

## The Cohen Rosenthal Diabetic Hypertensive Rat (CRDH) model (Ramot) code: 12-2013-434

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The construction of the Cohen Rosenthal Diabetic Hypertensive Rat (CRDH) model was initiated nearly a decade ago by cross-breeding between the Cohen Diabetic rat (CDR) and the SHR. The CDR is a rodent model that expresses the following phenotypes: when fed regular diet, it is non-diabetic; when fed a diabetogenic diet, it invariably develops diabetes reminiscent of type 2 in humans. The high-sucrose copper-poor diet consists of 18% casein, 72% sucrose, 4.5% butter, 0.5% corn oil, 5% salt No. II USP, water, and fat-soluble vitamins. Thus, a diet very poor in copper is required to develop the full diabetic phenotype. An outstanding feature of the CRDH rat is that it is a nonobese model of diabetes, which allows dissociation of the confounding obesity factor from other diabetogenic genes. Its pathology includes severe diffuse diabetic glomerulosclerosis and/or "onion skin" lesions, as well as by smooth muscle cell hyperplasia. Such vascular changes were not observed in the CDR or in the SHR. Diffuse glomerulosclerosis with marked expansion of mesangial matrix as well as lipohyalin lesions were also occasionally observed. Myocardial changes are prominent, with foci of ischemic necrosis and hyperplasic vascular changes. CRDH rats undergo cardiac hypertrophy and vascular changes affecting small-sized coronary arteries.

This animal model was used as an experimental tool for the investigation of therapeutic agents including telmisartan and other agents such as enalapril, losartan lercanidipine, endothelin antagonist-LU-135252, and allyl-mercaptocaptopril in collaboration with Weizmann institute of science.

We can provide a full spectrum of analysis for in vitro and in vivo assays, enabling us to evaluate and characterize the effects of drugs on kidney, heart and brain.

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