

## CARDIOVASCULAR MODELS

### Dahl/Salt-Sensitive (DSS) Rat

**Nomenclature:** SS/JrHsd/McwiCrI

**Origin:** Inbred from a congenic group of Dahl/SS rats (SS/JrHsd) from Dr. Theodore Kurtz at UCSF. Originally derived from the Harlan SS/Jr colony. To the Medical College of Wisconsin in 1991. To Charles River in 2001.

**Characteristics:** Hypertension, Insulin Resistance, Hyperinsulinemia, Hypertriglyceridemia, Hypercholesterolemia, Nephropathy, Cardiac Hypertrophy, Heart Failure

*References:* Rapp, J.P. and Dene, H., 1985, Development and characteristics of inbred strains of Dahl salt-sensitive and salt-resistant rats. *Hypertension* 7: 340-349.  
Chen, P.Y., St. John, P.L., Kirk, K.A., Abrahamson, D.R., and Sanders, P.W., 1993, Hypertensive nephrosclerosis in the Dahl/Rapp rat: initial sites of injury and effect of dietary L-arginine administration. *Lab Investigation* 68:174-349.  
Castrop, H. and Kurtz, A., 2001, Differential nNOS gene expression in salt-sensitive and salt resistant Dahl rats. *J. Hypertension* 19(7):1223-1231.

### SS-13<sup>BN</sup> Rat

**Nomenclature:** SS-13<sup>BN</sup>/McwiCrI

**Origin:** A consomic developed at the Medical College of Wisconsin, in which chromosome 13 from the normotensive inbred Brown Norway rat was introgressed into the background of the Dahl/Salt-Sensitive rat. This consomic is used as the control for the hypertensive Dahl/Salt-Sensitive rat.

**Characteristics:** Insulin Resistant, Hyperinsulinemia, Hypertriglyceridemia, Normotensive Control

*References:* Cowley, A. W., Jr., Roman, R.J., Kaldunski, M.L., Dumas, P., Dickhout, J.G., Greene, A.S. and Jacob, H.J. 2001 Brown Norway chromosome 13 confers protection from high salt to consomic Dahl S rat. *Hypertension*. 37(2 Part2):456-461.  
Liang, M., Yuan, B., Rute, E. Greene, A.S., Zou, A.P., et al. 2002. Renal medullary genes in salt-sensitive hypertension: a chromosomal substitution and cDNA microarray study. *Physiol. Genomics*. 28:8(2):139-149.

### Fawn Hooded Hypertensive (FHH) Rat

**Nomenclature:** FHH/EurMcwiCrI

**Origin:** Introduced in Europe by Tschopp in the early 1970s. To Erasmus University in Rotterdam, Netherlands. To the Medical College of Wisconsin in the 1990s. To Charles River in 2001.

**Characteristics:** Pulmonary Hypertension, Hypertriglyceridemia, Hypercholesterolemia, Nephropathy

*References:* Brown, D.M., Provoost, A.P., Lander, E.S., and Jacob, H. J., 1996, Renal disease susceptibility and hypertension are under independent genetic control in the Fawn-Hooded rat *Nature Genet.* 12: 44-51.  
Le Cras, T.D., Kim, D., Markham, N.E., and Abman, S.H., 2000, Early abnormalities of pulmonary vascular development in the Fawn-Hooded rat raised at Denver's altitude. *Am. J. Physiol. Lung Cell Mol. Physiol.* 279: L283-L291.

### SHR Rat

**Nomenclature:** SHR/NCrI

**Origin:** Okamoto at the Kyoto School of Medicine in 1963 from an outbred Wistar Kyoto male with marked elevation of blood pressure mated to a female with slightly elevated blood pressure. To NIH in 1966. To Charles River in 1973.

**Characteristics:** Hypertension, Insulin Resistance, Hyperinsulinemia, Hypertriglyceridemia, Hypercholesterolemia

*References:* Okamoto, K., 1969, Spontaneous hypertension in rats. *Int. Rev. Exp. Pathol.* 7: 227-270.  
Swislocki, A. and Tsuzuki, A., 1993, Insulin-resistance and hypertension-glucose-intolerance, hyperinsulinemia, and elevated free fatty-acids in the lean spontaneously hypertensive rat. *American Journal of the Medical Sciences* 306: 282-286.  
Palmer, B.M., Chen, Z., Lachapelle, R.R., Hendley, E.D. and Lewinter, M.M., 2005. Cardiomycocyte function associated with hyperactivity and/or hypertension in genetic models of LV hypertrophy. *Am. J. Physiol. Heart Circ. Physiol.*, Oct 21.

With the increase in cardiovascular disease worldwide, new tools to investigate these conditions can accelerate the process of finding solutions. Charles River's Disease Models Program supports these efforts by making available several rodent models of cardiovascular conditions, such as those noted on this sheet, which allow for direct *in vivo* studies of these conditions. 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; Edmonton, Canada in 1978. To Charles River in 2003.

**Characteristics:** Atherosclerosis, Myocardial Ischemia, Obesity, Insulin Resistance, Hyperinsulinemia, Hypertriglyceridemia, Hypercholesterolemia, 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. Vasopeptidase 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:** Congestive Heart Failure, Hypertension, Nephropathy, Obesity, Insulin Resistance, Hyperinsulinemia, Type 2 Diabetes, Hypertriglyceridemia, Hypercholesterolemia

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

*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 Ernberger, 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.

Velliouette, R.A., Friedman, J.E., Shao, J., Zhang, B.B., and Ernberger, 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., Velliouette, R.A., and Ernberger, P., 2003. The role of I(1)-imidazole 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.

## Stroke Prone (SHR/SP) Rat

**Nomenclature:** SHR/SPA3NCrI

**Origin:** Isolated from Wistar-Kyoto rats by Okamoto and Aoki in 1963. A3 subline transferred to NIH in 1975 from Yamori. To Charles River in 2002.

**Characteristics:** 82% of males will develop cerebrovascular lesions (cerebral hemorrhage) over 100 days of age. Hypertension, Nephropathy, Insulin Resistance, Hyperinsulinemia, Hypertriglyceridemia, Hypercholesterolemia

*References:* Nagaoka, A., Iwatsuka, H., Suzuoki, A., and Okamoto, K., 1976. Genetic predisposition to stroke in spontaneously hypertensive rats. *Am. J. Physiol.* 230: 1354-1359.

Okamoto, K., Yamori, Y., and Nagaoka, A., 1974. Establishment of stroke-prone spontaneously hypertensive rat (SHR). *Circ. Res.* 34-35 (suppl.), 1143-1153.

Masineni, S.N., Chander, P.N., Singh, G.D., Powers, C.A. and Stier, C.T., Jr., 2005. Male gender and not the severity of hypertension is associated with end-organ damage in aged stroke-prone spontaneously hypertensive rats. *Am. J. Hypertens.* 18(6):8780-784.

Sepehrdad, R., Chander, P.N., Singh, G. and Stier, C.T., Jr., 2004. Sodium transport antagonism reduces thrombotic microangiopathy in stroke-prone spontaneously hypertensive rats. *Am. J. Physiol. Renal Physiol.* 286(6):F1185-1192.



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