***Supplementary material***

**Digital Ventilated Cages**

Digital Ventilated Cages (DVC®), manufactured by Tecniplast SpA (Buguggiate, Italy), are based on a sensing board underneath each cage that is mechanically connected to the rack without influencing conventional IVC cage operations. This electronic board is composed of 12 electrodes connected to an integrated circuit that continuously measures their electrical capacitance.Since mice have a high water content, their movements while close to an electrode induce significant capacitance changes, and thus, by properly tracking these changes over time it is possible to monitor the animal’s spontaneous activity. Each electronic board is set up to collect capacitance measurements 4 times per second from each electrode of each cage, thus generating a set of 48 capacitance measurements per second (i.e. 12 electrodes sampled at 4 Hz). In addition, the DVC system also embeds infrared sensors to monitor the presence of food and water.

**Diastolic dysfunction assessment**

To evaluate diastolic dysfunction, the ratio of peak velocity blood flow from LV relaxation in early diastole (the E wave) to peak velocity flow in late diastole caused by atrial contraction (the A wave) will be calculated to evaluate the diastolic transmitral flow velocity (E/A). Since in mice these two peaks can be fused at physiological heart rates, the E to early diastolic mitral annular tissue velocity (E/e') will be further calculated to estimate LV filling pressures (E/e’). In addition, isovolumetric relaxation time (IVRT), which represents the time between aortic valve closure and mitral valve opening, will be measured as another indicator of diastolic dysfunction.

**Void spot assay (VSA)**

For VSA, single mice will be placed in a standard cage whose floor will be covered with absorbent paper and allowed to move freely for a determined period of time. After putting back the mice to their home cage, the filter paper will be dried and imaged under UV light to visualize the spots of urine. The number of urine spots, the total urine area and the ratio on edge voiding to center voiding will be calculated using imaging software.