Heterotopic Heart Transplantation

The donor rats were anesthetized with a single intra-peritoneal injection of xylazine (3 mg/kg) and ketamine (100 mg/kg). After the abdominal cavity was opened 400 IU/kg sodium heparin was injected into the inferior caval vein. Abdominal aorta was exposed and a 1 cm segment of the infrarenal aorta was occluded by small vessel forceps. A single intravenous cannula with PTFE catheter (Vygon GmbH & Co. KG, 52017 Aachen, Germany) was advanced into the aorta straight to the aortic arch by shortly opening the upper vessel forcep. The cannula was removed from the PTFE catheter. Then bilateral thoracotomy was performed and the heart exposed. Afterward cardiac arrest was induced by injection of 40 mL of HTK solution (Custodiol, Dr. Franz Köhler Chemie GmbH, Alsbach-Hähnlein, Germany) using the PTFE catheter. To reduce the load, the inferior caval vein was cut. After cardiac arrest, the superior and inferior caval vein and the pulmonary veins were tied en masse with a 4–0 single silk suture. The aorta and the pulmonary artery were divided and the heart was immediately placed into cold HTK solution (4°C).

The recipient rats were anesthetized with a single intra-peritoneal injection of xylazine (3 mg/kg) and ketamine (100 mg/kg) and heparinized with 400 IU/kg. The abdomen was opened by a midline incision and the aorta and inferior caval vein were exposed by reflecting the intestines to the left side. Two centimeter segments of the infrarenal aorta and the inferior caval vein were isolated and occluded by small vessel forceps. The aorta and the pulmonary artery of the donor heart were anastomosed end to side to the abdominal aorta and the inferior caval vein of the recipient rat, respectively. This was achieved using a 9–0 monofilament polyamide sutures operating under a 16-power magnification microscope. To minimize variability between experiments, the duration of the implantation was standardized at 60 min. After completion of the anastomoses, the vessels were released and the heart was then reperfused with blood in situ for a time period of 1 hr.

SUPPLEMENTAL FIGURE 1. cGMP-PKG pathway. Oxidative stress leads to an inhibition of sGC and activation of PDE-5 — both leading to a decreased intracellular cGMP level. PDE-5-inhibitors like vardenafil increase intracellular cGMP levels and thereby pharmacologically trigger cytoprotective pathways.

REDUCED ISCHEMIA/REPERFUSION INJURY
Nonischemic Heterotrophic Heart Transplantation

The technique of the ischemic heterotopic heart transplantation was slightly modified to implant the donor heart without a significant ischemic time. To assure a quick implantation of the donor heart, the recipients were prepared before explantation. The animals were heparinized with 400 IU/kg intravenously. The abdomen was opened by a middle and the aorta and inferior caval vein were exposed. One centimeter segments of the infrarenal aorta and inferior caval vein were isolated and occluded by small vessel forceps. Thin polyethylene tubes were inserted through a small incision into the abdominal aorta and inferior caval vein, respectively. The connections were tightened by local application of tissue glue. Afterward, the donor hearts were explanted as described above. The donor aorta and pulmonary artery were attached immediately to the corresponding aortic and caval tubes and fixed with 5–0 single silk sutures. Then the recipient vessels were released and the heart was perfused with blood for a 1-hr period.