



Research Models  
and Services  
Oncology - Mutant Rats

# Athymic Nude Rat

The *rnu* mutation was discovered in 1953 in an outbred colony of hooded rats at the Rowett Research Institute, Aberdeen, Scotland. Since 1978, Harlan Laboratories maintained this model as an outbred colony, produced within flexible-film isolators and monitored for microbiologic integrity. Athymic nude rats are suitable for use in transplantation, tumor therapy, and carcinogenesis research, among many other purposes. Harlan was renamed Envigo in 2015.

## Hsd:RH-Foxn1<sup>rnu</sup>

### Characteristics (7,9,19,23,27,33)

- + Autosomal recessive mutation on *rnu* locus of chromosome 10
- + T-cell deficient
- + Normal B-cell function
- + Increased Natural Killer (NK) and macrophage cell population
- + Thymic aplasia
- + Phenotypically hairless (sparse hair growth possible)

### Research Use

#### General

- Xenograft transplantation (2,4,8,10,11,12,16, 17,20,21,24,26,29,32,35,36,37)
- Tumor suppression therapy (3,8,16,24,30,38)
- Carcinogenesis regulation (6,26,28,35)
- Tumor angiogenesis (1,5)

#### Brain Cancer

- Rodent models of brainstem tumors (37)
- Oral fenretinide therapy for neuroblastoma (20)
- Anti-VEGF antibody treatment of glioblastoma (22)

- Tumor imaging by targeting peptide radiopharmaceuticals across blood-brain barrier (12)
- Tumor imaging by α-receptor ligands (32)
- Predicting resistance or response to chemotherapy in neuroblastoma by MRS (14,15)
- 11C-colchicine PET imaging of multiple drug resistance (13)
- Systemic immunity against intracranial T9 gliomas (6)

#### Breast Cancer

- MRI Monitoring of microvascular permeability in xenograft tumors (36)
- Treatment of bone metastasis induced by breast cancer cells (2)
- Eicosapentaenoic acid suppression of human breast cancer xenograft cells (24)
- Pentoxyfylline inhibition of tumor cell tissue factor and VEGF (1)

#### Lung Cancer

- Pharmacology of orally active taxane (21)
- Tumor imaging by α-receptor ligands (32)
- Pentoxyfylline inhibition of tumor cell tissue factor and VEGF (1)
- Gefitinib inhibition of EGF-stimulated tumorigenesis in human lung carcinoma (18)

#### Skin Cancer

- Modulation of chemotherapy resistance in regional melanoma therapy (31)
- Pentoxyfylline inhibition of tumor cell tissue factor and VEGF (1)

## Liver Cancer

- 4-phenylbutyrate treatment of liver tumor xenografts (28)
- Photodynamic diagnosis of hepatoblastoma (29)
- Hepatic artery infusion chemotherapy for hepatic metastases (16)
- Rat model of liver metastases with human colorectal cells (17)

## Colon Cancer

- Rat model of liver metastases with human colorectal cells (17)
- EGFP gene transfer and expression in human colon adenocarcinoma (34)
- Metastatic potential and variants from colorectal tumor cell lines (35)

## Sarcoma

- MDM2 antisense therapy suppresses growth of human soft tissue sarcoma (38)
- Electrochemotherapy treatment of human sarcoma xenografts (11)

## References:

- Amirkhosravi, A., Meyer, T., Warnes, G., Amaya, M., Malik Z., Biggerstaff, J.P., et al. (1998). Pentoxyfilline inhibits hypoxia-induced upregulation of tumor cell tissue factor and vascular endothelial growth factor. *Thromb. Haemost.*, 80, 598-602.
- Bäuerle, T., Peterschmitt, J., Hilbig, H., Kiessling, F., Armbruster, F.P., and Berger, M.R. (2006). Treatment of bone metastasis induced by MDA-MB-231 breast cancer cells with an antibody against bone sialoprotein. *Int'l. J. Oncol.*, 28, 573-83.
- Burch, S., Bogaards, A., Siewerdsen, J., Moseley, D., Yee, A., Finkelstein, J., et al. (2005). Photodynamic therapy for the treatment of metastatic lesions in bone: Studies in rat and porcine models. *Journal of Biomedical Optics*, 10, 034011-1-13.
- Buursma, A.R., Beeren, A.M.J., de Vries, E.F.J., van Waarde, A., Rots, M.G., Hospers, G.A.P. et al. (2005). The human norepinephrine transporter in combination with <sup>11</sup>C-m-Hydroxyephedrine as a reporter gene/reporter probe for PET of gene therapy. *J. Nucl. Med.*, 46, 2068-75.
- Cabrera, G., Porvasnik, S.L., DiCorleto, P.E., Siemionow, M. and Goldman, C.K. (2006). Intra-arterial adenoviral mediated tumor transfection in a novel model of cancer gene therapy. *Mol. Cancer*, 5, 32.
- Chen, Y., Douglass, T., Jeffes, E.W.B., Xu, Q., Williams, C.C., Arpaikarul, N., et al. (2002). Living T9 glioma cells expressing membrane macrophage colony-stimulating factor produce immediate tumor destruction by polymorphonuclear leukocytes and macrophages via a "paraptosis"-induced pathway that promotes systemic immunity against intracranial T9 gliomas. *Blood*, 100, 1373-80.
- Cook, J.L., Iklé, D.N. and Routes, B.A. (1995). Natural killer cell ontogeny in the athymic rat. *Journal of Immunology*, 155, 5512-8.
- Dauchy, R. T., Dauchy, E. M., Sauer, L. A., Blask, D. E., Davidson, L. K., Krause, J. A., et al. (2004). Differential inhibition of fatty acid transport in tissue-isolated steroid receptor negative human breast cancer xenografts perfused *in situ* with isomers of conjugated linoleic acid. *Cancer Letters*, 209, 7-15.
- Festing, M.F.W., May, D., Connors, T.A., Lovell, D. and Sparrow, S. (1978). An athymic nude mutation in the rat. *Nature*, 274, 5669, 365-6.
- Gossmann, A., Helbich, T. H., Mesiano, S., Shames, D. M., Wendland, M. F., Roberts, T. P. L., et al. (2000). Magnetic resonance imaging in an experimental model of human ovarian cancer demonstrating altered microvascular permeability after inhibition of vascular endothelial growth factor. *Journal of Obstetrics and Gynecology*, 183, 956-963.
- Jaroszeski, M.J., Coppola, D., Pottinger, C., Gilbert, R.A., and Heller, R. (2002). Electrochemotherapy for the treatment of human sarcoma in athymic rats. *Tech. Cancer Res. & Treat.*, 1, 393-9.
- Kurihara, A. and Pardridge, W.M. (1999). Imaging brain tumors by targeting peptide radiopharmaceuticals through the bloodbrain barrier. *Cancer Res.*, 59, 6159-63.
- Levchenko, A., Mehta, B.M., Lee, J., Humm, J.L., Augensen, F., Squire, O., et al. (2000). Evaluation of <sup>11</sup>C-colchicine for PET imaging of multiple drug resistance. *J. Nucl. Med.*, 41, 493-501.
- Lindskog, M., Kogner, P., Ponthan, F., Schweinhardt, P., Sandstedt, B., Heiden, T., et al. (2003). Noninvasive estimation of tumour viability in a xenograft model of human neuroblastoma with proton magnetic resonance spectroscopy (<sup>1</sup>H MRS). *British J. of Cancer*, 88, 478-85.
- Lindskog, M., Spenger, C., Jarvet, J., Graslund, A. and Kogner, P. (2004). Predicting resistance or response to chemotherapy by proton magnetic resonance spectroscopy in neuroblastoma. *J. Natl. Cancer Inst.*, 96,1457-66.
- Loesch, A., Turmaine, M., Loizidou, M., Crowe, R., Ashraf, S., Taylor, I., et al. (1997). Increase in immunoreactivity for endothelin-1 in blood vessels of rat liver metastases: Experimental sarcoma and carcinoma. *Journal of Anatomy*, 191, 291-299.
- Marchal, F., Tran, N., Marchal, S., Leroux, A., Marchal, C., Bolotine, L., et al. (2005). Development of an HT29 liver metastases model in nude rats. *Oncology Reports*, 14, 1203-7.
- McKillop, D., Partridge, E.A., Kemp, J.V., Spence, M.P., Kendrew, J., Barnett, S., et al. (2005). Tumor penetration of gefitinib (Iressa) an epidermal growth factor receptor tyrosine kinase inhibitor. *Mol. Cancer Ther.*, 4, 641-9.
- National Research Council. (Eds.). (1989). *Immunodeficient rodents: a guide to their immunology, husbandry and use*. Washington, D.C.: National Academy Press.
- Ponthan, F., Lindskog, M., Karnehed, N., Castro, J., and Kogner, P. (2003). Evaluation of anti-tumour effects of oral fenretinide (4-HPR) in rats with human neuroblastoma xenografts. *Oncology Reports*, 10, 1587-92.
- Rose, W.C., Long, B.H., Fairchild, C.R., Lee, F.Y.F., Kadow, J.F. (2001). Preclinical pharmacology of BMS-275183, an orally active taxane. *Clin. Cancer Res.*, 7, 2016-21.
- Rubenstein, J.L., Kim, J., Ozawa, T., Zhang, M., Deen, D.F. and Shuman, M.A. (2000). Anti-VEGF antibody treatment of glioblastoma prolongs survival but results in increased vascular cooption. *Neoplasia*, 2, 306-14.
- Rygaard, T., Brünner, N., Groen, N. and Spang-Thompson, M. (Eds.). (1987). *Immune-deficient animals in biomedical research*. Basel: Karger.
- Sauer, L.A., Dauchy, R.T., Blask, D.E., Krause, J.A., Davidson, L.K. and Dauchy, E.M. (2005). Eicosapentaenoic acid suppresses cell proliferation in MCF-7 human breast cancer xenografts in nude rats via a pertussis toxin-sensitive signal transduction pathway. *J. Nutr.*, 135, 2124-9.
- Schuurman, H., Hougen, H.P. and van Loveren, H. (1992). The rnu (Rowett Nude) and rnuN (nzu, New Zealand Nude) rat: an update. *ILAR Journal*, 34, 1-2.
- Siegall, C. B., Liggitt, D., Chace, D., Tepper, M. A., and Fell, H. P. (1994). Prevention of immunotoxin-mediated vascular leak syndrome in rats with retention of antitumor activity. *PNAS*, 91, 9514-9518.
- Suckow, M.A., Weisbroth, S.H. and Franklin, C.L. (2006). (Eds.). *The Laboratory Rat*. Amsterdam: Elsevier.
- Svechnikova, I., Gray, S.G., Kundrotiene, J., Ponthan, F., Kogner, P. and Ekstrom, T.J. (2003). Apoptosis and tumor remission in liver tumor xenografts by 4-phenylbutyrate. *Int'l. J. Oncol.*, 22, 579-88.
- Till, H., Bergmann, F., Metzger, R., Haeberle, B., Schaeffer, K., von Schweinitz, D., et al. (2005). Videoscopic fluorescence diagnosis of peritoneal and thoracic metastases from human hepatoblastoma in nude rats. *Surgical Endoscopy*, 19, 1483-1486.
- Trail, P.A., Willner, D., Bianchi, A. B., Henderson, A. J., TrailSmith, M. D., Girit, E., et al. (1999). Enhanced antitumor activity of Paclitaxel in combination with the anticancer immun conjugate BR96 Doxorubicin. *Clinical Cancer Research*, 5, 3632-3638.
- Ueno, T., Ko, S.H., Grubbs, E., Yoshimoto, Y., Augustine, C., Abdel-Wahab, Z., et al. (2006). Modulation of chemotherapy resistance in regional therapy: a novel therapeutic approach to advanced extremity melanoma using intra-arterial temozolamide in combination with systemic O<sub>6</sub>-benzylguanine. *Mol. Cancer Ther.*, 5, 732-8.
- Van Waarde, A., Buursma, A.R., Hospers, G.A.P., Kawamura, K., Kobayashi, T., Ishii, K., et al. (2004). Tumor imaging with 2 α-receptor ligands, 18F-FE-SA5845 and <sup>11</sup>C-SA4503: a feasibility study. *J. Nucl. Med.*, 45, 1939-45.
- Vos, J.G., Kreeftenberg, J.G., Krut, B.C., Kruizinga, W. and Steerenberg, P. (1980). The athymic nude rat: II. Immunological characteristics. *Clinical Immunology and Immunopathology*, 15, 229-37.
- Wang, M., Boenicek, L., Howard, B.D., Vogel, I. and Kalthoff, H. (2003). Gene transfer and expression of enhanced green fluorescent protein in variant HT-29c cells. *World J. Gastroenterol.*, 9, 2083-7.
- Wang, M., Vogel, I. and Kalthoff, H. (2003). Correlation between metastatic potential and variants from colorectal tumor cell line HT-29. *World J. Gastroenterol.*, 9, 2627-31.
- Wiart, M., Fournier, L.S., Novikov, V.Y., Shames, D.M., Roberts, T.P., Fu, Y., et al. (2004). Magnetic resonance imaging detects early changes in microvascular permeability in xenograft tumors after treatment with the matrix metalloprotease inhibitor prinomastat. *Tech. in Cancer Res. & Treatment*, 3, 377-82.
- Wu, Q., Tyler, B., Sukay, L., Rhines, L., DiMeco, F., Clatterbuck, R.E., et al. (2002). Experimental rodent models of brainstem tumors. *Vet. Pathol.*, 39, 293-9.
- Würl, P., Bartel, F., Meye, A., Kappler, M., Bache, M., Schmidt, H. et al. (2002). Growth reduction of a xenotransplanted human soft tissue sarcoma by MDM2 anti sense therapy via implanted osmotic minipumps. *Int'l. J. Oncol.*, 20, 1087-93.

## Contact us

North America 800.793.7287 EU and Asia [envigo.com/contactus](http://envigo.com/contactus) [info@envigo.com](mailto:info@envigo.com)

Envigo RMS Division, 8520 Allison Pointe Blvd., Suite 400, Indianapolis, IN 46250, United States