

## METABOLIC MODELS

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### ZDF Rat

**Nomenclature:** ZDF/Crl-*Lepr<sup>fa</sup>*

**Origin:** Originated in a colony of outbred Zucker rats in the laboratory of Dr. Walter Shaw at Eli Lilly Research Laboratories in Indianapolis, Indiana. To Dr. Julia Clark at the Indiana University Medical School (IUMS) in 1977. To Dr. Richard Peterson at IUMS in 1981. To Genetic Models, Inc. in 1991. To Charles River in 2001.

**Characteristics:** Obesity, Insulin Resistance, Hyperinsulinemia, Type 2 Diabetes, Hyperglycemia, Hypertriglyceridemia, Hypercholesterolemia, Nephropathy, Impaired Wound Healing, Mild Hypertension, Neuropathy

**References:** Clark, J., Palmer, C.J., and Shaw, W.N., 1983, The diabetic Zucker fatty rat. *Proc. Soc. Exp. Biol. Med.* 173: 68-75.

Peterson, R.G., Neel, M.A., Lithe, L.A., Kincaid, J.C., and Eichberg, J., 1990, Neuropathic complications in the Zucker diabetic fatty rat (ZDF/Drt-fa). In *Frontiers in Diabetes Research Lessons from Animal Diabetes III*, edited by E. Shafir, pp. 456-458. London: Smith-Gordon.

Peterson, R.G. 2001, The Zucker Diabetic Fatty (ZDF) Rat. In *Animal Models of Diabetes A Primer*, editors A.A.F. Sima and E. Shafir, pp. 109-128. The Netherlands: Harwood Academic Publishers.

Wijekoon, EP, Hall, B., Ratnam, S., Brosnan, M. E., et al. 2005. Homocysteine Metabolism in ZDF (Type 2) Diabetic Rats. *Diabetes*. 54(11):3245-3251.

### Zucker Rat

**Nomenclature:** Crl:ZUC-*Lepr<sup>fa</sup>*

**Origin:** The obese condition appeared spontaneously in the 13M strain of Dr. Theodore and Dr. Lois Zucker maintained at the laboratory of Comparative Pathology in Stow, MA. Colonies were established at many institutions from this nucleus colony. To Charles River Laboratories in 1985 from a research colony maintained at a pharmaceutical company.

**Characteristics:** Obesity, Insulin Resistance, Hyperinsulinemia, Hypertriglyceridemia, Hypercholesterolemia, Metabolic Syndrome

**References:** Zucker, L.M. and Zucker, T.F., 1961, Fatty, a new mutation in the rat *J. Hered.* 52: 275-278.

Zucker, T.F. and Zucker, L.M., 1962, Hereditary obesity in the rat associated with high serum fat and cholesterol. *Proc. Soc. Exp. Biol. Med.* 110: 165-171.

Frisbee, J.C., 2005. Hypertension-independent microvascular rarefaction in the obese Zucker rat model of the metabolic syndrome. *Microcirculation*, 12(5):383-392.

With the worldwide increase in metabolic diseases, new methods and technologies to investigate these conditions take on an ever increasing priority. Charles River's Disease Models Program makes rodent models available for the study of obesity, diabetes, hyperlipidemia and other metabolic complications. Additionally, our Preclinical Services division has extensive experience using multiple models and species within this therapeutic area.

## JCR Rat

**Nomenclature:** CrI:JCR(LA)-Lepr<sup>cp</sup>

**Origin:** Developed in the laboratory of Dr. Carl Hansen at NIH by crossing the SHROB rat with the LA/N rat. To Dr. Jim Russell at the University of Alberta in Edmonton, Canada in 1978. To Charles River in 2003.

**Characteristics:** Obesity, Insulin Resistance, Hyperinsulinemia, Hypertriglyceridemia, Hypercholesterolemia, Atherosclerosis, Myocardial Ischemia, Nephropathy

**References:** Russell, J.C. and Amy, R.M., 1986, Early atherosclerotic lesions in a susceptible rat model: the LA/N-corpulent rat *Atherosclerosis* 60: 119-129.

Russell, J.C. and Graham, S.E., 2001, The JCR:LA-cp rat: an animal model of obesity and insulin resistance with spontaneous cardiovascular disease, In *Animal Models of Diabetes A Primer*, editors A.A.F. Sima and E. Shafir, pp. 227-245. The Netherlands: Harwood Academic Publishers.

Russell, J. C. Kelly, S. E., and Schafer, S. 2004. Vasoepitaxial inhibition improves insulin sensitivity and endothelial function in the JCR:LA-cp rat. *J. Cardiovascular Pharmacology*, 44(2):258-265.

Proctor, S.D., Kelly, S.E. and Russell, J.C., 2005. A novel complex of argininesilicate improves micro-and macrovascular function and inhibits glomerular sclerosis in insulin-resistant JCR:LA-cp rats. *Diabetologia* 48(9):1925-1932.

## SHHF Rat

**Nomenclature:** SHHF/MccCrI-Lepr<sup>cp</sup>

**Origin:** Breed stock for this colony was transferred to Dr. Sylvia McCune at the University of Chicago Medical School in 1983, from the laboratory of Dr. J.E. Miller at G.D. Searle and Company. The animals were developed by backcrossing the SHROB rat to the SHR/N rat. To Genetic Models, Inc. in 1994. To Charles River in 2001.

**Characteristics:** Obesity, Insulin Resistance, Hyperinsulinemia, Type 2 Diabetes, Hypertriglyceridemia, Hypercholesterolemia, Congestive Heart Failure, Hypertension, Nephropathy

**References:** McCune S.A., Baker, P.B., and Stills, H.F., 1990, SHHF/Mcc-cp rat: model of obesity, non-insulin-dependent diabetes, and congestive heart failure. *ILAR News* 32: 23-27.

Heyen, J.R.R., Blasi, E.R., Nikula, K., Rocha, R., Daust, H. A., Friedrich, G., Van Bleet, J.F., De Ciechi, R., McMahon, E.G., and Rudolph, A.E., 2002, Structural, functional, and molecular characterization of the SHHF model of heart failure. *Am. J. Physiol. Heart Circ. Physiol.* 283: H1775-H1784.

Emter, C.A., McCune, S.A., Sparagna, G.C., Radin, M.J. and Moore, R.L., 2005. Low-intensity exercise training delays onset of decompensated heart failure in spontaneously hypertensive heart failure rats. *Am J. Physiol. Heart Circ. Physiol.* 289(5):H2030-2038.

## SHROB Rat

**Nomenclature:** SHR/OBKoI-CrI-Lepr<sup>cp</sup>

**Origin:** Originated in the laboratory of Dr. Simon Koletsky at Case Western Reserve University School of Medicine in 1969. Developed from a cross between a SHR female rat and a normotensive male Sprague Dawley rat. To Genetic Models, Inc. in 2000. To Charles River in 2001.

**Characteristics:** Obesity, Insulin Resistance, Hyperinsulinemia, Hypertriglyceridemia, Hypercholesterolemia, Hypertension, Syndrome X, Nephropathy

**References:** Koletsky, S., 1972, New type of spontaneously hypertensive rats with hyperlipidemia and endocrine gland defects. In *Spontaneous Hypertension: Its Pathogenesis and Complications*, edited by K. Okamoto pp. 194-197. Tokyo: Igaku Shoin W.

Koletsky, R.J., Friedman, J.E., and Ernsberger, R., 2001, The obese spontaneously hypertensive rat (SHROB, Koletsky Rat): a model of metabolic syndrome X. In *Animal Models of Diabetes A Primer*, edited by A.A.F. Sima and E. Shafir pp.143-158. The Netherlands: Harwood Academic Publishers.

Velliquette, R.A., Friedman, J.E., Shao, J., Zhang, B.B., and Ernsberger, P., 2005. Therapeutic actions of an insulin receptor activator and novel peroxisome proliferators-activated receptor gamma agonist in the spontaneously hypertensive obese rat model of metabolic syndrome X. *J. Pharmacol. Exp. Ther.* 314(1):422-430.

Koletsky, R.J., Velliquette, R.A., and Ernsberger, P., 2003. The role of I(1)-imidazoline receptors and alpha(2)-adrenergic receptors in the modulation of glucose and lipid metabolism in the SHROB model of metabolic syndrome X. *Ann. N.Y. Acad. Sci.* 1009:251-261.

## ZSF1 Rat

**Nomenclature:** CrI:ZSF1-Lepr<sup>fa</sup> Lepr<sup>cp</sup>

**Origin:** A hybrid between a ZDF female and SHHF male developed at Genetic Models, Inc. To Charles River in 2001.

**Characteristics:** Obesity, Type 2 Diabetes, Insulin Resistance, Hypertension, Hyperinsulinemia, Hypertriglyceridemia, Hypercholesterolemia, Congestive Heart Failure, Nephropathy

**References:** Tofovic, S.P., Kusaka, H., Kost, C.K., and Bastacky, S., 2000, Renal function and structure in diabetic, hypertensive, obese ZDFxSHHF-hybrid rats. *Renal Failure* 22: 387-406.

Tofovic, S.P., Kusaka, H., Jackson, E.K., and Bastacky, S.I., 2001, Renal and metabolic effects of caffeine in obese (fa/fa<sup>cp</sup>) diabetic hypertensive ZSF1 rats, *Renal Failure* 23 2: 159-173.



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