

Supplementary Table 3: Plasma glucose, plasma insulin and endogenous glucose production in the basal state and following the hyperinsulinaemic/euglycaemic clamp (Insulin Stimulated) in WT, Global-ARKO and PC-AR Gene Replacements fed a high caloric diet (HCD) for 18 weeks (24 weeks of age).

| Parameter | Basal | | | | | | Insulin Stimulated | | | | | |
|--|-------------------|-------------------|-------------------|-------------------------------|-------------------|-------------------|--------------------|------------------|------------------|---------------------------------|--------------------------------|----------------------------------|
| | WT Chow | ARKO Chow | PC-AR Rep Chow | WT HCD | ARKO HCD | PC-AR Rep HCD | WT Chow | ARKO Chow | PC-AR Rep Chow | WT HCD | ARKO HCD | PC-AR Rep |
| Plasma glucose (mmol/L) | 11.1 ± 1.5 (4) | 10.7 ± 0.7 (4) | 10.7 ± 1.7 (3) | 7.3 ± 1.7 (4) | 11.5 ± 4.6 (5) | 14.9 ± 4.0 (5) | 5.4 ± 0.4 (4) | 4.8 ± 0.6 (4) | 4.6 ± 1.0 (5) | 7.8 ± 1.9 (4) | 7.0 ± 2.1 (4) | 5.7 ± 2.6 (4) |
| Plasma insulin (ng/mL) | 1.4 ± 0.3 (4) | 3.2 ± 1.4 (4) | 1.9 ± 0.8 (3) | 7.3 ± 1.7 [#] (4) | 3.9 ± 3.3 (5) | 2.3 ± 1.0 (5) | 8.5 ± 3.9 (4) | 9.6 ± 1.9 (4) | 7.0 ± 2.2 (5) | 29.5 ± 6.3 ^{##} (4) | 17.5 ± 8.2 [*] (4) | 11.5 ± 5.4 ^{***} (4) |
| Endogenous Glucose Production/plasma insulin (µmol/min/kg)/(ng/mL) | - | - | - | - | - | - | 1.4 ± 3.4 (4) | 5.4 ± 3.2 (4) | 2.1 ± 3.4 (5) | 1.8 ± 14.4 (4) | 1.9 ± 11.4 (4) | 1.5 ± 1.2 (4) |

Values are mean ± SD, - not measured, n/group shown in parentheses. * $P < 0.05$, *** $P < 0.001$ versus WT within diet, [#] $P < 0.05$, ^{##} $P < 0.005$ versus chow within genotype.