willingham, T., Shuford, M., and Nisen, P.D. 1996. Tumor suppression and inhibition of aneuploid cell accumulation in human brain tumor cells by ectopic overexpression of the cyclin dependent kinase inhibitor p27KIP1. *J Clin Invest*, 97, 1983-8.
- Chen, Z., Sun, J., Pradines, A., Favre, G., Adnane, J., and Sefti, S.M. 2000. Both farnesylated and geranylgeranylated RhoB inhibit malignant transformation and suppress human tumor growth in nude mice. *J Biol Chem*, 275, 17974-8.
- DeFeo-Jones, D., Garsky, V.M., Wong, B.K., Feng, D.M., Bolyar, T., Haskell, K., et al. 2000. A peptide-doxorubicin 'prodrug' activated by prostate-specific antigen selectively kills prostate tumor cells positive for prostate-specific antigen *in vivo*. *Nature Medicine*, 6, 1248-52.
- Denmeade, S.R., Jakobsen, C.M., Janssen, S., Khan, S.R., Garrett, E.S., Lilja, H., et al. 2003. Prostate-specific antigen-activated thapsigargin prodrug as targeted therapy for prostate cancer. *J Natl Cancer Inst*, 95, 990-1000.
- Dikmen, Z.G., Gellert, G., Dogan, P., Mason, R., Antich, P., Richer, E., et al. 2005. A new diagnostic system in cancer research: Bioluminescent Imaging (BLI). *Turk J Med Sci*, 35, 65-70.
- Duyndam, M.C.A., Hilhorst, M.C.G., Schlüper, H.M.M., Verheul, H.M.W., van Diest, P.J., Kraal, G., et al. 2002. Vascular endothelial growth factor-165 overexpression stimulates angiogenesis and induces cyst formation and macrophage infiltration in human ovarian cancer xenografts. *Am J Pathol*, 160, 537-48.
- Dwyer, R.M., Bergert, E.R., O'Conner, M.K., Gendler, S.J., and Morris, J.C. 2006. Sodium iodide symporter-mediated radioiodide imaging and therapy of ovarian tumor xenografts in mice. *Gene Ther*, 13, 60-6.
- Ebel, W., Routhier, E.L., Foley, B., Jacob, S., McDonough, J.M., Patel, R.K., et al. 2007. Preclinical evaluation of MORAb-003, a humanized monoclonal antibody antagonizing folate receptor-alpha. *Cancer Immunity*, 7, 1-8.
- Fogh, J. and Giovanella, B.C., (Eds.) 1978. *The Nude Mouse in Experimental and Clinical Research*. New York: Academic Press.
- Fukasawa, M., and Korc, M. 2004. Vascular endothelial growth factor trap suppresses tumorigenicity of multiple pancreatic cancer cell lines. *Clin Cancer Res*, 10, 3327-32.
- Goldman, A.P., Williams, C.S., Sheng H., Lamps, L.W., Williams, V.P., Pairet, M., et al. 1998. Meloxicam inhibits the growth of colorectal cancer cells. *Carcinogenesis*, 19, 2195-99.
- Graff, J.R., Konicek, B.W., McNulty, A.M., Wang, Z., Houck, K., Allen, S., et al. 2000. Increased AKT activity contributes to prostate cancer progression by dramatically accelerating prostate tumor growth and diminishing p27Kip1 expression. *J Biol Chem*, 275, 24500-5.
- Gurfinkel, M., Ke, S., Wang, W., Li, C., and Sevick-Muraca, E.M. 2005. Quantifying molecular specificity of $\alpha\beta$ integrin-targeted optical contrast agents with dynamic optical imaging. *J Biomed Optics*, 10, 034019.
- Hardman, E.W., Munoz, J., Cameron, I.L. 2002. Role of lipid peroxidation and antioxidant enzymes in omega 3 fatty acids induced suppression of breast cancer xenograft growth in mice. *Cancer Cell Intl*, 2, 10.
- He, N., Li, C., Zhang, X., Sheng, T., Chi, S., Chen, K., et al. 2005. Regulation of lung cancer cell growth and invasiveness by β -TRCP. *Molecular Carcinogenesis*, 42, 18-28.
- Heinkelein, M., Hoffmann, U., Lücke, M., Imrich, H., Müller, J.G., Meixensberger, J., et al. 2005. Experimental therapy of allogeneic solid tumors induced in athymic mice with suicide gene-transducing replicationcompetent foamy virus vectors. *Cancer Gene Ther*, 12, 947-53.
- Hillman, G.G., Wang Y., Kucuk, O., Che, M., Doerge, D.R., Yudelev, M., et al. 2004. Genistein potentiates inhibition of tumor growth by radiation in a prostate cancer orthotopic model. *Mol Cancer Ther*, 3, 1271-9.
- Horton, H.M., Anderson, D., and Hernandez, P. 1999. A gene therapy for cancer using intramuscular injection of plasmid DNA encoding interferon α . *Proc Natl Acad Sci*, 96, 1553-8.
- Horton, H.M., Dorigo, O., Hernandez, P., Anderson, D., Berek, J.S. and Parker, S.E. 1999. IL-2 plasmid therapy of murine ovarian carcinoma inhibits the growth of tumor ascites and alters its cytokine profile. *The Journal of Immunology*, 163, 6378-85.
- Huang, Shyh-Min, Harari, Paul M. 2000. Modulation of Radiation Response after Epidermal Growth Factor Receptor Blockade in Squamous Cell Carcinomas: Inhibition of Damage Repair, Cell Cycle Kinetics, and Tumor Angiogenesis. *Clinical Cancer Research*, 6, 2166-74.
- Jenkins, D.E., Hornig, Y.S., Oei, Y., Dusich, J. and Purchio, T. 2005. Bioluminescent human breast cancer cell lines that permit rapid and sensitive *in vivo* detection of mammary tumors and multiple metastases in immune deficient mice. *Breast Cancer Res*, 7, R444-54.
- Kanga, Junghee, Kamalb, Adeela, Burrowsb, Francis J., Evers, B., Mark, Chunga, Dai H. 2006. Inhibition of Neuroblastoma Xenograft Growth by HSP90 Inhibitor. *Anticancer Res*, 26(3A), 1903-1908.
- Kruskal, J.B., Thomas, P., Kane, R.A. and Goldberg, S.N. 2004. Hepatic perfusion changes in mice livers with developing colorectal cancer metastases. *Radiology*, 231, 482-90.
- Kruskal, J.B., Thomas, P., Nassar, I., Osman, C. and Kane, RA. 2000. Hepatic colon cancer metastases in mice: Dynamic *in vivo* correlation with hypoechoic rims visible at US. *Radiology*, 215, 852-7.
- Lee, O.H., Fueyo, J., Xu, J., Yung, W.K.A., Lemoine, M.G., Lang, F.F., et al. 2006. Sustained angiopoietin-2 expression disrupts vessel formation and inhibits glioma growth. *Neoplasia*, 8, 419-28.
- Li, Zi-bo, Cai, Weibo, Cao, Qizhen, Chen, Kai, Wu, Zhanhong, He, Lina, Chen, Xiaoyuan. 2007. 64Cu-Labeled Tetrameric and Octameric RGD Peptides for Small-Animal PET of Tumor $\alpha\beta$ Integrin Expression. *The Journal of Nuclear Medicine*, 48(7), 1162-71.
- Löqvist, A., Humm, J.L., Sheikh, A., Finn, R.D., Koziorowski, J., Ruan, S., et al. 2001. PET imaging of 86Y-labeled anti-Lewis Y monoclonal antibodies in a nude mouse model: Comparison between 86Y and 111In radiolabels. *J Nucl Med*, 42, 1281-87.
- Mahasreshti, P.J., Navarro, J.G., Kataram, M., Wang, M.H., Carey, D., Siegal, G.P., et al. 2001. Adenovirus-mediated soluble FLT-1 gene therapy for ovarian carcinoma. *Clin Cancer Res*, 7, 2057-66.
- Malafa, Mokenge P., Fokum, Frida D., Mowlavi, Arian, Abusief, Mary, King, Michele. 2002. Vitamin E Inhibits Melanoma Growth in Mice. *Surgery*, Jan, 85-90.
- Malafa, M.P., Fokum, F.D., Smith, L., and Louis, A. 2002. Inhibition of angiogenesis and promotion of melanoma dormancy by vitamin E succinate. *Annals of Surgical Oncology*, 9(10), 1023-32.
- Manekjee, R. and Minna, J.D. 1992. Nonconventional opioid binding sites mediate growth inhibitory effects of methadone on human lung cancer cells. *Proc Natl Acad Sci*, 89, 1169-73.

- Mariotti, A., Kedeshtian, P.A., Dans, M., Curatola, A.M., Gagnoux-Palacios, L., and Giancotti, F.G. 2001. EGF-R signaling through Fyn kinase disrupts the function of integrin $\alpha 6\beta 4$ at hemidesmosomes: role in epithelial cell migration and carcinoma invasion. *J Cell Biol*, 155, 447-57.
- Menon, C., Iyer, M., Prabakaran, I., Canter, R.J., Lehr, S.C., and Fraker, D.L. 2003. TNF- α downregulates vascular endothelial Flk-1 expression in human melanoma xenograft model. *Am J Physiol Heart Circ Physiol*, 284, H317-29.
- Modesitt, S.C., Ramirez, P., Zu, Z., Bodurka-Bevers, D., Gershenson, D., and Wolf, J.K. 2001. *In vitro* and *in vivo* adenovirus-mediated p53 and p16 tumor suppressor therapy in ovarian cancer. *Clin Cancer Res*, 7, 1487-89.
- Montgomery, E., Goggins, M., Zhou, S., Argani, P., Wilentz, R.E., Kaushal, M., et al. 2001. Nuclear localization of Dpc4 (Madh4, Smad4) in colorectal carcinomas and relation to mismatch repair/transforming growth factor- β receptor defects. *Am J Pathol*, 158, 537-42.
- Pan, Y., Wang, L., and Dai, J.L. 2006. Suppression of breast cancer cell growth by Na $^+$ /H $^+$ exchanger regulatory Factor 1 (NHERF1). *Breast Cancer Res*, 8, R63.
- Park, B.H., Vogelstein, B., and Kinzler, K.W. 2001. Genetic disruption of PPAR δ decreases the tumorigenicity of human colon cancer cells. *Proc Natl Acad Sci* 98, 2598-2603.
- Petros, J.A., Baumann, A.K., Ruiz-Pesini, E., Amin, M.B., Sun, C.Q., Hall, J., et al. 2005. mtDNA mutations increase tumorigenicity in prostate cancer. *Proc Natl Acad Sci*, 102, 719-24.
- Presnell, S.C., Werdin, E.S., Maygarden, S., Mohler, J.L., and Smith, G.J. 2001. Establishment of short-term primary human prostate xenografts for the study of prostate biology and cancer. *Am J Pathol*, 159, 855-860.
- Prewett, M.C., Hooper, A.T., Bassi, R., Ellis, L.M., Waksal, H.W., and Hicklin, D.J. 2002. Enhanced antitumor activity of anti-epidermal growth factor receptor monoclonal antibody IMC-C225 in combination with Irinotecan (CPT-11) against human colorectal tumor xenografts. *Clin Cancer Res*, 8, 994-1003.
- Pyrko, P., Soriano, N., Kardosh, A., Liu, Y.T., Uddin, J., Petasis, N.A., et al. 2006. Downregulation of survivin expression and concomitant induction of apoptosis by celecoxib and its non-cyclooxygenase-2-inhibitory analog, dimethyl-celecoxib (DMC), in tumor cells *in vitro* and *in vivo*. *Mol Cancer*, 5, 19.
- Richert, M.M., Phadke, P.A., Matters, G., DiGirolamo, D.J., Washington, S., Demers, L.M., et al. 2005. Metastasis of hormone-independent breast cancer to lung and bone is decreased by α -difluoromethylornithine treatment. *Breast Cancer Res*, 7, R819-27.
- Roby, K.F., Taylor, C.C., Sweetwood, J.P., Cheng, Y., Pace, J.L., Tawfik, O., et al. 2000. Development of a syngeneic mouse model for events related to ovarian cancer. *Carcinogenesis*, 21, 585-91.
- Samuels, Y., Diaz, L.A., Schmidt-Kittler, O., Cummins, J., DeLong, L., Cheong, I., et al. 2005. Mutant PIK3CA promotes cell growth and invasion of human cancer cells. *Cancer Cell*, 7, 561-73.
- Santell, R.C., Kieu, N., and Helferich, W.G. 2000. Genistein inhibits growth of estrogen-independent human breast cancer cells in culture but not in athymic mice. *J Nutr*, 130, 1665-9.
- Shao, R., Xia, W., and Hung, M. 2000. Inhibition of angiogenesis and induction of apoptosis are involved in E1A-mediated bystander effect and tumor suppression. *Cancer Res*, 60, 3123-26.
- Sheffield, L.G., Eppler, C.M., Tucker, H.A., Welsch, C.W. 1988. Influence of Recombinant Deoxyribonucleic Acid-Derived Bovine Growth Hormone on α -Lactalbumin Production by Bovine Mammary Tissue Maintained in Athymic Nude Mice. *Journal of Dairy Science*, 71(1), 68-74.
- Sheng, H., Shao, J., Kirkland, S.C., Isakson, P., Coffey, R.J., Morrow, J., et al. 1997. Inhibition of human colon cancer cell growth by selective inhibition of Cyclooxygenase-2. *J Clin Invest*, 99, 2254-59.
- Sun, LuZhe, Chen, Changguo. 1997. Expression of Transforming Growth Factor β Type III Receptor Suppresses Tumorigenicity of Human Breast Cancer MDA-MB-231 Cells. *The Journal of Biological Chemistry*, 272(40), 25367-72.
- Truman RW, Andrews PK, Robbins NY, Adams LB, Krahenbuhl JL, et al. 2008. Enumeration of Mycobacterium leprae Using Real-Time PCR. *PLoS Negl Trop Dis*, 2(11), e328.
- Tsui, P., Rubenstein, M., and Guinan, P. 2005. Correlation between PSMA and VEGF expression as markers for LNCaP tumor angiogenesis. *J Biomed & Biotech*, 3, 287-90.
- Tuomela, Johanna M., Valtal, Maija P., Vaananen, Kalervo, Harkonen, Pirkko L. 2008. Alendronate decreases orthotopic PC-3 prostate tumor growth and metastasis to prostate-draining lymph nodes in nude mice. *BMC Cancer*, 8, 81.
- Venkataraman, S., Jiang, X., Weydert, C., Zhang, Y., Zhang, H.J., Goswami, P.C., et al. 2005. Manganese superoxide dismutase overexpression inhibits the growth of androgen-independent prostate cancer cells. *Oncogene*, 24, 77-89.
- Verhoef, Joost Jc, Stalpers, Lukas JA, Coumou, Annet W, Koedooder, Kees, Lavini, Cristina, Van Noorden, Cornelis, JF, Haverman, Jaap, Vandertop, William P, Van Furth, Wouter R. 2007. Experimental Iodine-125 Seed Irradiation of Intracerebral Brain Tumors in Nude Mice. *Radiation Oncology*, 2, 38.
- Weinberg, O.K., Marquez-Garban, D.C., Fishbein, M.C., Goodlick, L., Garban, H.J., Dubinett, S.M., et al. 2005. Aromatase inhibitors in human lung cancer therapy. *Cancer Res*, 65, 11287-91.
- Weydert, C., Roling, B., Liu, J., Hinkhouse, M.M., Ritchie, J.M., Oberley, L.W., et al. 2003. Suppression of the malignant phenotype in human pancreatic cancer cells by the overexpression of manganese superoxidizedismutase. *Mol Cancer Ther*, 2, 361-9.
- Wu, Licun, Tannock, Ian F. 2005. Effect of the Selective Estrogen Receptor Modulator Arzoxifene on Repopulation of Hormone-Responsive Breast Cancer Xenografts between Courses of Chemotherapy. *Clin Cancer Res*, 11(22), 8195-8200.
- Yahanda, A.M., Bruner, J.M., Donehower, L.A., and Morrison, R.S. 1995. Astrocytes derived from p53-deficient mice provide a multistep *in vitro* model for development of malignant gliomas. *Mol & Cell Biol*, 15, 4249-59.
- Yang, M., Zhong, W.W., Srivastava, N., Slavin, A., Yang, J., Hoey, T., et al. 2005. G Protein-coupled lysophosphatidic acid receptors stimulate proliferation of colon cancer cells through the β -catenin pathway. *Proc Natl Acad Sci*, 102, 6027-32.
- Zawel, Leigh, Yu, Jian, Torrance, Christopher J., Markowitz, Sanford, Kinzler, Kenneth W., Vogelstein, Bert, Zhou, Shihbin. 2002. DEC1 is a Downstream Target of TGF- β with Sequence-Specific Transcriptional Repressor Activities. *PNAS*, 99(5), 2848-2853.
- Zhang, N., Zhong, R., Wang, Z., and Deuel, T.F. 1997. Human breast cancer growth inhibited *in vivo* by a dominant negative pleiotrophin mutant. *J Biol Chem*, 272, 16733-6.
- Zhang, X., Cai, W., Cao, F., Schreibmann, E., Wu, Y., Wu, J.C., et al. 2006. 18F-Labeled bombesin analogs for targeting GRP receptors expressing prostate cancer. *J Nucl Med*, 47, 492-501.
- Zhang, X., Jiang, F., Li, P., Li, C., Ma, Q., Nicosia, S.V., et al. 2005. Growth suppression of ovarian cancer xenografts in nude mice by vitamin D analogue EB1089. *Clin Cancer Res*, 11, 323-28.
- Zhang, Y., Zhao, W., Zhang, H.J., Domann, F.E., Oberley, L.W. 2002. Overexpression of copper zinc superoxide dismutase suppresses human glioma cell growth. *Cancer Res*, 62, 1205-12.
- Zimmers, Teresa A., McKillop, Iain H., Pierce, Robert H., Yoo, Joo-Yeon, Koniaris, Leonidas G. 2003. Massive Liver Growth in Mice Induced by Systemic Interleukin 6 Administration. *Hepatology*, 38(2), 326-34.
- Zou, Y., Zong, G., and Ling, Y. 1998. Effective treatment of early endobronchial cancer with regional administration of Liposome-p53 complexes. *J Natl Cancer Inst*, 90, 1130-7.
- Zou, Yiyu, Peng, Hua, Zhou, Binhu, Wen, Yong, Wang, Shao-Chun, Tsai, Eing-Mei, Hung, Mien-Chie. 2002. Systemic Tumor Suppression by the Proapoptotic Gene bik1. *Cancer Research*, 62, 8-12.