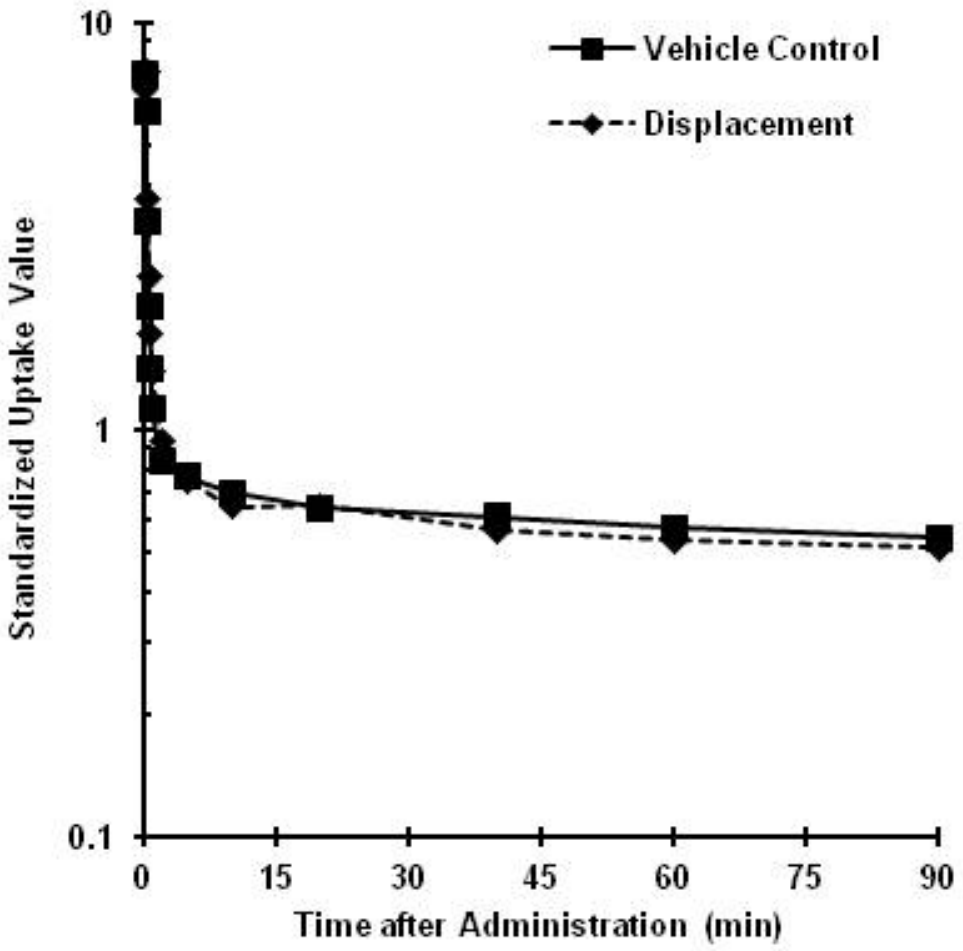
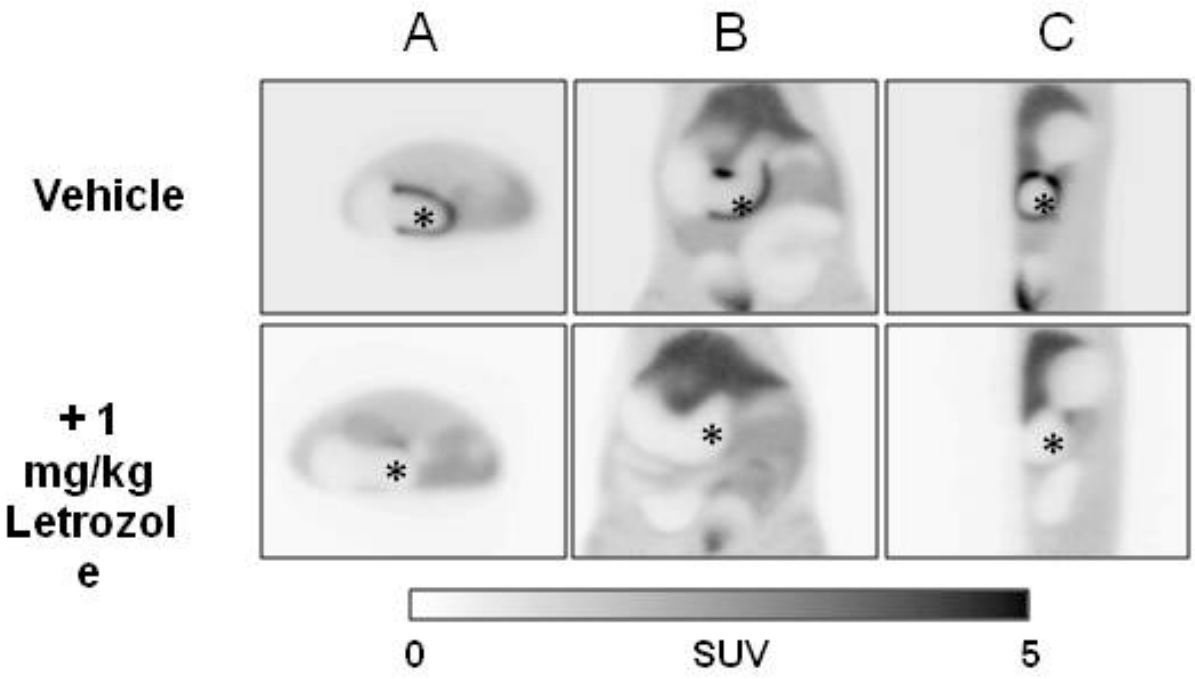
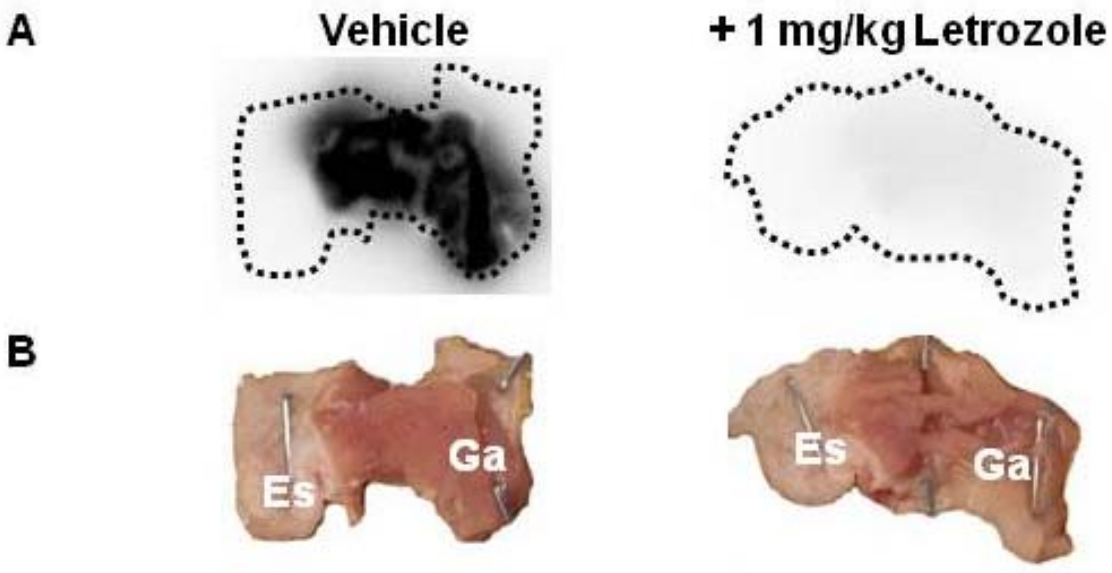


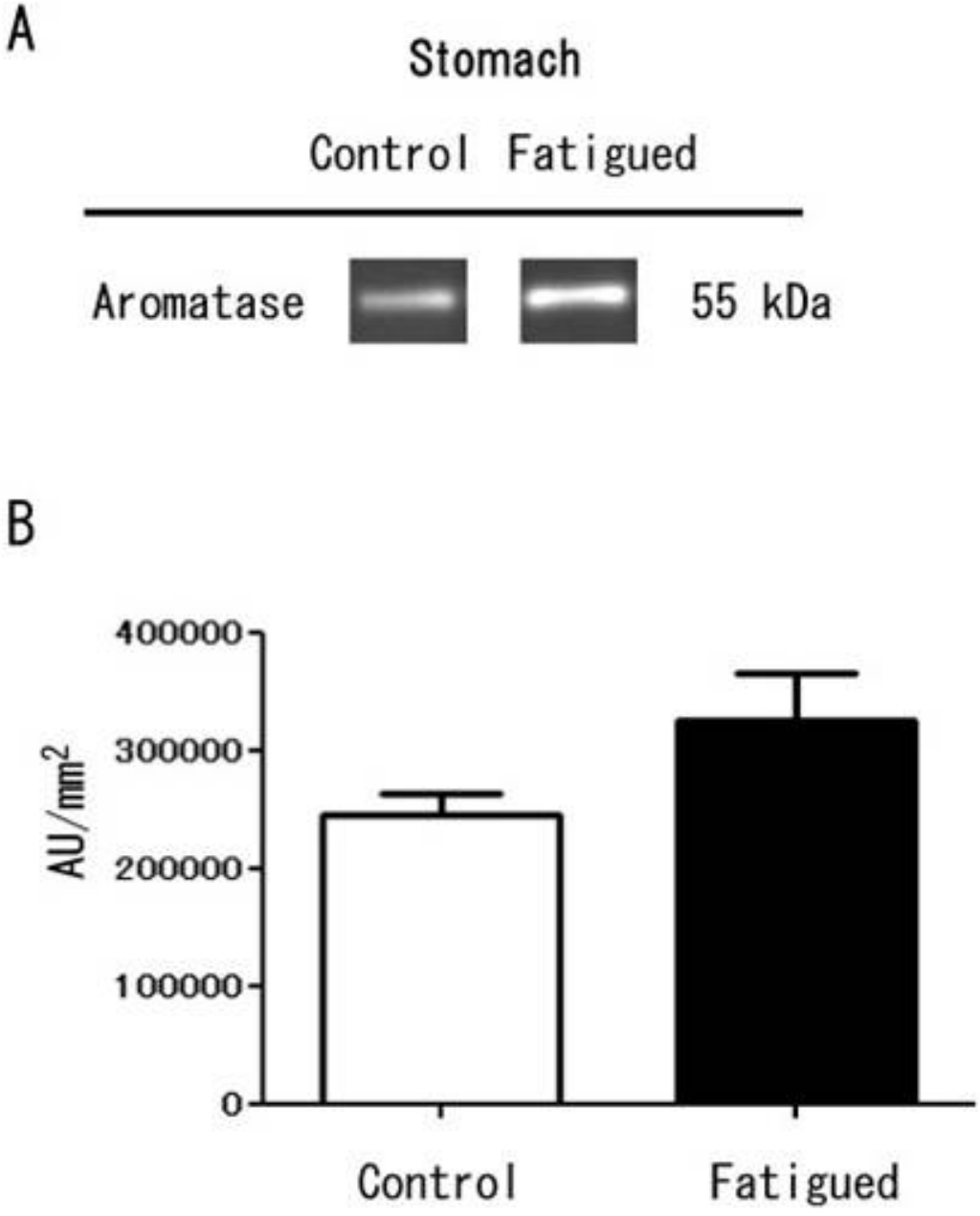
Supplemental Figure 1. Radioactivity of [^{11}C]vorozole in the plasma over time. A polyethylene catheter (SP31, Natsume, Tokyo, Japan) was inserted into the right femoral artery for blood collection in anesthetized condition with 1.5% isoflurane inhalation before the PET scan. Arterial blood was collected from the femoral artery at 10, 20, 30, 40, 50 sec, 1, 2, 5, 10, 20, 40, 60 and 90 min after [^{11}C]vorozole administration. The radioactivity of the blood and plasma was measured using a well-type gamma counter (Wallac1470, PerkinElmer, Waltham, MA, USA) and was corrected for decay. No significant difference was observed between the unlabeled ligand- and vehicle-treated groups.



Supplemental Figure 2. Representative maximum intensity projection (MIP) images in abdominal region of rat following administration of [^{11}C]vorozole with co-administration of unlabeled letrozole or vehicle. The PET images were summated from 5 to 60 min after the tracer injection and then the images of maximum intensity projection were constructed in coronal (A), B: Sagittal, and C: Transverse image. The accumulation of the radioactivity in the stomach was decreased by co-administration of letrozole. The asterisks indicate the area of the gastric glands.



Supplemental Figure 3. *Ex vivo* autoradiographic images with tissue photographs at 30 min post-injection of [^{11}C]vorozole (approximately 300 MBq/kg). (A) represents the autoradiographic images of stomach in control rat and letrozole-treated rat (1 mg/kg). (B) shows photographs of the stomach corresponding to autoradiographic images from the the rats as above. Black broken lines were corresponding shapes of the isolated stomach defined in the photographs, which were applied to the autoradiographic images. Es: Esophagel part of stomach, Ga: Gastric gland.



Supplemental Figure 4. Male SD rats weighing 251-272 g were randomly separated into 2 groups (control: n=4, fatigued condition: n=6). For fatigued-conditioned rats, fatigue-loading procedure was completed. Animals were sacrificed and glandular stomachs and adrenals were removed. Glandular stomachs and adrenals were homogenized in 10 volumes of ice-cold cell lysis buffer (10 mM Tris-HCl pH 7.2, 1% Triton X-100, 1% sodium deoxycholate, 0.1% SDS,

158 mM NaCl, 5 mM EDTA, 1 mM PMSF, 10 μg/ml aprotinin). Equal amounts of protein per lane (10 μg) were loaded onto an 10% polyacrylamide gel and separated by electrophoresis at 40 mA for 80 min. Proteins were then transferred to PVDF membranes at 15 V for 45 min and the membrane was blocked with 5% skim milk/0.1% Tween-20 in PBS (PBS-T; pH 7.4). The PVDF membranes were then incubated with monoclonal anti-aromatase antibody (1:250, AbD Serotec) in 5% skim milk/PBS-T at 4℃ overnight. Bound antibodies were detected using ECL peroxidase anti-mouse antibody (NA931VS, GE Healthcare) diluted 1:5000in PBS-T. The reaction was developed with ECL Plus Western Blotting Detection System (GE Healthcare) and detected using LAS-3000 (Fujifilm). The band intensity was quantified using Image Gauge (Fujifilm). The representative bands of glandular stomach samples were shown in panel A. The difference between fatigued condition and control did not reach the significance, however, the tendency that the aromatase expression level was higher in fatigued condition compared to control was observed (B), indicating fatigue loading induced aromatase expression. The signals of adrenal samples were not detected. These results are consistent with the results of our PET studies.