Online supplemental material, part 2

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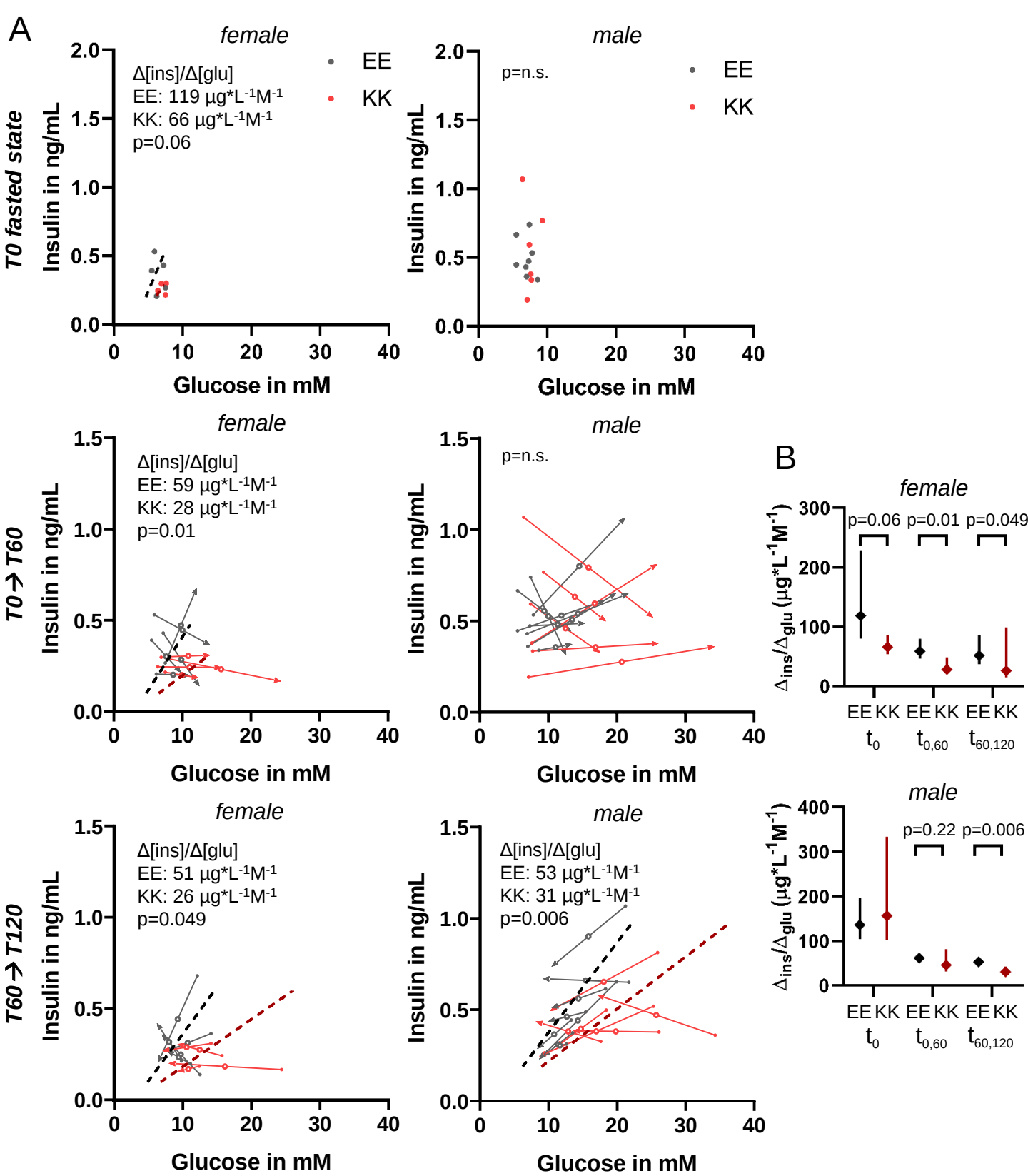
supplemental figures and tables

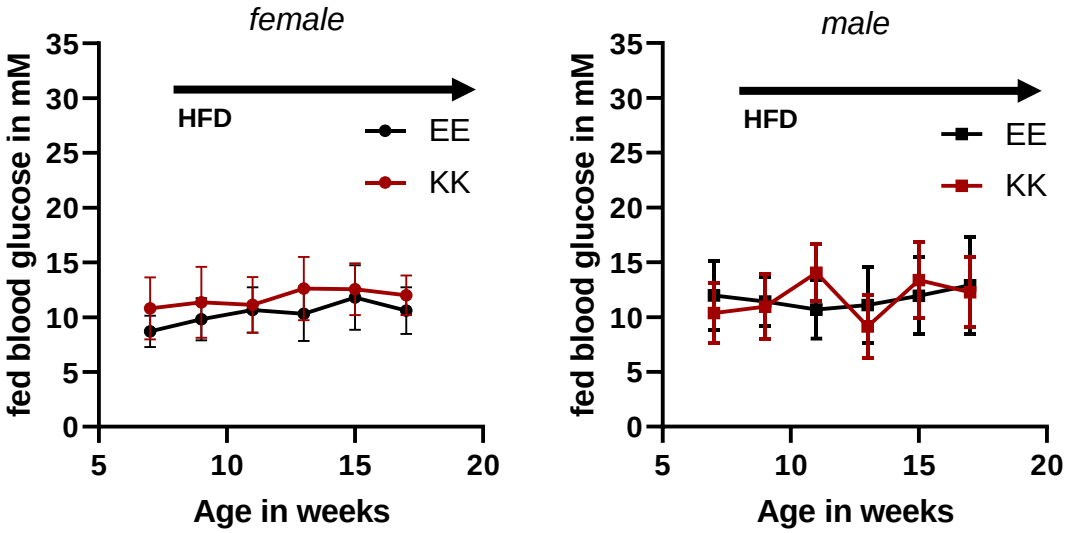


Supplemental Figure 1 – Blood insulin and glucose concentrations during IPGTT on a SD (12 weeks of age)

A Plasma insulin concentrations, plotted against the blood glucose concentration measured in the same animal, during an IPGTT at 12 weeks of age, for female (left) and male (middle) EE and KK mice (see Figure 3A). T0 denotes the overnight fasted state, pre-injection, and is shown at the top. Scatterplot symbols correspond to individual animals. Changes during IPGTT, from T0 to T60 post injection (middle) and from T60 to T120 post injection (bottom) are shown as arrows, each arrow representing the change in one animal. T0 data points, as well as T0→T60 and T60→T120 arrow centres (❶) were fitted by linear regression (dotted lines), assuming X_{3mM}=0.

B Slopes of the best fits ($\Delta_{ins}/\Delta_{glu}$) for EE and KK mice at t_0 and during $t_{0,60}$ and $t_{60,120}$ intervals. The statistical significance of the difference between the slopes was calculated using the extra sum-of-squares F-test. Error bars = 90% CI. Some error bars are smaller than the symbol.

Underlying data are available online (DOI: 10.6084/m9.figshare.12272873).

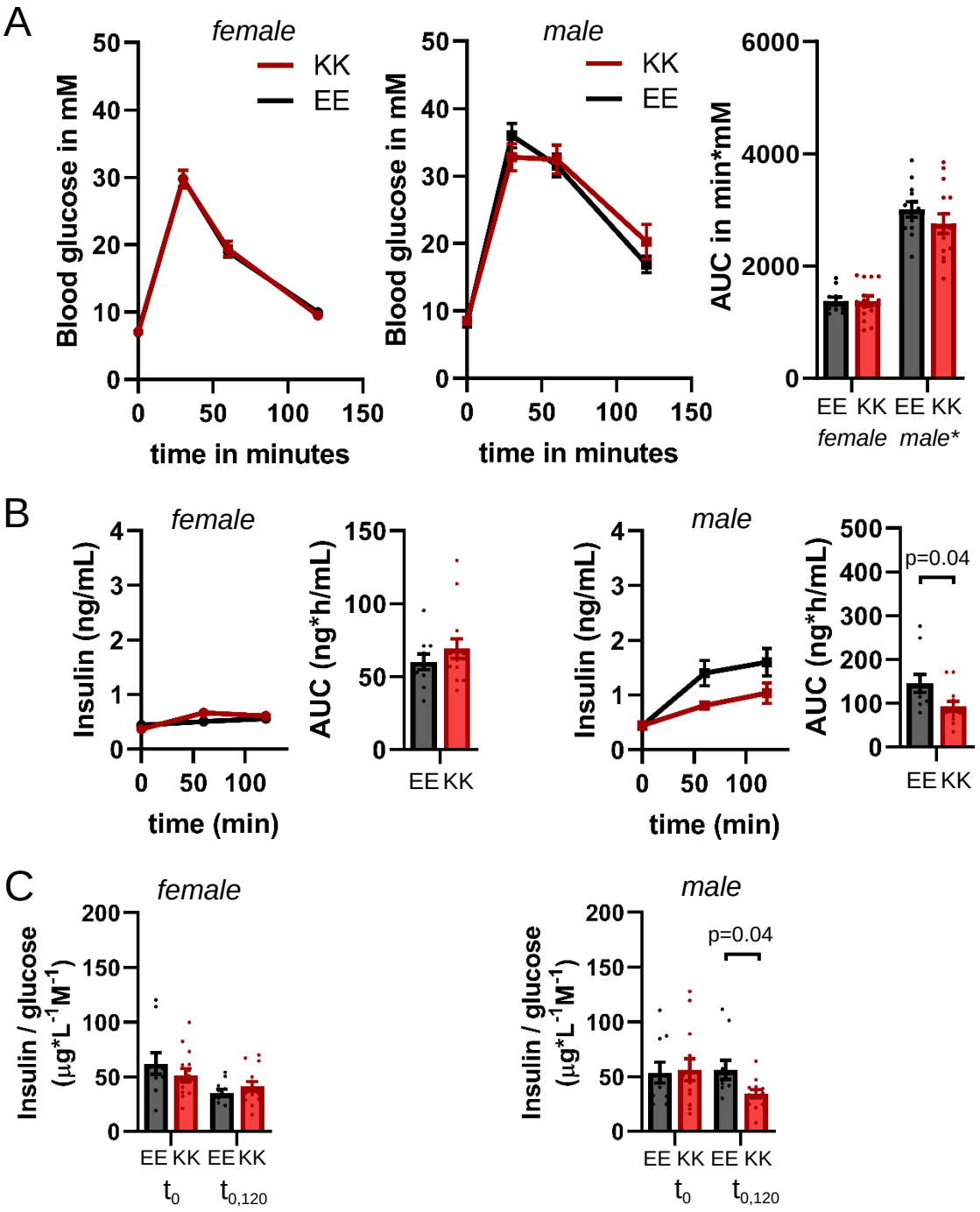


Supplemental Figure 2 – Mean fed blood glucose concentrations of female and male mice carrying two risk alleles (KK) or none (EE), on a HFD from 8 weeks of age

Number of mice: female EE, N=11; female KK, N=14; male EE, N=12; male KK, N=13. Error bars = SD. Average fed blood glucose across groups increased overall from 10.5±0.4 mM at week 7 to 12.0±0.4 mM at week 17 (SEM, N=50, p=0.01, Welch's t-test). At 27 weeks of age this increased to 12.4±0.4 mM (SEM, N=33, p=0.003, Welch's t-test). Underlying data available online (DOI: 10.6084/m9.figshare.12420839).

Supplemental Table 1 – overnight fasting blood glucose on a HFD

	Week 12 SD	Week 12 HFD from week 8		Week 26 HFD from week 8		
Experimental Group	MEAN±SEM	MEAN±SEM	p-value vs SD	MEAN±SEM	p-value vs SD	p-value vs week 12
Female EE	6.7±0.4mM (10)	7.0±0.2mM (10)	n.s.	7.5±0.5mM (7)	n.s.	n.s.
Female KK	6.8±0.2mM (10)	7.1±0.2mM (14)	n.s.	8.4±0.3mM (11)	0.0009	0.003
Male EE	6.6±0.3mM (13)	8.2±0.5mM (12)	0.01	10.3±0.6mM (6)	0.0006	0.01
Male KK	7.1±0.3mM (10)	7.6±0.2mM (14)	n.s.	10.5±0.8mM (9)	0.002	0.005
Number of animals given in brackets (N). p-values calculated using Welch's t-test.						



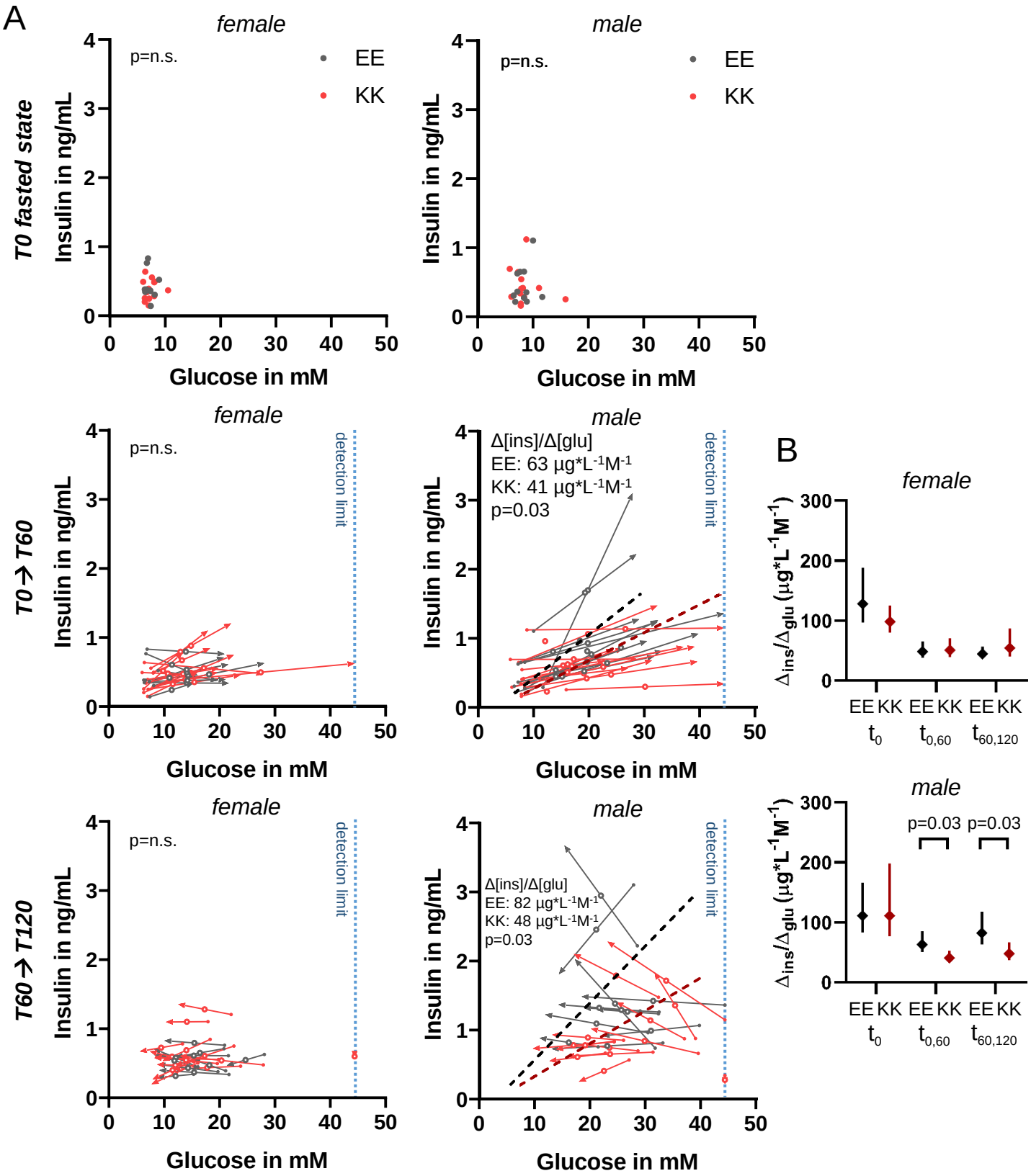
Supplemental Figure 3 – Glucose sensitivity at 12 weeks of age, after 4 weeks on a HFD

A IPGTT for female (left) and male (middle) mice carrying two risk alleles (KK) or none (EE), at 12 weeks of age. Right, area under the curve (AUC). *: Sporadically, data points reached the upper detection limit of 44 mM, affecting traces for 3 m-EE and 2 m KK mice.

B Plasma insulin concentrations measured during the IPGTT shown in A for female and male EE and KK mice. AUCs for the 1st hour post injection (t0,60) and the 2nd hour post injection (t60,120) are shown to the right of traces. Welch's t-test was used to test for statistically significant differences.

C Mean plasma insulin to blood glucose ratios during the IPGTT shown in A for female and male EE and KK mice. T0 denotes the overnight fasted state, pre-injection. Ratios were calculated by dividing insulin concentrations (t0) or AUC (t0,60 and t60,120) by their corresponding glucose values for each animal and then averaged. Data points shown correspond to individual animals. Welch's t-test was used to test for statistically significant differences.

AUC data points correspond to individual animals. Number of mice: (glucose measurements) female EE, N=10; female KK, N=14; male EE, N=12; male KK, N=13; (insulin measurements) female EE, N=10; female KK, N=14; male EE, N=10; male KK, N=13. Error bars = SEM . Some error bars are smaller than the symbol. Underlying data available online (DOI: 10.6084/m9.figshare.12420839).

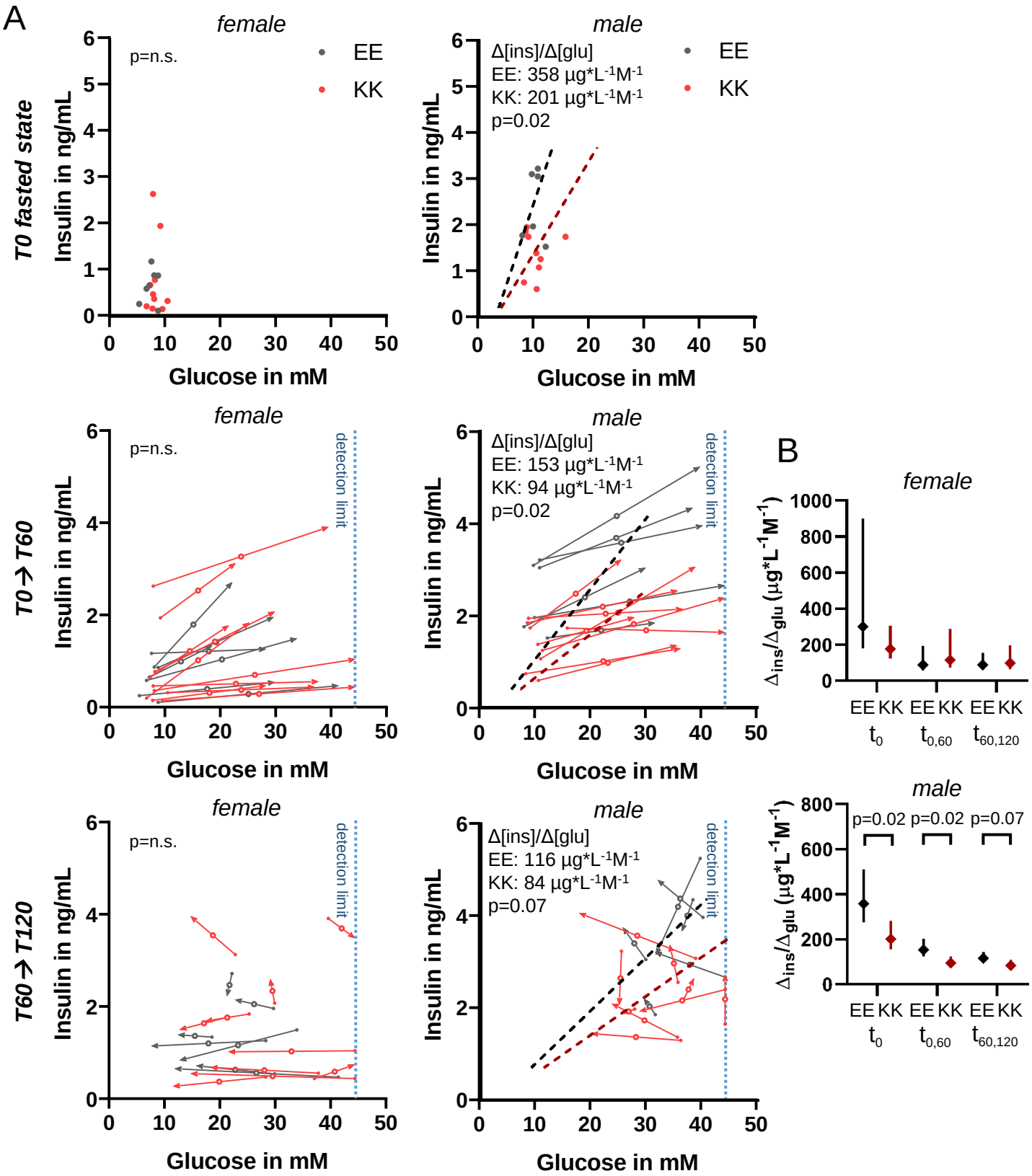


Supplemental Figure 4 – Blood insulin and glucose concentrations during an IPGTT (12 weeks, HFD from week 8)

A Plasma insulin concentrations, plotted against the blood glucose concentration measured in the same animal, during an IPGTT at 12 weeks of age, for female (left) and male (middle) EE and KK mice (see Supplemental Figure 3A). T0 denotes the overnight fasted state, pre-injection, and is shown at the top. Scatterplot symbols correspond to individual animals. Changes during IPGTT, from T0 to T60 post injection (middle) and from T60 to T120 post injection (bottom) are shown as arrows, each arrow representing the change in one animal. T0 data points, as well as T0→T60 and T60→T120 arrow centres (❍) were fitted by linear regression (dotted lines), assuming X_{3mM}=0.

B Slopes of the best fits ($\Delta_{ins}/\Delta_{glu}$) for EE and KK mice at t_0 and during $t_{0,60}$ and $t_{60,120}$ intervals. The statistical significance of the difference between the slopes was calculated using the extra sum-of-squares F-test. Error bars = 90% CI. Some error bars are smaller than the symbol.

Underlying data are available online (DOI: 10.6084/m9.figshare.12420839).



Supplemental Figure 5 – Blood insulin and glucose concentrations during an IPGTT (26 weeks, HFD from week 8)

A Plasma insulin concentrations, plotted against the blood glucose concentration measured in the same animal, during an IPGTT at 12 weeks of age, for female (left) and male (middle) EE and KK mice (see Figure 6B). T0 denotes the overnight fasted state, pre-injection, and is shown at the top. Scatterplot symbols correspond to individual animals. Changes during IPGTT, from T0 to T60 post injection (middle) and from T60 to T120 post injection (bottom) are shown as arrows, each arrow representing the change in one animal. T0 data points, as well as T0→T60 and T60→T120 arrow centres (❍) were fitted by linear regression (dotted lines), assuming X_{3mM}=0.

B Slopes of the best fits ($\Delta_{ins}/\Delta_{glu}$) for EE and KK mice at t_0 and during $t_{0,60}$ and $t_{60,120}$ intervals. The statistical significance of the difference between the slopes was calculated using the extra sum-of-squares F-test. Error bars = 90% CI. Some error bars are smaller than the symbol.

Underlying data are available online (DOI: 10.6084/m9.figshare.12420839).